The Effect of Guselkumab Induction Therapy on Inflammatory Biomarkers in Patients With Moderately to Severely Active Crohn's Disease: Week 12 Results From The Phase 2 GALAXI 1 Study

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BACKGROUND/OBJECTIVE

- Non-invasive inflammatory markers, specifically C-reactive protein (CRP) and fecal calprotectin (FeCal), are useful tools for the clinical management of patients with Crohn's disease (CD)[1]
- The Phase 2 GALAXI 1 study evaluated guselkumab (GUS), an interleukin-23 antagonist, for the treatment of moderately to severely active CD in patients who demonstrated inadequate response/intolerance to:
  - Conventional therapies (≥1 corticosteroids or immunosuppressives), and/or
  - Biologic therapies (≥1 TNF antagonists or vedolizumab)
- Week 12 biomarker results for GUS versus placebo are presented here for the interim analysis population (first 250 patients randomized)

METHODS

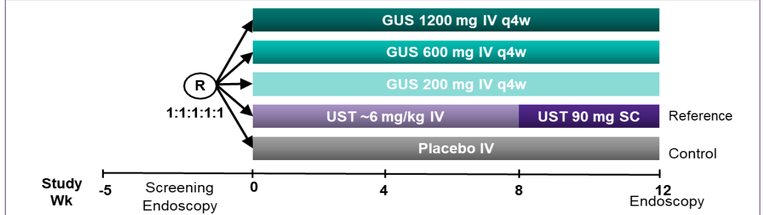
- Patients were randomized 1:1:1:1:1 into 5 arms: GUS 200, 600, or 1200 mg IV at Weeks 0, 4, 8; UST ~6 mg/kg IV at Week 0 and 90 mg SC at Week 8; or placebo IV (Figure 1)
- Interim analyses at Week 12 evaluated change from baseline in CRP, FeCal, and clinical-biomarker response for GUS versus placebo
- Clinical response was defined as ≥100-point reduction from baseline in Crohn's Disease Activity Index (CDAI) score or CDAI score <150
- Clinical-biomarker response was defined as clinical response and ≥50% reduction from baseline in CRP or FeCal
- The comparisons versus placebo at the interim analysis were not controlled for multiplicity; nominal p values are presented
- Data handling
  - Patients who had a missing CRP/FeCal value at Week 12 were considered not to have a normal CRP (≤3 mg/L)/FeCal (≤250 µg/g) level at Week 12
  - Patients who had missing CDAI score or who were missing both CRP and FeCal values at Week 12 were considered not to be in clinical-biomarker response at Week 12
  - Patients who had a prohibited change in concomitant CD medication, a CD-related surgery, or discontinued study agent due to lack of efficacy or an adverse event of worsening CD prior to Week 12 had their baseline CRP/FeCal carried forward from that timepoint on and were considered not to have achieved normalized CRP/FeCal or clinical-biomarker response at Week 12

CONCLUSIONS

- **Patients with moderately to severely active CD who were treated with GUS IV induction therapy had greater reductions in CRP and FeCal concentrations through Week 12 compared with those receiving placebo**
- **A higher proportion of patients treated with GUS (combined dosing regimens) achieved clinical-biomarker response and normalized CRP or FeCal at Week 12 compared with placebo**
- **These patterns of improvement were also observed in BIO-Failure and CON-Failure subgroup analyses**

RESULTS

Figure 1. Phase 2 GALAXI 1 Study Design



GUS, guselkumab; R, randomization; UST, ustekinumab; q4w, every 4 weeks; q8w, every 8 weeks; Wk, week.s

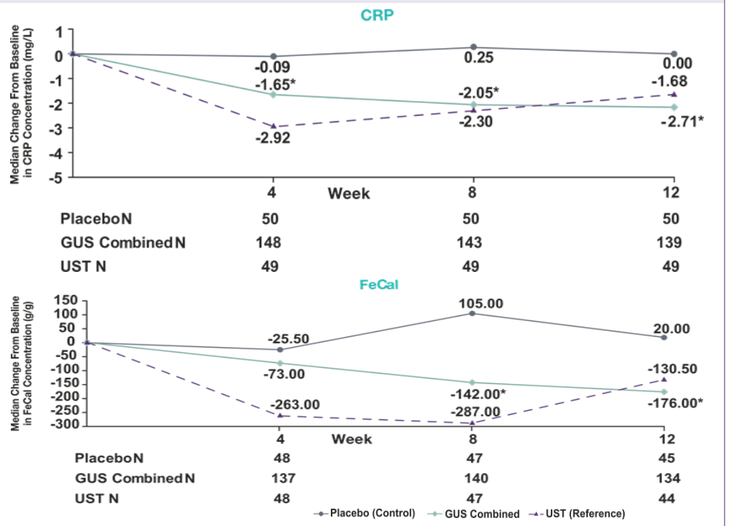
Table 2. Baseline Demographics and Disease Characteristics

