Efficacy and safety of 48 weeks of guselkumab for patients with Crohn's disease: maintenance results from the phase 2, randomised, double-blind GALAXI-1 trial

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Summary

Background Many patients with moderately to severely active Crohn's disease do not respond to available therapies or lose response over time. The GALAXI-1 study previously found that three intravenous guselkumab dosages showed superior clinical and endoscopic outcomes over placebo at week 12 in patients with moderately to severely active Crohn's disease. We report the safety and efficacy of subcutaneous guselkumab maintenance regimens to week 48 in the GALAXI-1 study.

Methods We did a phase 2, randomised, multicentre, double-blind trial. Adult patients with moderately to severely active Crohn's disease were randomly allocated with a computer-generated randomisation schedule to receive one of five treatment groups, with regimens consisting of an intravenous induction phase transitioning to a subcutaneous maintenance phase starting at week 12 in a treat-through design: (1) guselkumab 200→100 mg group (200 mg intravenous at weeks 0, 4, and 8, then 100 mg subcutaneous every 8 weeks; (2) guselkumab 600→200 mg group (600 mg intravenous at weeks 0, 4, and 8, then 200 mg subcutaneous every 4 weeks); (3) guselkumab 1200→200 mg group (1200 mg intravenous at weeks 0, 4, and 8, then 200 mg subcutaneous every 4 weeks); (4) ustekinumab group (approximately 6 mg/kg intravenous at week 0, then 90 mg subcutaneous every 8 weeks); or (5) placebo group (placebo induction followed by either placebo maintenance [for those with CDAI clinical response at week 12] or crossover to ustekinumab [for those without CDAI clinical response at week 12]). Endpoints assessed at week 48 included CDAI remission (CDAI score <150), endoscopic response (≥50% improvement from baseline in SES-CD or SES-CD score ≤2), and endoscopic remission (SES-CD score ≤2) in the primary efficacy analysis population of all randomised patients who received at least one dose of study drug, excluding those discontinued during a temporary study pause. Safety analyses included all randomised patients who received at least one study drug dose. This trial is registered at Clinical Trials.gov (NCT03466411) and is active but not recruiting.

Findings Among 700 patients screened, 309 (112 biologic-naive; 197 biologic-experienced) were included in the primary efficacy analysis population: 61 in the guselkumab 200→100 mg group, 63 in the guselkumab 600→200 mg group, 61 in the guselkumab 1200→200 mg group, 63 in the ustekinumab group, and 61 in the placebo group. 126 (41%) women and 183 (59%) men were included, with median age 36·0 years (IQR 28·0–49·0). At week 48, the numbers of patients with CDAI clinical remission were 39 (64%) in the guselkumab 200→100 mg group, 46 (73%) in the guselkumab 600→200 mg group, 35 (57%) in the guselkumab 1200→200 mg group, and 37 (59%) in the ustekinumab group. The corresponding numbers of patients with endoscopic response were 27 (44%), 29 (46%), 27 (44%), and 19 (30%), respectively, and endoscopic remission was seen in 11 (18%), 11 (17%), 20 (33%), and four (6%) patients, respectively. In the placebo group, 15 patients were in CDAI clinical response at week 12 and continued placebo; of these, nine (60%) were in clinical remission at week 48. 44 patients in the placebo group were not in CDAI clinical response at week 12 and crossed over to ustekinumab; of these, 26 (59%) were in clinical remission at week 48. Up to week 48, adverse events frequencies in the safety population (n=360) were 46 (66%) of 70 patients (464·9 events per 100 patient-years of follow-up) in the placebo group, 163 (74%) of 220 patients (353·1 per 100 patient-years) in the three guselkumab groups combined, and 60 (85%) of 71 patients (350·7 per 100 patient-years) in the ustekinumab group. Among patients treated with guselkumab or ustekinumab, the most frequently reported infections up to week 48 were nasopharyngitis (25 [11%] of 220 guselkumab recipients, 12 [11%] of 114 ustekinumab recipients) and upper respiratory infections (13 [6%] guselkumab recipients, eight [7%] ustekinumab recipients). After week 12, one patient who responded to placebo induction and two guselkumab-treated patients had serious infections. No active tuberculosis, opportunistic infections, or deaths occurred.

Interpretation Patients receiving guselkumab intravenous induction and subcutaneous maintenance treatment achieved high rates of clinical and endoscopic efficacy up to week 48. No new safety concerns were identified.

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See Online for appendix

Introduction

Crohn's disease, a chronic relapsing-remitting disease, requires lifelong management.[1] Currently, four classes of biological agents are approved for the treatment of moderately to severely active Crohn's disease: TNF antagonists (infliximab, adalimumab, certolizumab),[2–5] integrin antagonists (natalizumab, vedolizumab),[6,7] an antagonist of the p40 subunit of IL-12 and IL-23 (ustekinumab),[8] and the IL-23 p19 subunit-specific antagonist (risankizumab).[9,10] Recently, an oral, small-molecule JAK antagonist (upadacitinib) was also approved for Crohn's disease.[11] Although the introduction of biologics has substantially improved the medical management of Crohn's disease, many patients with moderately to severely active Crohn's disease do not respond to available therapies or lose response over time.[1] The unmet medical need for new treatment options, especially therapies that have the potential to raise the efficacy bar without compromising safety, could be realised with new treatment options and more efficient study designs (eg, seamless phase 2/3 studies and treat-through studies).[12,13]

An increased understanding of the pathogenesis of Crohn's disease has revealed a role for pathways related to IL-23. Genome-wide association studies have identified polymorphisms in the IL-23 receptor gene associated with Crohn's disease.[14] Clinically, the role of IL-12 and IL-23 in Crohn's disease has been shown in phase 3 induction and maintenance studies of ustekinumab in adults with moderately to severely active Crohn's disease.[8] Further evidence of the role of IL-23 in Crohn's disease has been provided by studies of risankizumab.[9,10]

Guselkumab is an IL23 p19 subunit antagonist that binds to IL-23 with high affinity and potency.[15] Guselkumab also binds to the CD64 receptor (high-affinity Fcγ receptor 1) on the surface of human inflammatory monocytes, which enables it to neutralise IL-23 at its predominant source of production, potentially enriching the presence of guselkumab in the inflamed tissue microenvironment.[16]

The GALAXI programme consists of three guselkumab efficacy and safety studies in patients with moderately to severely active Crohn's disease: a 48-week, phase 2, induction dose-finding study (GALAXI-1) and two identical 48-week phase 3 confirmatory studies (GALAXI-2 and GALAXI-3). These studies used a treat-through design in which patients were randomly allocated to receive guselkumab, ustekinumab, or placebo and continuously followed up from randomisation through induction (week 12), maintenance (weeks 12–48), and long-term extension phases (weeks 48–252) on their randomised treatment (except for patients who did not respond to placebo, who crossed over to ustekinumab at week 12). Results from the 12-week induction phase of GALAXI-1 showed that all three dosages of intravenous guselkumab induced clinically meaningful improvements, and differences between the individual dosage groups were small and not clinically meaningful.[17] In this Article, we present results from the maintenance phase of GALAXI-1.

Methods

Study design

GALAXI-1 is a phase 2, randomised, double-blind, parallel-group, multicentre trial assessing the efficacy

Research in context

Evidence before this study

Currently, four biological agent classes are approved for the treatment of moderately to severely active Crohn's disease: TNF antagonists (infliximab, adalimumab, certolizumab), integrin antagonists (natalizumab, vedolizumab), an IL-12 and IL-23 antagonist (ustekinumab), and an IL-23 antagonist (risankizumab); however, some patients do not respond to these available therapies. Over 12 weeks of therapy in GALAXI-1, three intravenous dosages of guselkumab, an IL-23 antagonist, showed superior clinical and endoscopic outcomes over placebo in patients with moderately to severely active Crohn's disease.

Added value of this study

This study presents comparative efficacy and safety data for guselkumab induction and maintenance therapy to week 48 for patients with moderately to severely active Crohn's disease, using a treat-through study design. High rates of clinical efficacy and endoscopy outcomes following intravenous induction continued to increase after week 12 and were maintained with subcutaneous maintenance therapy to week 48. Guselkumab intravenous induction doses of 1200 mg, 600 mg, or 200 mg then subcutaneous maintenance doses of 100 mg every 8 weeks or 200 mg every 4 weeks were generally well tolerated over 48 weeks in this patient population. No new safety concerns were identified.

