Efficacy of guselkumab intravenous and subcutaneous induction: symptoms, heath-related quality of life, and inflammatory biomarker results from the GALAXI and GRAVITI studies

Anita Afzali[1], Remo Panaccione[2], Silvio Danese[3], Tadakazu Hisamatsu[4], Geert D'Haens[5], Natalie A. Terry[6], Mobolaji Olurinde[6], Rian Van Rampelbergh[7], Leonardo Salese[6], Elizabeth Merrall[8], Kitty Yuen Yi Wan[9], Zijiang Yang[6], Bruce E. Sands[10], Ailsa Hart[11]

[1]Division on Digestive Diseases, University of Cincinnati, College of Medicine, Cincinnati, Ohio, USA; [2]Inflammatory Bowel Disease Unit, Division of Gastroenterology and Hepatology, University of Calgary, Calgary, Alberta, Canada; [3]Gastroenterology and Endoscopy, IRCCS Ospedale San Raffaele and University Vita-Salute San Raffaele, Milano, Italy; [4]Department Gastroenterology and Hepatology, Kyorin University School of Medicine, Tokyo, Japan; [5]Department of Gastroenterology, Amsterdam University Medical Centers, Amsterdam, The Netherlands; [6]Johnson & Johnson, Spring House, PA, USA; [7]Johnson & Johnson, Beerse, Belgium; [8]Johnson & Johnson, Leiden, The Netherlands; [9]Johnson & Johnson, Allschwil, Switzerland; [10]Ichan School of Medicine at Mount Sinai, New York, NY, USA; [11]London North-West University Healthcare NHS Trust, London, UK

Key Takeaways

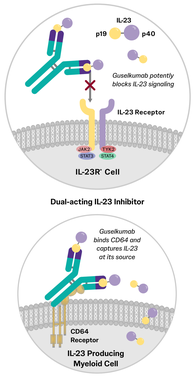
- **Induction treatment with either guselkumab IV or SC routes of administration provided rapid and robust improvements in symptoms and HRQoL as well as reductions in objective biomarkers of inflammation**
- **The differences between guselkumab and placebo were seen as early as the first assessment timepoint 4 weeks after the first IV or SC induction dose**
- **The rapidity and magnitude of the improvements were similar for IV and SC induction**

Background

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

The GALAXI and GRAVITI studies showed that induction with intravenous (IV) or subcutaneous (SC) guselkumab was effective in participants with moderately to severely active Crohn's disease[1,2]

Clinical and endoscopic outcomes from the GALAXI and GRAVITI studies demonstrate that the efficacy of guselkumab induction is similar for both IV and SC routes of administration



Objective

Here we assess the effect of guselkumab IV or SC induction on symptoms, health-related quality of life (HRQoL), and inflammatory markers in participants with Crohn's disease through week 12

Methods

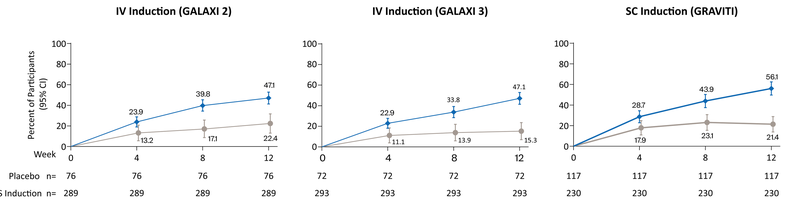
- Eligible participants in all 3 studies were at least 18 years of age and diagnosed with moderately to severely active Crohn's disease of at least three months' duration based on:
  - A Crohn's Disease Activity Index (CDAI) score of 220–450 AND:
    - A mean daily stool frequency count based on the unweighted CDAI component of liquid or very soft stools of >3 in GALAXI 2 & 3, and ≥4 in GRAVITI

    OR
    - A mean daily abdominal pain score based on the unweighted CDAI component of abdominal pain of >1 in GALAXI 2 & 3, and ≥2 in GRAVITI
  - Endoscopic evidence of ileocolonic Crohn's disease at the screening endoscopy with a Simple Endoscopic Score for Crohn's Disease (SES-CD) ≥6 (or ≥4 for participants with isolated ileal disease) and presence of ulceration in any one of the five ileocolonic segments
- Participants were required to have a history of intolerance or inadequate response to oral corticosteroids, AZA, 6-MP or MTX, or to biologic therapies (TNF antagonists or vedolizumab) for Crohn's disease
  - Participants who had demonstrated an inadequate response/intolerance to ustekinumab were not eligible for study entry (although ustekinumab exposed participants could be enrolled in GALAXI)
- During the induction period in GALAXI 2 (N=508) & 3 (N=513), participants received either:
  - IV induction with guselkumab 200 mg at weeks 0, 4, and 8
  - IV ustekinumab ~6 mg per kg at week 0, followed by SC 90 mg at week 8
  - Placebo at weeks 0, 4, and 8
- During the induction period in GRAVITI (N=347), participants received SC induction with guselkumab 400 mg or placebo at weeks 0, 4, and 8
- These studies were enrolled during the same time using some of the same study sites and countries
- To evaluate the improvement in symptoms, HRQoL, and inflammation, we assessed abdominal pain and stool frequency using the respective Crohn's Disease Activity Index subscore components, Inflammatory Bowel Disease Questionnaire (IBDQ) remission (defined as an IBDQ total score ≥170), C-reactive protein (CRP), and fecal calprotectin through week 12

