Title

Comparative Efficacy and Speed of Onset of Action of Infliximab vs Golimumab in Ulcerative Colitis

Journal

Clinical Gastroenterology and Hepatology, 18(2)

ISSN

1542-3565

Authors

Singh, Siddharth
Proudfoot, James A
Dulai, Parambir S
et al.

Publication Date

2020-02-01

DOI

10.1016/j.cgh.2019.05.019

Peer reviewed

Published in final edited form as:

Clin Gastroenterol Hepatol. 2020 February ; 18(2): 424–431.e7. doi:10.1016/j.cgh.2019.05.019.

Efficacy and Speed of Induction of Remission of Infliximab vs Golimumab for Patients With Ulcerative Colitis, Based on Data From Clinical Trials

Siddharth Singh[1,2], **James A. Proudfoot**[3], **Parambir S. Dulai**[1], **Ronghui Xu**[3,4], **Brian G. Feagan**[5,6], **William J. Sandborn**[1], **Vipul Jairath**[5,6]

[1]Division of Gastroenterology, University of California San Diego, La Jolla, California

[2]Division of Biomedical Informatics, University of California San Diego, La Jolla, California

[3]Biostatistics Unit, Altman Clinical and Translational Research Institute

[4]Department of Family Medicine and Public Health and Department of Mathematics, University of California San Diego, La Jolla, California

[5]Division of Epidemiology and Biostatistics, Western University, London, Ontario, Canada

[6]Department of Medicine, Division of Gastroenterology, University Hospital, Ontario, Canada

Abstract

Background & Aims: With several options available for patients with moderate–severe ulcerative colitis (UC), rapidity of symptom resolution could be an important differentiator. We compared the efficacy and speed of onset of action of infliximab vs golimumab induction therapy using patient-level data from phase 3 trials (ACT-1, ACT-2, and PURSUIT-SC).

Methods: We compared differences in proportions of patients who achieved the composite outcome of a rectal bleeding score=0 and stool frequency score ≤1 (patient-reported outcome 2 remission) at weeks 2 and 6 of treatment with standard-dose infliximab vs golimumab using logistic generalized estimating equation. Overall efficacy for inducing clinical remission (Mayo clinic score <3) was compared using logistic regression. Analyses were adjusted for sex, disease

Corresponding authors: Siddharth Singh, MD, MS, Assistant Professor of Medicine, Division of Gastroenterology and Division of Biomedical Informatics University of California San Diego 9452 Medical Center Dr., ACTRI 1W501, La Jolla, CA 92093, sis040@ucsd.edu, Phone: 858-246-2352, Fax: 858-657-7259. Vipul Jairath MBChB, DPhil, MRCP, Associate Professor of Medicine, Epidemiology and Biostatistics, Western University, London Health Sciences Centre-University Hospital, 339 Windermere Road, Room A10-228, London, ON, Canada, N6A 5A5, Phone: 519.685.8500 ext. 33655, Fax: 519.663.3658, vjairath@uwo.ca.

Author Contribution:

- Study concept and design: SS, VJ
- Acquixsition of data: SS, JAP
- Analysis and interpretation of data: SS, JAP, RX, VJ
- Drafting of the manuscript: SS
- Critical revision of the manuscript for important intellectual content: JAP, PSD, RX, BGF, WJS, VJ
- Approval of the final manuscript: SS, JAP, PSD, RX, BGF, WJS, VJ
- Guarantor of the article: SS

extent, baseline clinical and endoscopic severity, C-reactive protein, albumin, body weight and concomitant medications (immunomosuppressives, corticosteroids, and 5-aminsalicylates).

Results: Trial populations were similar and no differences were observed among the placebo groups in the studies. A significantly higher proportion patients treated with infliximab than golimumab achieved patient-reported outcome 2 remission at week 2 (35% vs 30%; adjusted odds ratio [OR], 1.71; 95% CI, 1.15–2.55) and at week 6 (50.0% vs 38.9%; adjusted OR, 2.0; 95% CI, 1.40–2.94). Infliximab-treated patients were also significantly more likely to achieve clinical remission than golimumab-treated patients (adjusted OR, 3.01; 95% CI, 1.95–4.70), with consistent findings in patients with moderate or severe UC.