Implications of all the available evidence

The treat-through design of this study, in which patients were randomly allocated to individual treatment regimens that included both induction and maintenance therapy and were followed up to week 48, allowed for evaluation of all patients on active treatment, regardless of their response to induction. This contrasts with recent registrational trials of inflammatory bowel disease therapies, in which induction and maintenance treatment regimens are evaluated in separate studies, and maintenance study populations consisted only of patients who responded to induction treatment. The results show that evaluation of guselkumab maintenance treatment in larger phase 3 studies is warranted.

and safety of guselkumab for patients with moderately to severely active Crohn's disease. This trial took place at 128 centres globally, including hospitals, academic medical centres, and private practices (appendix p 3).

Patients were randomly allocated to receive one of five treatment regimens that consisted of an intravenous induction phase and subcutaneous maintenance phase (figure 1). Those allocated to receive guselkumab (one of three different dosages) or ustekinumab were transitioned to their respective subcutaneous maintenance regimen regardless of response status at week 12 (the first subcutaneous dose for patients allocated to receive ustekinumab was at week 8). Patients allocated to receive intravenous placebo transitioned to either subcutaneous placebo (if they had a clinical response at week 12, as defined below) or ustekinumab rescue therapy (for those with no clinical response at week 12). Subcutaneous injections were administered on site after study procedures and assessments were completed. In this treat-through design, patients who lost response during maintenance had their disease managed at the investigators' discretion according to local practice, or they could be discontinued for reasons related to lack of efficacy, at the investigators' discretion.

The study protocol was approved by the institutional review boards or ethics committees at each recruiting centre, and the study was conducted in compliance with the Declaration of Helsinki, Good Clinical Practice guidelines, and applicable local regulations. All patients provided written informed consent before any study procedure was done. Safety data were periodically reviewed by an independent, external data monitoring committee. The study protocol is provided in the appendix (pp 34–237).

Participants

We enrolled adult patients (aged ≥18 years) with moderately to severely active Crohn's disease of at least 3 months duration, defined as Crohn's Disease Activity Index (CDAI) score of 220–450 (inclusive), with either a mean daily stool frequency count greater than 3 or a mean daily abdominal pain score greater than 1, and a Simple Endoscopic Score for Crohn's Disease (SES-CD) of 3 or greater.

We included two patient subgroups: those with documented inadequate response or intolerance to previous conventional therapy, or to previous biological therapy. Patients in the previous conventional therapy subgroup had documented inadequate response or intolerance to at least one of the following therapies: oral corticosteroids (including budesonide or beclomethasone dipropionate), immunomodulators (azathioprine, 6-mercaptopurine, or methotrexate), or corticosteroid dependence (appendix p 7). Patients in this subgroup could be naive to biologic therapy (ie, a TNF antagonist or approved biosimilars for these agents, or vedolizumab) or could have been exposed to biologic therapy without inadequate response or intolerance (appendix p 8).

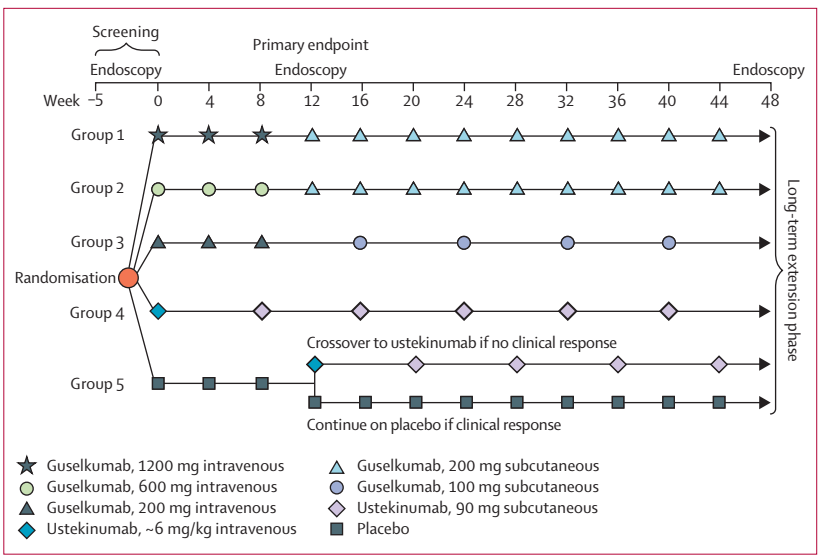

Figure 1: **Study design**
This schematic illustrates only the dosing for the treatment groups, and does not provide a complete illustration of all dummy (placebo) administrations done to maintain blinding.

Limited ustekinumab exposure was permitted, provided that the last dose was administered at least 16 weeks before study entry, with no evidence of ustekinumab failure or intolerance.

Patients in the subgroup with previous inadequate response or intolerance to biological therapy had a documented primary non-response, secondary non-response, or intolerance to one or more biological therapies (appendix p 8).

In all patients, stable doses of 5-aminosalicylates and immunomodulators were maintained from induction baseline to maintenance week 48, unless otherwise stated in protocol (appendix p 7). Corticosteroid therapy at a prednisone-equivalent dose at or below 40 mg/day, or 9 mg/day of budesonide, or 5 mg/day beclomethasone dipropionate was permitted at entry, with mandatory tapering from week 12 according to a protocol-recommended tapering schedule (appendix p 7), unless not medically feasible. Exclusion criteria are listed in the appendix (pp 114-118). Key exclusion criteria were presence of complications of Crohn's disease that could require surgery, presence or suspicion of an abscess, draining stoma or ostomy, recent surgery, and evidence of enteric infection (in the past 4 months). Patients who previously received a biological agent targeting IL-12 and IL-23, or IL-23 alone, were ineligible, except for patients with limited exposure to ustekinumab, as described above. Patients receiving the following medications within the specified time periods before baseline were excluded: intravenous corticosteroids (3 weeks); ciclosporin, tacrolimus, sirolimus, or mycophenolate mofetil (8 weeks); biological anti-TNF therapy (8 weeks); vedolizumab or ustekinumab (16 weeks); or other immunomodulatory biological agents (12 weeks or 5 half-lives, whichever is longer).

Randomisation and masking

Central randomisation was implemented. Patients were randomly assigned (1:1:1:1:1) to one of five treatment groups: three groups receiving guselkumab of various dosages, an ustekinumab group, and a placebo group. We used a computer-generated randomisation schedule prepared before the study. The randomisation was balanced by using randomly permuted blocks and was stratified by baseline CDAI score (≤300 or >300) and history of biologic failure status (yes or no). The interactive web response system assigned a unique treatment code, which dictated the treatment assignment and matching study intervention kits for the patient. Clinical outcome assessors were masked to study treatment and visit. Patients were masked to study treatment.

Procedures

Patients were allocated to one of the following five treatment groups (figure 1): (1) guselkumab 200→100 mg group (200 mg intravenous guselkumab at weeks 0, 4, and 8, then 100 mg subcutaneous guselkumab every 8 weeks); (2) guselkumab 600→200 mg group (600 mg intravenous guselkumab at weeks 0, 4, and 8, then 200 mg subcutaneous guselkumab every 4 weeks); (3) guselkumab 1200→200 mg group (1200 mg intravenous guselkumab at weeks 0, 4, and 8, then 200 mg subcutaneous guselkumab every 4 weeks); (4) ustekinumab group (approximately 6 mg/kg intravenous ustekinumab at week 0, then 90 mg subcutaneous ustekinumab every 8 weeks); or (5) placebo group (intravenous placebo followed by either subcutaneous placebo for patients with a clinical response on the CDAI at week 12, or rescue therapy with ustekinumab [a single intravenous dose of approximately 6 mg/kg, then 90 mg subcutaneous every 8 weeks] for patients with no CDAI clinical response to placebo at week 12). To maintain blinding, all groups received two intravenous infusions at week 0 (either one active and one placebo, or two placebo), and one intravenous infusion at weeks 4, 8, and 12 (either active or placebo). Additionally, all groups received one subcutaneous injection (either active or placebo) at week 8, and up to three subcutaneous injections (either active or placebo) at each visit from week 12 onwards.