Results

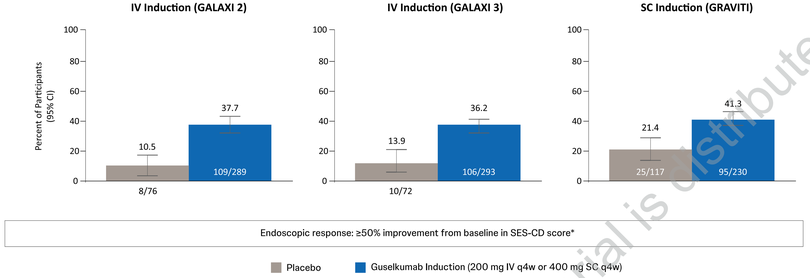
- **As presented previously, participants treated with guselkumab IV induction in GALAXI[1] or guselkumab SC induction in GRAVITI[2] had significantly greater rates of clinical remission at week 12 and endoscopic response at week 12 compared with placebo**

Clinical Remission Through Week 12



Clinical remission: CDAI score <150

Endoscopic Response at Week 12



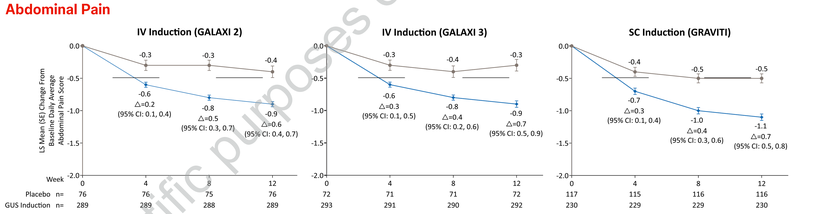
Endoscopic response: ≥50% improvement from baseline in SES-CD score*

In GALAXI 2 and 3, endoscopic response was defined as: ≥50% improvement from baseline in SES-CD or SES-CD ≤2

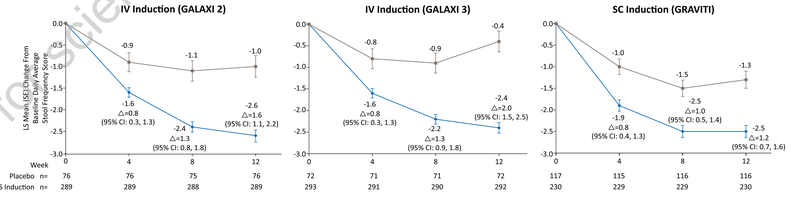
CDAI=Crohn's Disease Activity Index; CI=Confidence interval; GUS=Guselkumab; IV=Intravenous; q4w=Every 4 weeks; SC=Subcutaneous; SES-CD=Simple Endoscopic Score for Crohn's Disease

- **Compared with placebo, improvement in symptom-based outcomes was seen through week 12 for both guselkumab IV and SC; improvements with guselkumab were evident at the first assessment at Week 4**
- **Proportions of participants achieving IBDQ remission were greater for guselkumab-treated participants at both weeks 8 and 12 compared to placebo**

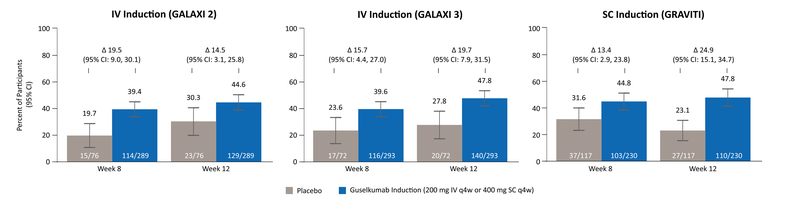
Abdominal Pain



Stool Frequency



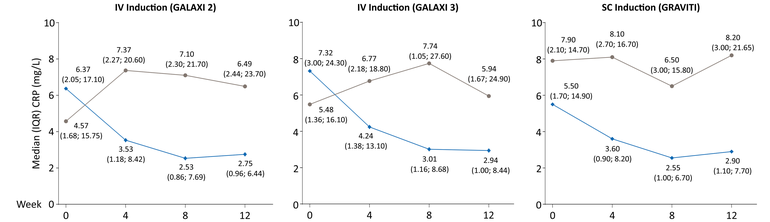
IBDQ Remission



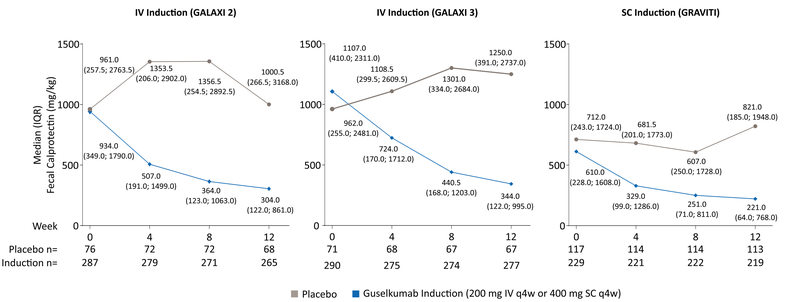
CI=Confidence interval; GUS=Guselkumab; IBDQ=Inflammatory Bowel Disease Questionnaire; IV=Intravenous; LS=Least squares; q4w=Every 4 weeks; SC=Subcutaneous; SE=Standard error

- **Median CRP and fecal calprotectin levels decreased in guselkumab-treated participants starting at week 4 following IV or SC induction, while levels increased or remained static in participants receiving placebo**

CRP



Fecal Calprotectin



CRP=C-reactive protein; GUS=Guselkumab; IQR=Interquartile range; IV=Intravenous; q4w=Every 4 weeks; SC=Subcutaneous

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