Conclusions: Based on a patient-level analysis of data from phase 3 trials, infliximab resolves symptoms more rapidly and has greater efficacy for inducing remission than golimumab in patients with moderate–severe UC.

Keywords

Comparative efficacy; patient-reported outcomes; open science; inflammatory bowel diseases

INTRODUCTION

Treatment options for moderate-severe ulcerative colitis (UC) have increased over the last 5 years, with availability of several tumour necrosis factor (TNF)-α antagonists, antiintegrin agents such as vedolizumab and oral janus kinase inhibitors, such as tofacitinib.[1, 2] However, because no clinical trials have compared the effectiveness of these agents, their relative positioning in treatment algorithms is unknown.[3, 4] Amongst TNF-α antagonists, indirect treatment comparison network meta-analyses have suggested that infliximab may be superior to adalimimab or golimumab for induction of remission.[3, 5, 6] However, such studies are unable to control for patient-level covariates such as baseline disease activity and corticosteroid use that could affect meaningful interpretation of observed differences in efficacy amongst these agents.

Rapid relief of symptoms is a treatment attribute of critical importance to patients that can influence positioning of agents.[7, 8] TNF-α antagonists are generally considered to be rapidly acting induction drugs and this property could be considered an advantage over other classes. However, comparisons of rapidity of onset for the currently available TNFα antagonists are unavailable. Accordingly, we performed a post-hoc analysis with individual participant level data (IPD) from phase III registration clinical trials of infliximab (ACT-1 and −2) and golimumab (PURSUIT-SC) available through Yale Open Database Access (YODA) to compare the overall efficacy and speed of onset of action of infliximab and golimumab in patients with moderate-severe UC.[9]

METHODS

Data Sources

Clinical trials of infliximab and golimumab in patients with moderate-severe UC were accessed through the YODA project.[9] This pioneering data-sharing model, started in 2011 at

Yale University, provides access to de-identified IPD data, shared by data holders, Johnson&Johnson, Medtronic, Inc. and SI-BONE, Inc. A detailed research proposal for this project was approved by the YODA scientific committee (Protocol # 2018–3121) on May 16, 2018. Through this project, we accessed phase III trials of infliximab (ACT-1 [NCT00036439, C0168T37], ACT-2 [NCT00096655, C0168T46]) and golimumab in UC (PURSUIT-SC [NCT00487539, C0524T17]).[10, 11] Overall clinical trial characteristics including study design, setting, inclusion and exclusion criteria including prior medication use, outcome measures and outcomes of interest were very similar for the included trials (eTable 1).

Exposures

The primary exposures of interest were standard-dose induction therapy with infliximab (5mg/kg intravenously at weeks 0, 2 and 6) and golimumab (200mg subcutaneously at week 0, followed by 100mg at week 2 and week 6). We also evaluated the following secondary comparisons: (a) high-dose infliximab induction therapy (10mg/kg intravenously at weeks 0, 2 and 6) vs. high-dose golimumab (400mg subcutaneously at week 0, followed by 200mg at week 2 and week 6); (b) standard- and high-dose infliximab vs. placebo in ACT-1 and −2 trials, and standard- and high-dose golimumab vs. placebo in PURSUIT-SC trial; and (c) placebo comparisons for infliximab vs. golimumab trials.

Outcomes

Speed of onset of action: The primary outcome of interest for comparing rapidity of symptom resolution was remission defined by patient-reported outcome-2 (PRO2, derived from the Mayo Clinic Score [MCS]), defined as achieving rectal bleeding score (RBS) of 0 and stool frequency score (SFS) ≤1), at week 2.[12] PRO2 is validated index that correlates highly with endoscopic remission. Secondary outcomes were: (a) PRO2 remission at week 6, (b) RBS=0 at weeks 2 and 6, and (c) SFS≤1 at weeks 2 and 6. Briefly, RBS=0 corresponds to complete resolution of rectal bleeding, and SFS≤1 corresponds either normalization of stool frequency, or 1–2 stools more than normal.[13] In addition, we calculated mean percentage changes from baseline in partial MCS (RBS, SFS and physician global assessment) in infliximab- (week 2, 6 and 8) and golimumab-treated patients (week 2, 4, 6).