Among demographic characteristics collected, sex was self-reported as female or male. Clinical efficacy was evaluated at each visit (weeks 0, 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, and 48) using the CDAI.[18] Endoscopic assessments of the terminal ileum and colon, using the SES-CD, were done at baseline and weeks 12 and 48, and were scored by a single central reader masked to study treatment and visit. Video endoscopies were assessed by a single central reader masked to treatment group and visit; software assigned each patient's video to a reader. Health-related quality of life was assessed using the Inflammatory Bowel Disease Questionnaire (IBDQ)[19] at weeks 0, 8, 12, 24, and 48. Inflammatory biomarkers (C-reactive protein [CRP] and faecal calprotectin) were assessed at weeks 0, 4, 8, 12, 24 and 48. CRP was also assessed at weeks 16, 20, 32, and 40. Patients were evaluated for adverse events and serious adverse events at each study visit.

Serum guselkumab concentrations were measured every 4 weeks until week 24, then every 8 weeks, with a validated, specific, and sensitive electrochemiluminescence immunoassay method using the Meso Scale Discovery platform (Gaithersburg, MD, USA). Serum antibodies to guselkumab were assessed every 4 weeks until week 12, then every 8 weeks beginning at week 24, using a validated, drug-tolerant assay with an acid dissociation step to improve detection of antibodies to guselkumab in the presence of excess guselkumab.

Outcomes

The primary and major secondary endpoints were reported previously.[17] Prespecified clinical endpoints examined at week 48 that assessed the efficacy of long-term maintenance subcutaneous administration after intravenous induction infusion included CDAI clinical remission (CDAI <150), CDAI clinical response (either CDAI clinical remission or a ≥100-point decrease in CDAI from baseline), and corticosteroid-free CDAI remission (at week 48, and within 30 or 90 days of week 48). Another prespecified clinical endpoint was durable CDAI clinical remission (CDAI score <150 for ≥80% of all visits between week 12 and week 48 [ie, at least eight of ten visits], which must include week 48). Prespecified composite clinical and biomarker endpoints evaluated to week 48 were clinical-biomarker response (CDAI clinical response and a ≥50% reduction from baseline in CRP or faecal calprotectin), and clinical-biomarker remission (CDAI clinical remission and CRP concentrations ≤3 mg/L or faecal calprotectin concentration ≤250 µg/g, or both).

Prespecified endoscopic endpoints assessed at week 48 were endoscopic response (≥50% improvement from baseline in SES-CD, or SES-CD ≤2) and endoscopic remission (SES-CD ≤2).[20] As patients with non-passable strictures were eligible, an alternative post-hoc definition of endoscopic remission was also assessed (SES-CD ≤4 and at least a 2 point reduction from baseline, with no subscore >1 in any individual variable). Prespecified patient-reported outcomes assessed at week 48 were IBDQ remission (IBDQ score >170), IBDQ response (≥16-point improvement from baseline in IBDQ score), and 2-Item Patient-Reported Outcomes (PRO-2) remission (unweighted mean daily CDAI components of abdominal pain ≤1 and stool frequency ≤3, and no worsening from baseline).

A post-hoc analysis of week 48 outcomes in patients with a clinical response at week 12 was done with use of the prespecified CDAI clinical response definition and post-hoc symptom-based clinical response definition (a decrease of at least 30% in average daily stool frequency or average daily abdominal pain score, or both, and no

worsening from baseline). A post-hoc analysis of week 48 outcomes in patients who did not have a clinical response at week 12 was also done.

A list of all prespecified long-term efficacy endpoints and definitions is provided in the appendix (p 14). More detailed pharmacokinetic, immunogenicity, and biomarker analyses will be reported elsewhere.

Statistical analysis

Sample size calculation for this study was based on the primary endpoint comparison between guselkumab and placebo at week 12, which was reported previously (appendix pp 21–22).[17]

Except for the post-hoc analyses mentioned above, week 48 endpoints were prespecified but not controlled for

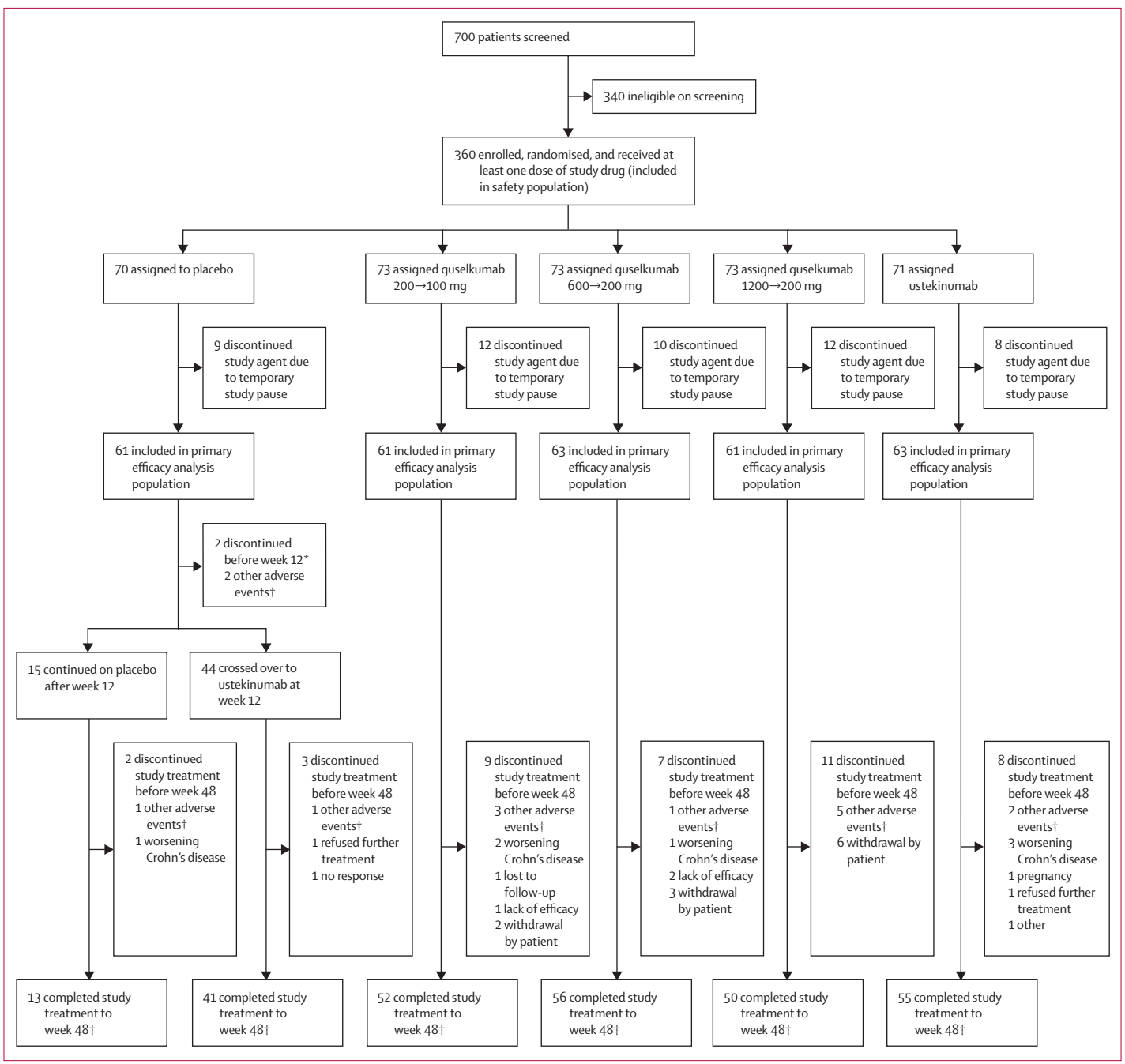

Figure 2: **Trial profile showing disposition of patients to week 48**

*Two patients in the placebo group discontinued study drug before week 12 and did not receive maintenance dosing. †Other than worsening Crohn's disease. ‡Patients who completed the study to week 48 continued into the long-term extension or completed their final efficacy and safety visit.