	Placebo (Control)	GUS 200 mg IV	GUS 600 mg IV	GUS 1200 mg IV	UST (Reference)	Total
Primary analysis set, n	51	50	50	50	49	250
Age in years, mean (SD)	40.2 (13.31)	41.6 (14.05)	38.8 (14.34)	40.3 (14.05)	36.1 (12.10)	39.4 (13.61)
Male, n (%)	29 (56.9)	31 (62.0)	29 (58.0)	25 (50.0)	35 (71.4)	149 (59.6)
CD duration in years, mean (SD)	8.9 (6.76)	11.7 (13.06)	9.9 (8.66)	6.2 (6.28)	7.5 (6.16)	8.8 (8.73)
CDAI score, mean (SD)	300.9 (49.91)	307.8 (56.23)	305.5 (59.02)	303.7 (53.49)	313.4 (61.57)	306.2 (55.85)
CRP, median (IQR)	4.2 (1.4; 8.5)	6.1 (1.3; 19.6)	6.2 (1.6; 28.1)	5.6 (2.3; 14.0)	7.3 (1.7; 18.5)	5.4 (1.7; 16.3)
FeCal, median (IQR)	433.5 (178.0; 1587.0)	530.0 (178.0; 1637.0)	603.0 (230.0; 1619.0)	724.0 (185.0; 1662.0)	675.5 (241.0; 1818.5)	594.0 (189.0; 1665.5)
Pts with abnormal CRP (>3 mg/L), n(%)	31 (60.8)	34 (68.0)	31 (62.0)	31 (62.0)	32 (65.3)	159 (63.6)
Pts with abnormal FeCal (>250 µg/g)*, n(%)	33 (64.7)	30 (60.0)	37 (74.0)	35 (70.0)	36 (73.5)	171 (68.4)
Pts with biologic therapy failure (BIO-Failures) , n(%)	23 (45.1)	24 (48.0)	25 (50.0)	27 (54.0)	26 (53.1)	125 (50.0)
Pts who failed conventional therapy, but not biologic therapy (CON-Failures) , n(%)	28 (54.9)	26 (52.0)	25 (50.0)	23 (46.0)	23 (46.9)	125 (50.0)
Biologic-naïve	17 (33.3)	22 (44.0)	21 (42.0)	22 (44.0)	17 (34.7)	99 (39.6)

CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; CRP, C-reactive protein; FeCal, fecal calprotectin; GUS, guselkumab; IQR, interquartile range; SD, standard deviation; UST, ustekinumab.
*Six patients had missing FeCal at baseline.

Patients treated with GUS had greater reductions in CRP and FeCal through Week 12 compared with placebo

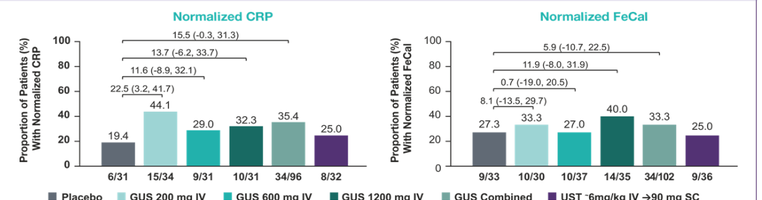
Figure 2. Median Change From Baseline in CRP and FeCal



*Nominal p-value GUS vs. placebo <0.05. CRP, C-reactive protein; FeCal, fecal calprotectin; GUS, guselkumab; UST, ustekinumab; Wk, week

Among patients who had elevated CRP (>3 mg/L) or FeCal (> 250 µg/g) at baseline, a higher proportion of combined GUS-treated patients had normal CRP (≤3 mg/L) or FeCal (≤ 250 µg/g) at Week 12 compared with placebo-treated patients