Overall efficacy for induction of remission: We compared overall efficacy in achieving clinical remission, defined as MCS <3. This outcome was reported at week 8 in trials of infliximab and week 6 in trials of golimumab (2 weeks after completion of induction therapy).

Confounding Variables

Potential confounders were determined a priori based upon biological plausibility and published literature. We abstracted data on relevant confounding variables including: sex, disease extent (limited to splenic flexure vs. extensive), baseline disease activity (based on MCS as a continuous variable), body weight, concomitant (current) use of immunosuppressives (thiopurines or methotrexate), corticosteroids and/or 5aminosalicylates, and baseline biochemical parameters including albumin and C-reactive protein. While we

intended to adjust for disease duration also, this data was not accurately captured in the YODA platform for the PURSUIT-SC trial.

Statistical Analysis

Baseline characteristics of trials participants were summarized as mean (standard deviation) or medians (range) for continuous variables, and as frequency (%) for categorical variables. Statistical differences in patient characteristics by exposure to infliximab vs. golimumab were assessed using two sample t-tests for continuous variables and chi-squared test for categorical variables. As noted above, in unadjusted analysis, we compared proportion of patients achieving PRO2 remission with standard-dose infliximab vs. golimumab at week 2 as primary outcome. Additionally, we compared rates of PRO2 remission at week 6, RBS=0 at week 2 and 6 and SFS≤1 at week 2 and 6, as well as mean percentage change in partial MCS from baseline. Similar analyses were performed for secondary comparisons with different exposure categories (high-dose infliximab vs. high-dose golimumab, infliximab vs. placebo and golimumab vs. placebo, and placebo arms of infliximab trials vs. placebo arms of golimumab trials). Subsequently, we performed logistic generalized estimating equations, with an exchangeable working correlation structure assumed.[14] This analysis was adjusted for all covariates including sex, body weight, disease extent, baseline disease activity, concomitant use of immunosuppressives, corticosteroids and/or 5-aminosalicylates, and baseline biochemical parameters including albumin and C-reactive protein. Similarly, to compare overall efficacy, we performed multivariable logistic regression analysis, after adjusting for all relevant covariates. All analyses were performed using R (the R Project for Statistical Computing).

RESULTS

A total of 1793 patients were included in three trials – 484 treated with infliximab (240 with standard induction dosing), 734 treated with golimumab (330 treated with standard induction dosing), and 575 patients treated with placebo. Baseline characteristics of included patients are shown in Table 1. Patients treated with infliximab were less likely to be receiving concomitant corticosteroids (34.5% vs. 47.6%, $p<0.01$), and had modestly lower albumin (4.1±0.4 g/dl vs. 4.2±0.4, $p<0.01$). Otherwise, the groups were similar. As anticipated, both standard and high-dose infliximab regimens (Figure 1A–C, eTable 2) and standard and high-dose golimumab regimens (Figure 2A–C, eTable 3) were superior to placebo for inducing PRO2 remission, RBS=0, SFS≤1 at week 2 and 6, and overall clinical remission at week 8.

Comparative Speed of Onset of Action of Infliximab vs. Golimumab

At week 2, more patients treated with infliximab achieved PRO2 remission, as compared to patients treated with golimumab (35.0% vs. 30.0%; adjusted odds ratio [OR], 1.71; 95% confidence intervals [CI], 1.15–2.55) (Table 2). Similarly, at week 6, infliximab-treated patients had 2-times higher odds of achieving PRO2 remission (50.0% vs. 38.9%; aOR, 2.03; 95% CI, 1.40–2.94). Based upon analysis of individual outcomes, patients treated with infliximab were significantly more likely to achieve rapid resolution of rectal bleeding (RBS=0) at week 2 and 6, and achieving SFS≤1 at week 6 (Table 2). No differences in the

frequency of achieving PRO2 remission at week 2 or 6 for patients assigned to placebo in trials of infliximab and golimumab was observed (eTable 4). When comparing high-dose infliximab with high-dose golimumab, similar results were obtained although the difference in achieving PRO2 remission was not statistically significant at week 2 (eTable 5). Likewise, the mean percentage decline in partial MCS was significantly higher for infliximab-treated patients as compared to golimumab-treated patients at week 2 and 6 after adjusting for covariates (eTable 6).