	Placebo group* (n=61)	Guselkumab 200→100 mg group (n=61)	Guselkumab 600→200 mg group (n=63)	Guselkumab 1200→200 mg group (n=61)	Ustekinumab group† (n=63)
Sex,					
Men	37 (61%)	38 (62%)	36 (57%)	31 (51%)	41 (65%)
Women	24 (39%)	23 (38%)	27 (43%)	30 (49%)	22 (35%)
Median age, years	36·0 (29·0–47·0)	39·0 (29·0–49·0)	37·0 (26·0–50·0)	35·0 (30·0–51·0)	36·0 (26·0–42·0)
Race					
American Indian or Alaska Native	0	2 (3%)	0	0	0
Asian	3 (5%)	9 (15%)	8 (13%)	3 (5%)	6 (10%)
Black or African American	3 (5%)	0	1 (2%)	2 (3%)	1 (2%)
Native Hawaiian or Other Pacific Islander	0	1 (2%)	0	1 (2%)	0
White	53 (87%)	46 (75%)	52 (83%)	54 (89%)	56 (89%)
Not reported	2 (3%)	3 (5%)	2 (3%)	1 (2%)	0
Ethnicity					
Hispanic or Latino	2 (3%)	4 (7%)	4 (6%)	2 (3%)	0
Not Hispanic or Latino	57 (93%)	54 (89%)	55 (87%)	58 (95%)	61 (97%)
Not reported	2 (3%)	3 (5%)	4 (6%)	1 (2%)	2 (3%)
Mean weight, kg	67·0 (16·2)	71·1 (15·9)	67·5 (14·7)	73·9 (19·7)	69·4 (16·2)
Median duration of Crohn's disease, years	7·3 (3·5–12·4)	6·1 (2·3–14·3)	7·6 (2·9–16·2)	4·6 (2·1–9·7)	5·9 (2·1–10·6)
Mean CDAI score	300·8 (49·9)	304·6 (57·2)	305·8 (58·8)	305·8 (54·5)	313·3 (61·3)
PRO-2					
Weighted mean score	143·3 (42·0)	147·2 (45·1)	141·9 (42·8)	146·1 (39·5)	147·2 (42·4)
Daily stool frequency >3	49 (80%)	47 (77%)	52 (83%)	48 (79%)	56 (89%)
Abdominal pain >1	58 (95%)	57 (93%)	58 (92%)	59 (97%)	60 (95%)
Mean SES-CD score	12·8 (8·0)	12·6 (8·0)	12·4 (7·4)	11·7 (7·1)	15·1 (8·7)
Median C-reactive protein concentration, mg/L	4·4 (1·9–10·2)	6·3 (1·3–27·8)	5·8 (1·6–28·1)	4·8 (2·2–13·9)	8·8 (1·8–21·1)
Median faecal calprotectin, µg/g	488·5 (192·5–1692·0), n=60	561·5 (169·0–1669·0), n=58	596·0 (222·0–1641·0), n=63	687·0 (190·0–1689·5), n=60	957·0 (339·0–1852·0), n=62
Mean IBDQ score	120·8 (30·12), n=57	126·8 (33·97), n=60	128·2 (32·46), n=63	122·8 (37·95), n=61	130·6 (32·12), n=63
Disease location					
Ileum only	11 (18%)	17 (28%)	22 (35%)	13 (21%)	11 (17%)
Colon only	26 (43%)	27 (44%)	18 (29%)	31 (51%)	29 (46%)
Ileum and colon	24 (39%)	17 (28%)	23 (37%)	17 (28%)	23 (37%)
History of fistula	18 (30%)	18 (30%)	23 (37%)	17 (28%)	23 (37%)
≥1 open fistula at baseline	3 (5%)	7 (11%)	9 (14%)	8 (13%)	10 (16%)
History of stricturing complication of Crohn's disease	16 (26%)	16 (26%)	13 (21%)	12 (20%)	11 (17%)
Crohn's disease medications taken at baseline					
≥1 medications for Crohn's disease	45 (74%)	44 (72%)	47 (75%)	46 (75%)	53 (84%)
Immunomodulatory therapy‡	26 (43%)	15 (25%)	18 (29%)	25 (41%)	26 (41%)
Corticosteroids including budesonide and beclomethasone dipropionate	24 (39%)	24 (39%)	19 (30%)	20 (33%)	26 (41%)
Corticosteroids excluding budesonide and beclomethasone dipropionate	19 (31%)	18 (30%)	12 (19%)	8 (13%)	20 (32%)
Median prednisone-equivalent corticosteroid dose (excluding budesonide and beclomethasone dipropionate), mg/day	20 (10·0–30·0)	20 (20·0–25·0)	20 (10·0–25·0)	20 (15·0–22·5)	20 (15·0–32·5)

(Table 1 continues on next page)

	Placebo group* (n=61)	Guselkumab 200→100 mg group (n=61)	Guselkumab 600→200 mg group (n=63)	Guselkumab 1200→200 mg group (n=61)	Ustekinumab group† (n=63)
(Continued from previous page)					
Previous biologic use§	42 (69%)	36 (59%)	39 (62%)	36 (59%)	44 (70%)
Inadequate response or intolerance to previous biological therapy	30 (49%)	32 (52%)	35 (56%)	34 (56%)	37 (59%)
Anti-TNF only	25 (41%)	26 (43%)	27 (43%)	31 (51%)	32 (51%)
≥1 anti-TNF	29 (48%)	30 (49%)	35 (56%)	33 (54%)	37 (59%)
Vedolizumab	5 (8%)	6 (10%)	8 (13%)	3 (5%)	5 (8%)
Vedolizumab and ≥1 anti-TNF	4 (7%)	4 (7%)	8 (13%)	2 (3%)	5 (8%)
Biologic-naive patients	19 (31%)	25 (41%)	24 (38%)	25 (41%)	19 (30%)
Biologic-experienced, without documented failure	12 (20%)	4 (7%)	4 (6%)	2 (3%)	7 (11%)

Data are n (%), median (IQR), or mean (SD). Denominators for each parameter are non-missing values. The primary efficacy analysis set consisted of all randomised patients who received at least one dose (full or partial) of study drug, excluding 51 patients whose induction dosing and study participation were discontinued during a temporary study pause. CDAI=Crohn's Disease Activity Index. IBDQ=Inflammatory Bowel Disease Questionnaire. PRO-2=2-Item Patient-Reported Outcomes. SES-CD=Simple Endoscopic Score for Crohn's Disease. *Includes all patients randomly allocated to receive placebo; at week 12, patients who were clinical responders continued placebo treatment, and those who were non-responders crossed over to ustekinumab. †Includes all patients randomly allocated to receive ustekinumab. ‡Immunomodulatory therapy included azathioprine, mercaptopurine, and methotrexate. §Biologics included infliximab, adalimumab, certolizumab pegol, vedolizumab, and ustekinumab.

Table 1: **Demographics and baseline disease characteristics of the primary efficacy analysis set**

multiplicity. The study was not powered to evaluate efficacy differences among the guselkumab maintenance dose groups or between guselkumab and ustekinumab. The ustekinumab group was included as a reference group only.

All efficacy analyses used the primary efficacy analysis set, defined as all randomly allocated patients who received at least one dose (full or partial) of study drug, excluding 51 patients whose induction dosing and study participation were discontinued during a temporary study pause to evaluate a serious adverse event of toxic hepatitis in one guselkumab-treated patient.[17]

Patients who had a Crohn's disease-related surgery, a prohibited change in Crohn's disease medications, or discontinued study agent due to lack of efficacy or an adverse event of worsening Crohn's disease (in the opinion of the investigator) before the designated analysis timepoint were considered not to have met the endpoint from that timepoint onward. For patients who discontinued study agent for any other reason before the designated analysis timepoint but continued to undergo study evaluations, observed data from these evaluations were used to determine the endpoint at that timepoint. Patients with missing data at the designated analysis timepoint were considered not to have met the endpoint at that timepoint.

Safety analyses included all randomised patients who received at least one dose (full or partial) of study drug.

Confidence intervals for all binary endpoints were based on an exact method. Analyses were done with SAS version 9.4 M6.

Role of the funding source

Employees of the funder had a role in study design, data collection, data analysis, data interpretation, and writing of the report.

Results

From May 10, 2018, to Aug 20, 2020, 360 patients were randomly allocated and treated: 73 were allocated to each of the guselkumab groups, 71 to the ustekinumab group, and 70 to the placebo group (figure 2). After exclusion of 51 patients whose induction dosing and participation were interrupted during a pause in the study, 309 patients were included in the primary efficacy analysis set: 61 patients randomly allocated to the guselkumab 200→100 mg group, 63 to the guselkumab 600→200 mg group, 61 to the guselkumab 1200→200 mg group, 63 to the ustekinumab group, and 61 to the placebo group.

