THE EFFECT OF GUSELKUMAB INDUCTION THERAPY ON INFLAMMATORY BIOMARKERS IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE ULCERATIVE COLITIS: QUASAR PHASE 2B INDUCTION RESULTS THROUGH WEEK 12

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G.R. Lichtenstein,[1] A. Dignass,[2] W.J. Sandborn,[3] K.G. Huang,[4] M. Germinaro,[4] R. Wilson,[4] H. Zhang,[4] B. Chen,[5] M. Chen,[5] T. Hisamatsu,[6] B.G. Feagan,[7] J. Panés,[8] L. Peyrin-Biroulet[9] on behalf of the QUASAR Investigators

[1]University of Pennsylvania, Philadelphia, PA, USA; [2]Agaplesion Markus Hospital, Frankfurt, Germany; [3]University of California San Diego, La Jolla, CA, USA; [4]Janssen Research & Development, LLC, Spring House, PA, USA; [5]The First Affiliated Hospital of Sun Yat-sen University; [6]Kyorin University, Tokyo, Japan; [7]Alimentiv Inc, London, ON, Canada; [8]Hospital Clínic de Barcelona, IDIBAPS, CIBERehd, Barcelona, Spain; [9]Nancy University Hospital, Université de Lorraine, Nancy, France

BACKGROUND/OBJECTIVE

Serum C-reactive protein (CRP) and fecal calprotectin (FeCal) are non-invasive inflammatory biomarkers used to assess disease activity in patients with ulcerative colitis (UC)

QUASAR Phase 2b Induction Study is a randomized, double-blind, placebo-controlled study of guselkumab (GUS), an IL-23 p19 subunit antagonist, in patients with moderately to severely active UC who had inadequate response or intolerance to:

- Conventional therapy (ie, thiopurines or corticosteroids) or
- Advanced therapy (ie, tumor necrosis factor alpha antagonists, vedolizumab, or tofacitinib)

Here we report inflammatory biomarker results through Week 12 with GUS IV treatment in the QUASAR Phase 2b Induction Study

METHODS

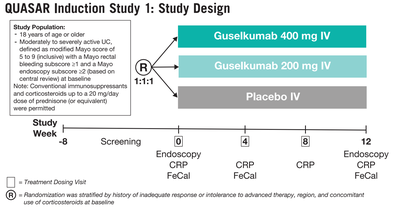
Biomarker Assessments

- Normalized CRP was defined as ≤ 3 mg/L and normalized FeCal was defined as ≤ 250 mg/kg

Data Handling

- The primary analysis population included all randomized patients with a modified Mayo score of 5 to 9 who received at least 1 (partial or complete) dose of study intervention
- For change from baseline in CRP or FeCal concentration
  - Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an adverse event worsening of UC prior to the designated timepoint had their baseline value carried forward from the time of the event onward
- For normalized or 50%/75% reduction in CRP or FeCal concentration
  - Patients who had a prohibited change in UC medication, an ostomy or colectomy, or discontinued study agent due to lack of efficacy or an adverse event of worsening of UC prior to the designated timepoint were considered not to have achieved normalized CRP or FeCal or a 50%/75% reduction
  - Patients who had a missing CRP or FeCal value at the designated timepoint were considered not to have achieved normalized CRP or FeCal or a 50%/75% reduction
- Data after a discontinuation of study agent due to COVID-19 related reasons (excluding COVID-19 infection) were considered to be missing

QUASAR Induction Study 1: Study Design



CONCLUSIONS

- Patients with moderately to severely active UC who received GUS IV induction treatment had greater reductions in CRP and FeCal concentrations through Week 12 compared with placebo with no dose dependent effect for GUS 200 mg and 400 mg
- Reductions in CRP and FeCal were observed as early as Week 4 with GUS and continued to Week 12
- Higher proportions of patients had normalized CRP and normalized FeCal levels at Week 12 with GUS compared with placebo