Comparative Efficacy of Infliximab vs. Golimumab

After adjusting for patient-level covariates, including sex, body weight, baseline disease activity, disease extent, concomitant corticosteroids, immunosuppressives and 5aminosalicylates and baseline albumin and C-reactive protein, standard-dose infliximab was superior to standard-dose golimumab in achieving overall clinical remission (MCS<3) (aOR, 3.01; 95% CI, 1.95–4.70) (Table 3). These results were consistent on subgroup analysis by baseline disease severity (moderate UC vs. severe UC).

DISCUSSION

There has been limited assessment of the comparative efficacy and speed of onset of action of different agents available for the treatment of patients with moderate-severe UC, due to paucity of head-to-head treatment trials. Indirect comparisons through meta-analysis are limited by the inability to adjust for patient level covariates. Through a post-hoc analysis of patient level data from similarly designed phase III clinical trials of infliximab and golimumab in biologic-naïve adults with moderate-severe UC, we have attempted to address this knowledge gap, and have made several key observations. In comparing infliximab vs. golimumab, after adjusting for key patient-level covariates, we observed that infliximab has a more rapid onset of action with higher odds of achieving PRO2 remission and resolution of rectal bleeding at week 2. We also observed that patients treated with infliximab have 3-times higher odds of achieving overall clinical remission with induction therapy as compared to golimumab; of note, clinical remission was assessed at week 8 in infliximab trials and week 6 in golimumab trials (2 weeks after completion of induction therapy). Finally, we confirmed that both infliximab and golimumab are superior to placebo for rapidly inducing resolution of symptoms within 2 weeks of administration. These findings have important clinical implications for the selection of TNF-α antagonist therapy for patients with moderate-severe UC. It is vital to choose the most effective agent upfront while treating patients with moderate-severe UC. It is well recognized that response to a second TNF-α antagonist is often inferior to that of the first TNF-α antagonist,[15] and mechanistic failure to TNF-α antagonist is associated with inferior response to a second line non-TNF biologic agent.[16]

Speed of onset of action is an essential attribute when choosing different medications with otherwise similar efficacy and safety.[7, 8] We observed infliximab had a faster onset of action than golimumab, particularly for resolution of rectal bleeding. This property may be due to specific aspects of the pharmacokinetics of monoclonal antibodies. Infliximab is administered intravenously, which allows for administration of a larger volume of drug and

immediate central distribution with 100% bioavailability, and eliminates variability in drug absorption between subjects.[18, 19] The concentration–time profile of infliximab is characterized by high peak-to-trough ratios because of the relatively large intravenous dose and long infusion interval, which may facilitate rapid target engagement and clinical response. In contrast, subcutaneous administration of golimumab is only ~50% bioavailable and the peak concentration is typically reached 5 to 7 days post-injection.[20 ,21] Biologically, resolution of rectal bleeding is more likely to reflect endoscopic remission, since it may indicate the absence of mucosal breaks that would allow blood to enter the fecal stream. In contrast, only 40% patients with endoscopic remission achieve normalization of stool frequency.[22, 23] In patients with endoscopic remission, lack of normalization of stool frequency may be accounted by other mechanisms such as chronic rectal inflammation leading to bowel damage.[22]

We also observed that, after adjusting for key patient-level covariates, infliximab may be superior to golimumab for induction of remission. These findings are similar to findings from indirect treatment comparison network meta-analysis, which have suggested numerically, but not statistically, higher efficacy of infliximab over golimumab.[3, 5, 6] Prior population-based observational comparative effectiveness studies have suggested that infliximab is associated with lower rates of hospitalization and corticosteroid use as compared to adalimumab-treated patients.[4, 17] This may be related to difference in pharmacokinetics and bioavailability with different dosing schema (weight-based vs. fixed dose), adequacy of dose finding studies to fully explore dose response, and route of administration. Findings from the anticipated SERENE trials of adalimumab in moderate-severe UC comparing higher vs. standard dose would be very informative regarding the impact of drug dosing (NCT02065622).