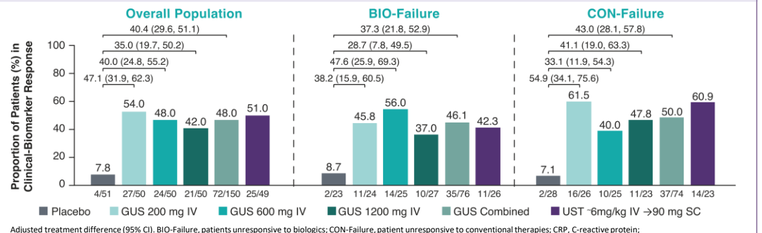
Figure 3. Patients With Normalized CRP or Normalized FeCal at Week 12 Who Were Abnormal at Baseline



Adjusted treatment difference (95% CI). CRP, C-reactive protein; FeCal, fecal calprotectin; GUS, guselkumab; IV, intravenous; UST, ustekinumab; Wk, week

Clinical-biomarker response was achieved by a higher proportion of patients treated with GUS compared with placebo at Week 12. Results were similarly higher in the subgroups and slightly more pronounced in the CON-Failure cohort at Week 12.

Figure 4. Patients in Clinical-Biomarker Response at Week 12 by Population



Adjusted treatment difference (95% CI). BIO-Failure, patients unresponsive to biologics; CON-Failure, patient unresponsive to conventional therapies; CRP, C-reactive protein; FeCal, fecal calprotectin; GUS, guselkumab; IV, intravenous; UST, ustekinumab; Wk, week

Disclosure of Financial Relationships
BES: 4D Pharma, AbbVie, Akros Pharma, Allergan, Amgen, Arena Pharmaceuticals, AstraZeneca, Boehringer-Ingelheim, Bristol-Myers Squibb, Capella Bioscience, Celgene, EnGene, Ferring, Forward Pharma, Gilead, Hoffman-La Roche Immune Pharmaceuticals, Ironwood Pharmaceuticals, Janssen Research & Development, LLC, Lilly, Lycera, Lyndra, MedImmune, Oppilan Pharmaceuticals, Otsuka, Palatin Technologies, Pharmaceuticals, Prometheus Laboratories, Takeda, Pfizer, Protagonist Therapeutics, Receptos, Rheos Medicines, Saliv, Seres Therapeutics, Shire, Synergy Pharmaceuticals, Target PharmaSolutions, Theravance Biopharma R&D, TiGenix, TopiVert Pharma, UCB, Vivelix. **SD:** AbbVie, Janssen Research & Development, LLC., Takada California, Inc. **JMA:** Abbott, AbbVie, Allergan, Anatara, AstraZeneca, Bayer, Celegene, Ferring, Gilead, Hospira, Immunic, Janssen, MSD, Nestle, Pfizer, Shire, Takeda, Vifor. **RP:** AbbVie, Janssen Research & Development, LLC., Takada California, Inc. **INBH:** Abbott, AbbVie, Celltrion, Eisai, Ferring, Janssen Research & Development, LLC., Johnson and Johnson, LF Asia, Takeda **AA:** AbbVie, Celgene, Janssen, Pfizer, Takeda, UCB. **WJS:** AbbVie, Allergan, Amgen, Arena Pharmaceuticals, Atlantic Healthcare Limited, Avexegen Therapeutics, BeiGene, Boehringer Ingelheim, Celgene/Receptos, Celltrion, Conatus, Cosmo, Escalier Biosciences, Ferring, Forbion, Genentech, Gilead Sciences, Gossamer Bio, Incyte, Janssen Research & Development, LLC, Kyowa Kirin Pharmaceutical Research, Landos Biopharma, Lilly, Oppilan Pharma, Otsuka, Pfizer, Progenity, Prometheus Biosciences (merger of Precision IBD and Prometheus Laboratories), Reistone, Ritter Pharmaceuticals, Robarts Clinical Trials (owned by Health Academic Research Trust, HART), Series Therapeutics, Shire, Sienna Biopharmaceuticals, Sigmoid Biotechnologies, Sterna Biologicals, Sublimity Therapeutics, Takeda, Theravance Biopharma, Tigenix, Tillotts Pharma, UCB Pharma, Ventyx Biosciences, Vimalan Biosciences, Vivelix Pharmaceuticals. **KW, DC, JJ, MEF, ZY, MC, LG**: Employees of Johnson & Johnson and own company stock/stock options.

References
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