42 (14%) of 309 patients in the primary efficacy set discontinued study drug between weeks 0 and 48, most commonly for other adverse events (15 [5%] patients) and withdrawal by patient (11 [4%] patients). Ten patients (3%) discontinued because of lack of efficacy or an adverse event of worsening Crohn's disease. One placebo-treated patient who crossed over to ustekinumab at week 12 received the scheduled ustekinumab intravenous dose at week 12, subcutaneous placebo at week 16, and subcutaneous ustekinumab at week 20, but erroneously received guselkumab 100 mg subcutaneous instead of placebo at week 24.

Overall, 126 (41%) women and 183 (59%) men with a median age of 36·0 years (IQR 28·0–49·0) and median duration of Crohn's disease of 6·3 years (IQR 2·5–11·7) participated (table 1). 168 (54%) patients had had an inadequate response or intolerance to a previous biological therapy, and 112 (36%) were naive to biologics. Two patients (one in the guselkumab 600→200 mg group and one in the guselkumab 1200→200 mg group) had previous brief exposure to ustekinumab. Baseline demographic and disease characteristics were generally similar.[17]

Clinical outcomes at each visit are summarised in figure 3. After the induction period (week 12), clinical outcome rates generally increased until week 48 with subcutaneous maintenance dosing. At week 48, CDAI clinical remission was observed in 39 (64%) of 61 patients in the guselkumab 200→100 mg group, 46 (73%) of 63 in the guselkumab 600→200 mg group, 35 (57%) of 61 in the 1200→200 mg group, and 37 (59%) of 63 in the ustekinumab group (figure 3A). Corresponding numbers of patients with CDAI response were 45 (74%), 53 (84%), 41 (67%), and 43 (68%; figure 3B), respectively, and with PRO-2 remission were 35 (57%), 44 (70%), 31 (51%), and 29 (46%; figure 3C), respectively. Corresponding numbers of patients with durable CDAI clinical remission were 31 (51%), 39 (62%), 25 (41%), and 30 (48%), respectively.

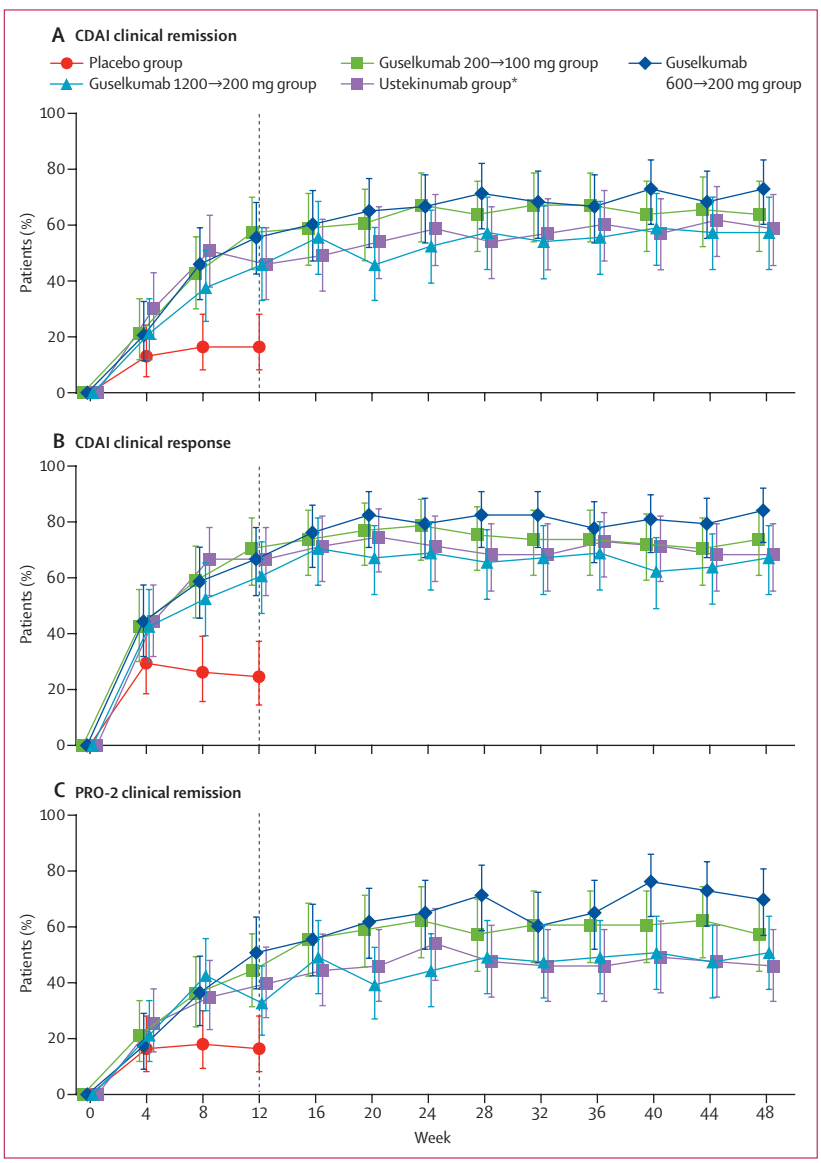

Figure 3: **Clinical efficacy outcomes to week 48**
(A) CDAI clinical remission, defined as a CDAI score less than 150. (B) CDAI clinical response, defined as a reduction of at least 100 points from baseline CDAI score, or a CDAI score less than 150. (C) PRO-2 clinical remission, defined as a daily average abdominal pain score no higher than 1 and a daily stool frequency of no more than 3, and no worsening of abdominal pain or stool frequency from baseline. The dashed vertical line represents the point of transition from the intravenous to the subcutaneous regimen. Error bars are 95% CIs, calculated with an exact method. Patients who had a prohibited change in concomitant Crohn's disease medication, a Crohn's disease-related surgery, or discontinued study agent due to lack of efficacy or an adverse event of worsening Crohn's disease before the designated analysis timepoint were considered not to be in clinical response from that timepoint onwards. For patients who discontinued study agent due to any other reasons before the designated analysis timepoint, observed data were used, if available, to determine response and non-response status from that timepoint onwards. Patients who had missing data at the designated analysis timepoint were considered not to have met the endpoint at that timepoint. CDAI=Crohn's Disease Activity Index. PRO-2=2-Item Patient-Reported Outcomes. *Includes only patients randomly allocated to the ustekinumab group.

Corticosteroid-free CDAI clinical remission rates at week 48 were 36 (59%) of 61 in the guselkumab 200→100 mg group, 45 (71%) of 63 in the guselkumab 600→200 mg group, 34 (56%) of 61 in the guselkumab 1200→200 mg group, and 37 (59%) of 63 in the ustekinumab group. The percentages of patients who were corticosteroid-free for at least 30 days or at least 90 days before week 48 and in CDAI remission at week 48 were nearly identical to those corticosteroid-free and in CDAI remission at week 48 (appendix p 23). Among patients in CDAI clinical remission, more than 95% were corticosteroid free.

For endoscopic outcomes at week 48, 27 (44%) of 61 patients in the guselkumab 200→100 mg group, 29 (46%) of 63 in the guselkumab 600→200 mg group, 27 (44%) of 61 in the guselkumab 1200→200 mg group, and 19 (30%) of 63 in the ustekinumab group showed an endoscopic response (figure 4A), and endoscopic remission was seen in 11 (18%), 11 (17%), 20 (33%), and four (6%) patients, respectively (figure 4B). Endoscopic remission based on the alternative definition was observed in 16 (26%), 19 (30%), 24 (39%), and nine (14%) patients, respectively (figure 4C).

Rates of CDAI clinical remission, PRO-2 remission, CDAI clinical response, and endoscopic response at week 48 among patients with inadequate response or intolerance to previous biological or conventional therapy are presented in the appendix (p 24).

Health-related quality-of-life outcomes, as measured by the IBDQ, show trends that are consistent with those of efficacy endpoints (appendix p 25). IBDQ remission at week 48 was achieved by 34 (56%) of 61 in the guselkumab 200→100 mg group, 39 (62%) of 63 in the guselkumab 600→200 mg group, 30 (49%) of 61 in the guselkumab 1200→200 mg group, and 30 (48%) of 63 in the ustekinumab group. Corresponding numbers of patients with IBDQ response at week 48 were 41 (67%), 48 (76%), 39 (64%), and 44 (70%), respectively.