Recent studies have evaluated the speed of onset of action of vedolizumab and tofacitinib. In a recent post-hoc analysis of GEMINI 1 trial, 22.3%, 31.5% and 40.8% biologic-naïve vedolizumab-treated patients achieved PRO2 remission at weeks 2, 4 and 6, respectively; corresponding rates in placebo-treated patients in the trial were 6.6%, 13.2% and 13.2%, respectively.[24] Tofacitinib, recently approved for use in patients with moderate-severe UC, also has been suggested to have a rapid onset of action.[25] Based on patient-reported symptom diaries in OCTAVE-1 and −2 trials, resolution of rectal bleeding at day 15 was observed in ~45% biologic-naïve tofacitinib-treated patients vs. ~25% placebo-treated patients; the corresponding placebo-adjusted difference of infliximab and golimumab at week 2 was 20.1 percentage points and 17.8 percentage points, respectively.

Our study has important limitations. First, this does not represent a head-to-head trial of infliximab and golimumab which would be the gold standard for comparing speed of onset and efficacy and thus should not be considered as definitive proof that infliximab is superior to golimumab for resolution of symptoms and in achieving clinical remission. We acknowledge that all known and unknown confounders cannot be accounted for given the nature of the design; nonetheless we believe this study provides the best available comparison in the absence of a head-to-head trial. Second, our study focused only on induction therapy, and we are unable to comment on the comparative efficacy of infliximab and golimumab for maintenance of remission due to differences in trial design of

maintenance therapy. Third, overall clinical remission was assessed at week 8 in infliximab trials (2 weeks after completion of induction therapy) and week 6 in golimumab trials (4 weeks after completion of induction therapy). However, we feel this is unlikely to significantly affect findings, considering that PRO2, RBS and SFS for golimumab at week 4 and 6 began to level off, suggesting the likelihood of significant incremental symptomatic remission at week 8 to be low. Fourth, we were unable to study pharmacokinetics for infliximab and golimumab in detail, and hence, are unable to assess whether these differences observed could be related to differences in drug exposure. However, we were able to account for key covariates that are well established to influence pharmacokinetics including sex, albumin, C-reactive protein and disease activity. Fifth, we were unable to assess differences that might be achieved through variable or accelerated dosing during induction, since the analyses were restricted to the fixed dosing regimens utilised in the pivotal registration trials and resulting drug label. Finally, we were unable to adjust for disease duration in this analysis as these data were not accurately reported for PURSUIT-SC in the YODA platform. However it is unlikely that this limitation would materially change the study conclusions. At a study-level, there was no significant difference in disease duration in trials of infliximab and golimumab. In contrast to Crohn's disease, disease duration has not been shown to significantly impact response to biologic therapy.[26, 27] Sixth, although a decade had elapsed between the two trials, the trial designs, eligibility and outcome criteria were very similar.

In conclusion, based on post-hoc analysis of individual patient-level data from phase III clinical trials of infliximab and golimumab in patients with moderate-severe UC, we observed a faster onset of action and efficacy of infliximab over golimumab for inducing PRO2 remission. These findings were most consistent for resolution of rectal bleeding, which is a more sensitive and specific marker of endoscopic remission. These findings may inform clinical practice in choosing TNF-α antagonists in patients with UC. Future head-to-head trials of non-TNF-based biologics and targeted small molecules should be interpreted in comparison with infliximab.