RESULTS

- Median baseline CRP and FeCal concentrations were similar across treatment groups
- Greater median reductions in CRP and FeCal were observed at the earliest timepoint assessed (ie, Week 4) in patients treated with GUS compared with placebo and continued through Week 12
- Median decreases from induction baseline in CRP levels were similar between the GUS 200 mg and 400 mg IV treatment groups; a similar trend was observed for FeCal levels
- At Week 12, higher proportions of patients treated with GUS had normalized CRP and normalized FeCal compared with placebo among patients with elevated CRP or FeCal levels at baseline

Baseline Demographics and Disease Characteristics: Primary Analysis Population

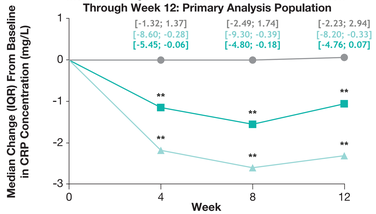
		Guselkumab		
	Placebo IV	200 mg IV	400 mg IV	Total
Primary analysis set, n	105	101	107	313
Age in years, mean (SD)	41.2 (15.05)	43.3 (14.28)	40.4 (13.84)	41.6 (14.40)
Male, n (%)	66 (62.9)	60 (59.4)	59 (55.1)	185 (59.1)
UC duration (years), mean (SD)	7.72 (7.157)	7.03 (5.996)	7.86 (7.147)	7.55 (6.789)
Mayo score, mean (SD)	9.0 (1.31)	9.2 (1.29)	9.3 (1.35)	9.2 (1.32)
Modified Mayo score, mean (SD)	6.9 (1.06)	7.0 (1.06)	7.0 (0.99)	7.0 (1.04)
Modified Mayo score of 7-9, n (%)	69 (65.7)	71 (70.3)	78 (72.9)	218 (69.6)
Mayo endoscopy subscore of 3 (severe), n (%)	75 (71.4)	66 (65.3)	78 (72.9)	219 (70.0)
Extensive UC, n (%)	46 (43.8)	48 (47.5)	59 (55.1)	153 (48.9)
Extraintestinal manifestations present, n (%)	13 (12.4)	15 (14.9)	22 (20.6%)	50 (16.0)
CRP concentration (mg/L), median (IQR)	4.9 (1.4; 10.8)	4.3 (1.6; 17.8)	4.4 (1.9; 8.8)	4.6 (1.6; 11.3)
Elevated CRP (>3mg/L), n (%)	64 (61.0)	63 (62.4)	66 (61.7)	193 (61.7)
FeCal concentration (mg/kg), median (IQR)	1457.0 (749.0; 3054.0)	1667.0 (771.0; 2859.0)	1578.0 (811.0; 2860.0)	1564.0 (767.0; 2860.0)
Elevated FeCal (>250mg/kg), n (%)	81 (77.1)	85 (84.2)	91 (85.0)	257 (82.1)

UC Medications: Primary Analysis Population

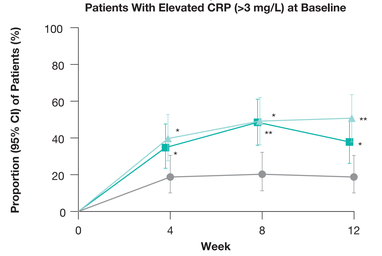
		Guselkumab		
	Placebo IV	200 mg IV	400 mg IV	Total
Primary analysis set, n	105	101	107	313
Receiving any of the following conventional therapy for UC at baseline, n (%)	95 (90.5)	92 (91.1)	96 (89.7)	283 (90.4)
Oral corticosteroids	40 (38.1)	41 (40.6)	44 (41.1)	125 (39.9)
Immunosuppressant drugs	17 (16.2)	25 (24.8)	27 (25.2)	69 (22.0)
Oral aminosalicylates	79 (75.2)	74 (73.3)	89 (83.2)	242 (77.3)
History of inadequate response or intolerance to 1 or more advanced therapies for UC,* n (%)	51 (48.6)	46 (45.5)	51 (47.7)	148 (47.3)
1 advanced therapy class	23 (21.9)	27 (26.7)	25 (23.4)	75 (24.0)
2 or more advanced therapy classes	28 (26.7)	19 (18.8)	26 (24.3)	73 (23.3)

*Advanced therapies indicate tumor necrosis factor alpha antagonists, vedolizumab, or tofacitinib.