Clinical-biomarker response at week 48 was observed in 29 (48%) of 61 patients in the guselkumab 200→100 mg group, 42 (67%) of 63 in the guselkumab 600→200 mg group, 32 (52%) of 61 in the guselkumab 1200→200 mg group, and 26 (41%) of 63 in the ustekinumab group (appendix p 26). At week 48, clinical-biomarker remission was observed in 32 (52%), 42 (67%), 24 (39%), and 24 (38%) patients, respectively (appendix p 26).

At week 12, 44 (72%) of 61 patients in the placebo group did not respond to induction treatment and were transitioned to ustekinumab as a rescue strategy (intravenous ~6 mg/kg at week 12 followed by 90 mg subcutaneously every 8 weeks); clinical and endoscopic outcomes for this subgroup of patients are reported in the appendix (pp 27–29). Of these patients, at week 48, 26 (59%) were in CDAI clinical remission, 25 (57%) were in PRO-2 clinical remission, 28 (64%) were in CDAI clinical response, 23 (52%) were in endoscopic response, and 13 (30%) were in endoscopic remission. Notably, although none of these 44 patients were in clinical response at week 12, seven (16%) were in endoscopic response at week 12.

17 (28%) of 61 patients in the placebo group did not cross over to ustekinumab during maintenance; two of these patients discontinued placebo before week 12 and did not receive maintenance placebo, and 15 were in clinical response at week 12 and continued to receive placebo after week 12. Clinical and endoscopic outcomes for this subgroup of patients are shown in the appendix (pp 27–29). At week 48, nine (60%) of 15 patients who continued receiving placebo maintenance treatment had CDAI clinical remission, eight (53%) had PRO-2 remission, and 11 (73%) had a CDAI clinical response. Only two (13%) of the 15 patients had an endoscopic response at week 48 (figure 4).

Key safety findings until week 48 in the safety analysis population (n=360) are summarised by adverse event frequency and adverse events per 100 patient-years of follow-up (table 2). Overall, adverse event frequencies were 46 (66%) of 70 patients (464·9 events per 100 patient-years of follow-up) in the placebo group, 163 (74%) of 220 patients (353·1 per 100 patient-years) in the three guselkumab groups combined, and 60 (85%) of 71 patients (350·7 per 100 patient-years) randomly assigned to the ustekinumab group. Specifically, infections occurred in 17 (24%) patients (121·8 per 100 patient-years), 81 (37%) patients (84·8 per 100 patient-years), and 26 (37%) patients (63·8 per 100 patient-years). The most frequently reported infections until week 48 in guselkumab-treated and ustekinumab-treated participants were nasopharyngitis (25 [11%] of 220 guselkumab recipients; 12 [11%] of 114 ustekinumab recipients) and upper respiratory tract infections (13 [6%] guselkumab recipients; eight [7%] ustekinumab recipients).

Serious adverse events frequencies were six (9%) of 70 patients (33·2 per 100 patient-years of follow-up) in the placebo group, 16 (7%) of 220 patients (11·2 events per 100 patient-years) in the three guselkumab groups combined, and nine (13%) of 71 patients (18·5 per 100 patient-years) randomised to the ustekinumab group. Serious infections were recorded in one (1%) patient (3·7 infections per 100 patient-years of follow-up), five (2%) patients (3·5 per 100 patient-years), and one (1%) patient (1·7 per 100 patient-years), respectively. Three serious infections in the combined guselkumab groups and one serious infection in the ustekinumab group occurred before week 12, and were reported previously.[17] After week 12, serious infections occurred in two guselkumab-treated patients (one with an anal abscess in the guselkumab 200→100 mg group, and

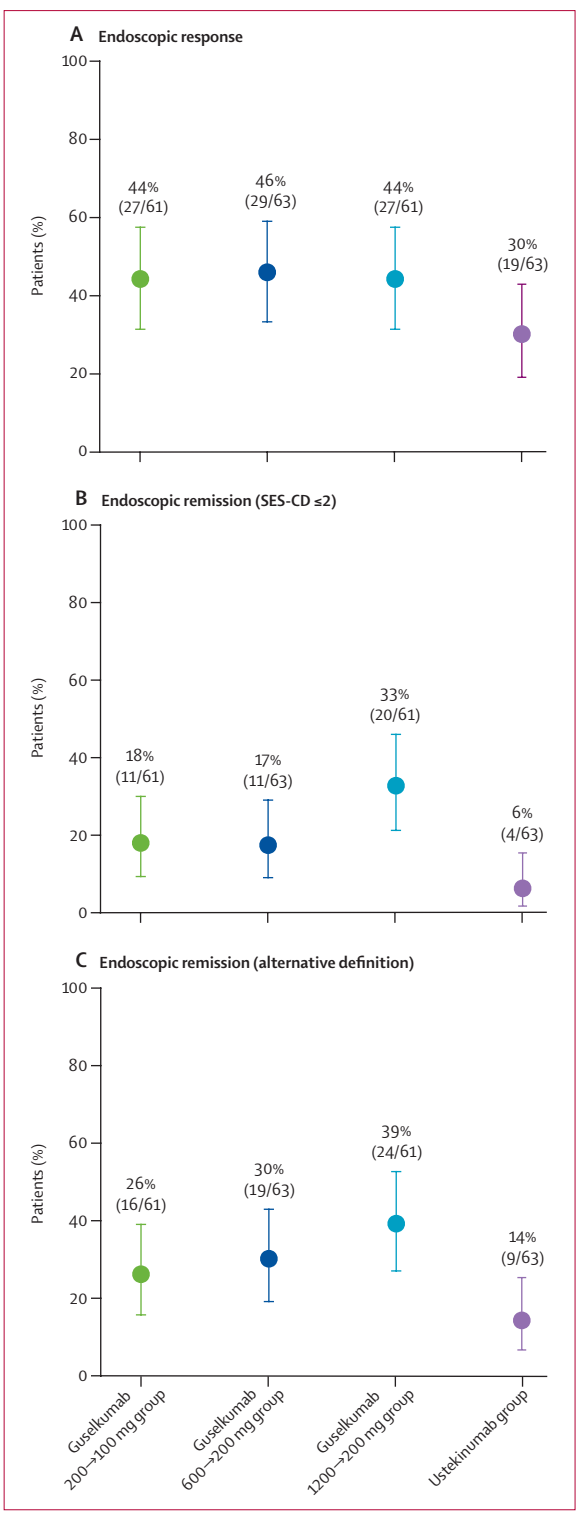

Figure 4: **Endoscopic outcomes at week 48**
(A) Endoscopic response, defined as an improvement of at least 50% from baseline in SES-CD, or an SES-CD of 2 or lower. (B) Endoscopic remission, defined as an SES-CD of 2 or lower. (C) Endoscopic remission (alternative definition), defined as an SES-CD of 4 or lower, at least a 2-point reduction versus baseline, and no subscore greater than 1 in any individual variable. Numbers below each percentage show n/N corresponding to the percentage for that group. Error bars are 95% CI based on an exact method. Patients who had a prohibited change in concomitant Crohn's disease medication, a Crohn's disease-related surgery, or discontinued study agent due to lack of efficacy or an adverse event of worsening Crohn's disease before the designated analysis timepoint were considered not to be in clinical response from that timepoint onwards. For patients who discontinued study agent due to any other reasons before the designated analysis timepoint, observed data were used, if available, to determine response and non-response status from that timepoint onwards. SES-CD score at week 48 was based on all observed segments scored at week 48. Patients who had insufficient data to calculate total SES-CD score at week 48 were considered not have met the endpoint at week 48. SES-CD=Simple Endoscopic Score for Crohn's Disease.