Acknowledgments

Funding: Dr. Singh is supported by the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health under award number K23DK117058, the American College of Gastroenterology Junior Faculty Development Award and the Crohn's and Colitis Foundation Career Development Award (#404614). The project was also partially supported by the National Institutes of Health, Grant UL1TR001442. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Disclosures:

This study, carried out under YODA Project # 2018–3121, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C.. The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C.

Siddharth Singh: Research support from AbbVie, consulting fees from AbbVie, Takeda and AMAG Pharmaceuticals outside the submitted work;

Parambir Dulai: Grant support from Pfizer, Janssen and Takeda, advisory board/consulting fees from Takeda and Janssen, and speaker honorarium from Takeda outside the submitted work;

Vipul Jairath: Consulting fees from AbbVie, Sandoz, Takeda, Janssen, Robarts Clinical Trials; speakers fees from Takeda, Janssen, Shire, Ferring;

Brian Feagan: Received grant/research support from Millennium Pharmaceuticals, Merck, Tillotts Pharma AG, AbbVie, Novartis Pharmaceuticals, Centocor Inc., Elan/Biogen, UCB Pharma, Bristol-Myers Squibb, Genentech, ActoGenix, and Wyeth Pharmaceuticals Inc.; consulting fees from Millennium Pharmaceuticals, Merck, Centocor Inc., Elan/Biogen, Janssen-Ortho, Teva Pharmaceuticals, Bristol-Myers Squibb, Celgene, UCB Pharma, AbbVie, Astra Zeneca, Serono, Genentech, Tillotts Pharma AG, Unity Pharmaceuticals, Albireo Pharma, Given Imaging Inc., Salix Pharmaceuticals, Novonordisk, GSK, Actogenix, Prometheus Therapeutics and Diagnostics, Athersys, Axcan, Gilead, Pfizer, Shire, Wyeth, Zealand Pharma, Zyngenia, GiCare Pharma Inc., and Sigmoid Pharma; and speakers bureaux fees from UCB, AbbVie, and J&J/Janssen;

William Sandborn: consulting fees from Abbvie, Akros Pharma, Allergan, Ambrx Inc., Amgen, Ardelyx, Arena Pharmaceuticals, Atlantic Pharmaceuticals, Avaxia, Biogen, Boehringer Ingelheim, Bristol Meyers Squibb, Celgene, Conatus, Cosmo Technologies, Escalier Biosciences, Ferring, Ferring Research Institute, Forward Pharma, Galapagos, Genentech, Gilead Sciences, Immune Pharmaceuticals, Index Pharmaceuticals, Janssen, Kyowa Hakko Kirin Pharma, Lilly, Medimmune, Mesoblast, Miraca Life Sciences, Nivalis Therapeutics, Novartis, Nutrition Science Partners, Oppilan Pharma, Otsuka, Palatin, Paul Hastings, Pfizer, Precision IBD, Progenity, Prometheus Laboratories, Qu Biologics, Regeneron, Ritter Pharmaceuticals, Robarts Clinical Trials (owned by Health Academic Research Trust or HART), Salix, Seattle Genetics, Seres Therapeutics, Shire, Sigmoid Biotechnologies, Takeda, Theradiag, Theravance, Tigenix, Tillotts Pharma, UCB Pharma, Vascular Biogenics, Vivelix; research grants from Atlantic Healthcare Limited, Amgen, Genentech, Gilead Sciences, Abbvie, Janssen, Takeda, Lilly, Celgene/Receptos; payments for lectures/speakers bureau from Abbvie, Janssen, Takeda; and holds stock/stock options in Escalier Biosciences, Oppilan Pharma, Precision IBD, Progenity, Ritter Pharmaceuticals

James Proudfoot and Ronghui Xu have nothing to declare.