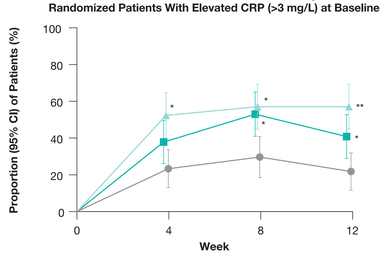
Median Change from Baseline in CRP Concentration Through Week 12: Primary Analysis Population



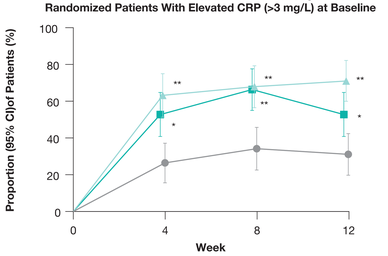
Normalized CRP Through Week 12: Randomized Patients With Elevated CRP (>3 mg/L) at Baseline



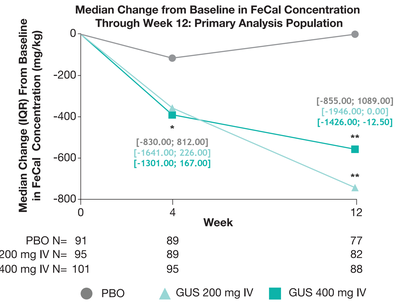
Normalized CRP or 75% Reduction in CRP Through Week 12: Randomized Patients With Elevated CRP (>3 mg/L) at Baseline



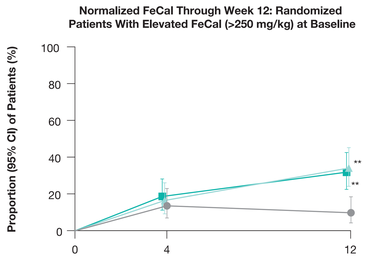
Normalized CRP or 50% Reduction in CRP Through Week 12: Randomized Patients With Elevated CRP (>3 mg/L) at Baseline



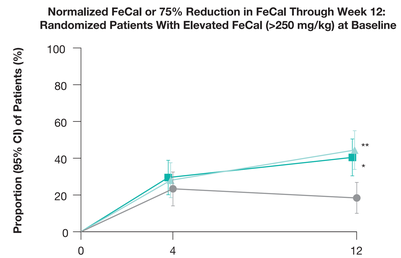
Median Change from Baseline in FeCal Concentration Through Week 12: Primary Analysis Population



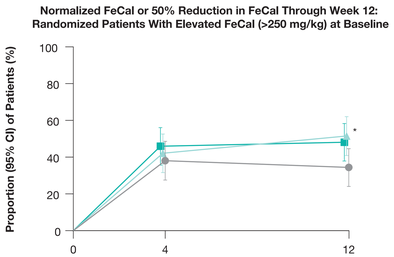
Normalized FeCal Through Week 12: Randomized Patients With Elevated FeCal (>250 mg/kg) at Baseline



Normalized FeCal or 75% Reduction in FeCal Through Week 12: Randomized Patients With Elevated FeCal (>250 mg/kg) at Baseline



Normalized FeCal or 50% Reduction in FeCal Through Week 12: Randomized Patients With Elevated FeCal (>250 mg/kg) at Baseline



*Nominal p-value <0.05. **Nominal p-value <0.001. Includes only treated patients with modified Mayo score of 5-9 at induction baseline.

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