	Placebo		Guselkumab				Ustekinumab	
	Placebo only* (n=70)	Ustekinumab crossover† (n=43)	200→100 mg group (n=73)	600→200 mg group (n=73)	1200→200 mg group (n=73)	Combined‡ (n=220)	Ustekinumab only§ (n=71)	Combined¶ (n=114)
Median duration of follow-up, weeks	12·5 (12·1–17·1)	36·1 (35·9–36·9)	48·0 (38·6–48·4)	48·1 (47·3–48·4)	48·1 (29·6–48·6)	48·1 (37·5–48·4)	48·1 (47·1–48·6)	40·4 (36·1–48·1)
Frequency of adverse events								
Any adverse event	46 (66%)	27 (63%)	52 (71%)	59 (81%)	51 (70%)	163 (74%)	60 (85%)	87 (76%)
Serious adverse events	6 (9%)	0	6 (8%)	5 (7%)	5 (7%)	16 (7%)	9 (13%)	9 (8%)
Adverse events that led to treatment discontinuation	4 (6%)	1 (2%)	5 (7%)	2 (3%)	6 (8%)	13 (6%)	6 (8%)	7 (6%)
Infections‖	17 (24%)	15 (35%)	25 (34%)	30 (41%)	25 (34%)	81 (37%)	26 (37%)	41 (36%)
Serious infections‖	1 (1%)	0	2 (3%)	2 (3%)	1 (1%)	5 (2%)	1 (1%)	1 (1%)
Deaths	0	0	0	0	0	0	0	0
Adverse event rate per 100 patient-years of follow-up								
Adverse events	464·9	245·7	296·8	388·3	375·7	353·1	350·7	316·0
Serious adverse events	33·2	0·0	14·1	10·3	9·2	11·2	18·5	12·4
Adverse events that led to discontinuation of treatment	29·5	10·4	8·8	3·4	14·7	8·8	10·1	10·2
Infections‖	121·8	76·1	56·5	106·5	90·2	84·8	63·8	67·7
Serious infections‖	3·7	0·0	5·3	3·4	1·8	3·5	1·7	1·1
Deaths	0·0	0·0	0·0	0·0	0·0	0·0	0·0	0·0

Data are median (IQR), n (%), or rate per 100 patient-years. The safety population consisted of all randomly allocated patients who received at least one dose (full or partial) of study drug. *Includes all events among patients randomly allocated to the placebo group up to week 12; after week 12, only events among patients who responded and continued to receive placebo are included. †Includes patients who did not respond to placebo and crossed over to ustekinumab at week 12, excluding the patient who received guselkumab in error; events counted occurred after the patient switched to ustekinumab treatment. ‡Includes one patient initially allocated to the placebo group who crossed over to ustekinumab and received guselkumab in error. §Includes only patients randomly allocated to receive ustekinumab. ¶Includes patients who crossed over from placebo to ustekinumab and those randomly allocated to the ustekinumab group. ‖Infection as assessed by the investigator.

Table 2: **Summary of key adverse events to week 48 in the safety population**

one with pelvic abscess in the guselkumab 1200→200 mg group) and one placebo-treated patient (infectious enterocolitis). No active tuberculosis, opportunistic infections, or deaths were reported up to week 48.

One case of basal cell carcinoma (guselkumab 600→200 mg group) and one case of prostate cancer (guselkumab 1200→200 mg group) were reported and were considered by the investigator to be unrelated to study drug. The investigator determined that the prostate cancer event was possibly a pre-existing condition.

No hypersensitivity reactions were reported before week 12. At week 12, anaphylaxis occurred in one patient who crossed over from placebo to ustekinumab. This event was considered by the investigator to be of moderate severity and related to ustekinumab, which was discontinued. Of the patients in the safety analysis set who had received at least one subcutaneous injection of guselkumab, seven (4%) of 178 had injection-site reactions (primarily erythema).

By week 48, one pregnancy was reported in the ustekinumab group. This patient discontinued the study.

A post-hoc analysis of week 48 outcomes in patients who showed a response to guselkumab or ustekinumab induction regimen at week 12 was done to evaluate the long-term impact of early response to treatment and to present the week 48 results in the context of a study in which those who respond to induction are randomised to maintenance therapy. Two definitions of clinical response at week 12 were used: a symptom-based definition or the prespecified CDAI-based clinical response definition. Patients who had a clinical response to induction therapy were more likely to have positive clinical and endoscopic outcomes at week 48 compared with the overall patient population that included patients with and without response to induction treatment at week 12 (appendix p 30). Among 122 patients in the combined guselkumab groups who were in CDAI clinical response at week 12, 102 (84%) were in CDAI clinical response, 94 (77%) in CDAI clinical remission, 83 (68%) in PRO-2 clinical remission, and 63 (52%) in endoscopic response at week 48. Outcomes at week 48 were similar for patients regardless of week 12 clinical response definition.

Among 63 patients who did not have a CDAI clinical response to guselkumab at week 12, continued treatment with subcutaneous guselkumab resulted in nearly half (29 patients [46%]) having clinical response at week 24. At week 48, 37 (59%) were in CDAI clinical response, 26 (41%) in CDAI clinical remission, 27 (43%) in PRO-2 clinical remission, and 20 (32%) in endoscopic response (appendix p 32).

Pharmacokinetic and immunogenicity results to week 12 were reported previously.[17] During maintenance

treatment, serum guselkumab concentrations generally reached a steady state in each guselkumab group by week 24. Serum trough guselkumab concentrations for patients receiving subcutaneous maintenance guselkumab every 4 weeks (guselkumab 600→200 mg and guselkumab 1200→200 mg groups) were greater than those receiving subcutaneous guselkumab every 8 weeks (guselkumab 200→100 mg group). At week 24, median serum trough guselkumab concentrations were 1·04 µg/mL (IQR 0·48–1·61) for patients in the guselkumab 200→100 mg group, 9·55 µg/mL (5·91–11·51) for those in the guselkumab 600→200 mg group, and 7·71 µg/mL (5·46–11·84) for those in the guselkumab 1200→200 mg group. Median serum trough guselkumab concentrations between weeks 16 and 48 are summarised in the appendix (p 33).

Antibodies to guselkumab were detected in three (1%) of 215 patients up to week 48; none were positive for neutralising antibodies. Antibodies to ustekinumab were detected in one (1%) of 113 patients up to week 48, and these antibodies were neutralising. Because of the small number of patients with antidrug antibodies, the relationships between efficacy, pharmacokinetics, and frequency of antidrug antibodies were not assessed.

Discussion

In this phase 2b study of patients with moderately to severely active Crohn's disease, we evaluated three treatment regimens of guselkumab induction and maintenance therapy using a treat-through design in which patients with and without responses to induction therapy on active treatment were followed up throughout the 48-week treatment period. More than half of the study population consisted of patients with previous inadequate response or intolerance to biological therapy, and just over a third were biologic-naive. As previously reported,[17] all intravenous induction doses (200, 600, and 1200 mg at weeks 0, 4, and 8) met the primary study endpoint of CDAI score improvement from baseline at week 12 compared with placebo, and the differences between individual induction dose groups were small and not clinically meaningful.

Following intravenous induction therapy, two subcutaneous maintenance doses were evaluated to week 48: a low dose of 100 mg every 8 weeks that followed the 200 mg intravenous induction dose, and a high dose of 200 mg every 4 weeks that followed the 600 mg and 1200 mg intravenous induction doses. After 48 weeks of guselkumab maintenance treatment, substantial proportions of patients in all three treatment groups had CDAI clinical remission (ranging from 57% to 73% across groups), CDAI clinical response (67% to 84%), and PRO-2 clinical remission (46% to 70%). Adverse event rates up to week 48 indicate a safety profile that is consistent with the known profile of guselkumab in currently approved indications. The group of patients randomly allocated to receive ustekinumab was included as a reference group to inform phase 3 study design, and no formal comparisons with guselkumab were conducted.

Although the study had a randomised placebo group at baseline, only a small number of patients (n=15) who were in clinical response at week 12 remained on placebo thereafter. Patients in the placebo subgroup who were not in clinical response at week 12 received rescue ustekinumab therapy (n=44) starting at week 12. After week 12, data from these two placebo subgroups, in which maintenance treatment was determined by week 12 clinical response status, were not comparable with the randomised guselkumab and ustekinumab treatment groups, in which maintenance treatment after week 12 followed the randomised allocation assigned at baseline, regardless of week 12 response.

Endoscopic evaluation in inflammatory bowel disease is important as an objective measure of disease activity and severity. Previous studies have used endoscopic assessments as a guide to reduce Crohn's disease flare.[21–24] In this study, at week 48, the percentages of patients showing an endoscopic response ranged from 44% to 46% in the guselkumab groups, and percentages with endoscopic remission (SES-CD ≤2) ranged from 17% to 33%. Because of the unique study protocol, which allowed for inclusion of patients with non-passable strictures, we did a post-hoc analysis using an alternative definition of endoscopic remission (SES-CD ≤4 and ≥2 point reduction from baseline and no subscore >1 in any individual variable). The percentages of patients with endoscopic remission according to the alternative definition (26% to 39%) were 7–13% percentage points greater than the percentages according to the protocol-specified definition. Further study is needed to assess which definition of endoscopic remission better predicts favourable long-term outcomes.

Registrational study design plays an important role in informing treatment decisions following regulatory approval. The GALAXI studies have treat-through designs in which patients are randomly allocated to individual treatment groups that specified both induction and maintenance therapy regimens, and patients on active treatment are followed up to week 48, regardless of their responses to induction treatment. More often in recent registrational trials, induction and maintenance treatment regimens are evaluated in separate studies, and maintenance study populations consisted only of patients who responded to induction.[8–10,25–28] The treat-through design in GALAXI-1 allows for the evaluation of patients with or without response to treatment after week 12. In a post-hoc analysis, we evaluated week 48 outcomes in patients who responded to induction treatment at week 12, using both symptom-based and CDAI-based clinical response definitions to evaluate induction clinical response. Week 48 clinical and endoscopic outcomes for those with clinical response to induction therapy at week 12 were greater than those of the overall population that included those with and

without responses at week 12 in the original treat-through design. Also, a majority of those without clinical response at week 12 showed clinical response at week 48—albeit at lower rates than in patients who had a response at week 12—indicating that continued treatment after week 12 can be beneficial in patients without clinical response to induction therapy.

Previous studies of ustekinumab, an IL-12 and IL-23 antagonist, showed that concomitant immunosuppression did not affect efficacy or pharmacokinetics in Crohn's disease[29] or ulcerative colitis.[30] Like ustekinumab, guselkumab also has low immunogenicity, so the effect of concomitant immunosuppression on efficacy and pharmacokinetics is expected to be low. Overall, just over a third of patients in GALAXI-1 were receiving immunosuppressants at baseline, and the percentages receiving immunosuppressants in the individual guselkumab treatment groups ranged from 25% to 41%. Because of the small numbers of patients and the imbalances in the treatment groups at baseline, this study is underpowered to evaluate the effect of concomitant immunosuppression on guselkumab efficacy and pharmacokinetics. These effects will be investigated in larger phase 3 studies.

Several limitations of this study should be considered when interpreting the results. As previously reported, the primary objective of this study was to measure the short-term (ie, induction to week 12) efficacy of guselkumab, as measured by the change from baseline in CDAI score (primary efficacy endpoint), in patients with moderately to severely active Crohn's disease.[17] The current study showed that the associated subcutaneous maintenance guselkumab doses maintained efficacy to week 48; however, this study was not designed or powered to evaluate differences in efficacy and safety between individual guselkumab maintenance dose groups, or between randomised guselkumab and ustekinumab groups (ustekinumab was included as a reference group only), or between randomised guselkumab or ustekinumab groups and placebo subgroups after week 12. Differences in the efficacy of guselkumab maintenance doses (100 mg every 8 weeks and 200 mg every 4 weeks), as well as active comparison of guselkumab with ustekinumab, will be evaluated in larger phase 3 trials. Maintenance endpoints were prespecified in the protocol and statistical analysis plan, but analyses were exploratory, and no formal statistical testing was done. Overall, the efficacy analysis in this report might be subject to measurement bias, as patients who discontinued treatment for any reason, including those unrelated to efficacy, and had missing data at a visit were considered to be non-responders. In addition, efficacy results by previous Crohn's disease medication subgroups (appendix p 17) should be interpreted with caution, as these data are limited by small sample sizes.

In conclusion, the clinical and endoscopic efficacy that was observed after intravenous guselkumab induction continued to increase after week 12 and was maintained with continued subcutaneous guselkumab to week 48. Safety results were consistent with the known safety profile of guselkumab in approved indications. These results require confirmation in larger phase 3 studies of patients with moderately to severely active Crohn's disease. The GALAXI-2 and GALAXI-3 phase 3 studies (NCT03466411) are ongoing.

Contributors

SD, RP, BGF, AA, DTR, BES, WR, JP, AS, NAT, DC, CH, MEF, ZY, WJS, TH, JMA, and GRD'H designed the study. SD, RP, BGF, AA, DTR, BES, WR, JP, WJS, TH, JMA, and GRD'H were involved in data acquisition. AS, NAT, MEF, and ZY verified the underlying data. All authors had full access to all the data in the study and accept responsibility to submit for publication. MEF and ZY analysed the data. All authors drafted the article or revised it critically for important intellectual content with the assistance of a professional medical writer employed by Janssen Scientific Affairs. All authors agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of interests

SD reports consultancy fees from AbbVie, Alimentiv, Allergan, Amgen, AstraZeneca, Athos Therapeutics, Biogen, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Enthera, Ferring Pharmaceuticals, Gilead, Hospira, Inotrem, Janssen, Johnson & Johnson, MSD, Mundipharma, Mylan, Pfizer, Roche, Sandoz, Sublimity Therapeutics, Takeda, TiGenix, UCB Inc, and Vifor; and reports lecture fees from AbbVie, Amgen, Ferring Pharmaceuticals, Gilead, Janssen, Mylan, Pfizer, and Takeda. RP has received consulting fees from Abbott, AbbVie, Abbivax, Alimentiv (formerly Robarts), Amgen, Arena Pharmaceuticals, AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Celltrion, Cosmos Pharmaceuticals, Eisai, Elan, Eli Lilly, Ferring, Galapagos, Fresenius Kabi, Genentech, Gilead Sciences, GlaxoSmithKline, 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, Takeda Pharmaceuticals, Theravance Biopharma, Trellus, Viatris, Ventyx, and UCB; speaker's fees from 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; and research support from AbbVie, Takeda, Janssen, and Pfizer. BGF has received consulting fees from AbbVie, AbolerIS, AgomAB Therapeutics, Allianthera, Amgen, AnaptysBio, Applied Molecular Transport, Arena Pharma, Avoro Capital Advisors, Atomwise, BioJamp, Biora Therapeutics, Boehringer-Ingelheim, Boxer, Celsius Therapeutics, Celgene/Bristol-Myers Squibb, Connect BioPharma, Cytoki, Disc Medicine, Duality, EcoR1, Eli Lilly, Equillium, Ermium, First Wave, First Word Group, Galapagos, Galen Atlantica, Genentech/Roche, Gilead, Gossamer Pharma, GlaxoSmithKline, Hinge Bio, Hot Spot Therapeutics, Index Pharma, Imhotex, Immunic Therapeutics, JAKAcademy, Janssen, Japan Tobacco Inc, Kaleido Biosciences, Landos Biopharma, Leadiant, LEK Consulting, LifeSci Capital, Lument, Millennium, MiroBio, Morphic Therapeutics, Mylan, OM Pharma, Origo BioPharma, Orphagen, Pandion Therapeutics, Pendopharm, Pfizer, Prometheus Therapeutics and Diagnostics, PlayToKnow, Progenity, Protagonist, PTM Therapeutics, Q32 Bio, Rebiotix, REDX, Roche, Sandoz, Sanofi, Seres Therapeutics, Silverback Therapeutics, Surrozen, Takeda, Teva, Thelium, Tigenix, Tillotts, Ventyx Biosciences, VHSquared, Viatris, Ysios, Ysopia, and Zealand Pharma; is a member of the speakers bureau for AbbVie, Janssen, Takeda, and Boehringer Ingelheim; has received payment for expert testimony from Morgan Lewis and Lenczner Slaght; has received support for attending meetings or for travel from Janssen, AbbVie, Pfizer, Takeda, and Boehringer Ingelheim; has participated on a data safety monitoring board or advisory board for AbbVie, Amgen, AMT, AnaptysBio, Boehringer-Ingelheim, Celgene/Bristol-Myers Squibb, Eli Lilly, Genentech/Roche, Janssen, MiroBio, Origo BioPharma, Pfizer, Prometheus, RedX Pharma, Sanofi, Takeda, Tillotts Pharma, Teva, Progenity, Index, Ecor1Capital, Morphic, GlaxoSmithKline, and Axio

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Data sharing

The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at https://www.janssen.com/clinical-trials/transparency. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access Project site at http://yoda.yale.edu.

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