REFERENCES

1. Ungaro R, Mehandru S, Allen PB, et al. Ulcerative colitis. Lancet 2017;389:1756–1770. [PubMed: 27914657]
2. Hindryckx P, Vande Casteele N, Novak G, et al. The Expanding Therapeutic Armamentarium for Inflammatory Bowel Disease: How to Choose the Right Drug[s] for Our Patients? J Crohns Colitis 2018;12:105–119. [PubMed: 28961959]
3. Singh S, Fumery M, Sandborn WJ, et al. Systematic review with network meta-analysis: first- and second-line pharmacotherapy for moderate-severe ulcerative colitis. Aliment Pharmacol Ther 2018;47:162–175. [PubMed: 29205406]
4. Singh S, Andersen NN, Andersson M, et al. Comparison of Infliximab and Adalimumab in Biologic-Naive Patients With Ulcerative Colitis: A Nationwide Danish Cohort Study. Clin Gastroenterol Hepatol 2017;15:1218–1225. [PubMed: 27913244]
5. Bonovas S, Lytras T, Nikolopoulos G, et al. Systematic review with network meta-analysis: comparative assessment of tofacitinib and biological therapies for moderate-to-severe ulcerative colitis. Aliment Pharmacol Ther 2018;47:454–465. [PubMed: 29205421]
6. Danese S, Fiorino G, Peyrin-Biroulet L, et al. Biological agents for moderately to severely active ulcerative colitis: a systematic review and network meta-analysis. Ann Intern Med 2014;160:704–11. [PubMed: 24842416]
7. Gray JR, Leung E, Scales J. Treatment of ulcerative colitis from the patient's perspective: a survey of preferences and satisfaction with therapy. Aliment Pharmacol Ther 2009;29:1114–20. [PubMed: 19222412]
8. Vaucher C, Maillard MH, Froehlich F, et al. Patients and gastroenterologists' perceptions of treatments for inflammatory bowel diseases: do their perspectives match? Scand J Gastroenterol 2016;51:1056–61. [PubMed: 26891800]
9. Krumholz HM, Waldstreicher J. The Yale Open Data Access (YODA) Project--A Mechanism for Data Sharing. N Engl J Med 2016;375:403–5. [PubMed: 27518657]
10. Rutgeerts P, Sandborn WJ, Feagan BG, et al. Infliximab for induction and maintenance therapy for ulcerative colitis. N Engl J Med 2005;353:2462–76. [PubMed: 16339095]
11. Sandborn WJ, Feagan BG, Marano C, et al. Subcutaneous golimumab induces clinical response and remission in patients with moderate-to-severe ulcerative colitis. Gastroenterology 2014;146:85–95. [PubMed: 23735746]

12. Jairath V, Khanna R, Zou GY, et al. Development of interim patient-reported outcome measures for the assessment of ulcerative colitis disease activity in clinical trials. Aliment Pharmacol Ther 2015;42:1200–10. [PubMed: 26388424]
13. Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. A randomized study. N Engl J Med 1987;317:1625–9. [PubMed: 3317057]
14. Buzkova P, Brown ER, John-Stewart GC. Longitudinal data analysis for generalized linear models under participant-driven informative follow-up: an application in maternal health epidemiology. Am J Epidemiol 2010;171:189–97. [PubMed: 20007201]
15. Gisbert JP, Marin AC, McNicholl AG, et al. Systematic review with meta-analysis: the efficacy of a second anti-TNF in patients with inflammatory bowel disease whose previous anti-TNF treatment has failed. Aliment Pharmacol Ther 2015;41:613–23. [PubMed: 25652884]
16. Singh S, George J, Boland BS, et al. Primary Non-Response to Tumor Necrosis Factor Antagonists is Associated with Inferior Response to Second-line Biologics in Patients with Inflammatory Bowel Diseases: A Systematic Review and Meta-analysis. J Crohns Colitis 2018;12:635–643. [PubMed: 29370397]
17. Singh S, Heien HC, Sangaralingham LR, et al. Comparative effectiveness and safety of infliximab and adalimumab in patients with ulcerative colitis. Aliment Pharmacol Ther 2016;43:994–1003. [PubMed: 26991059]
18. Vande Casteele N, Gils A. Pharmacokinetics of anti-TNF monoclonal antibodies in inflammatory bowel disease: Adding value to current practice. J Clin Pharmacol 2015;55 Suppl 3:S39–50. [PubMed: 25707962]
19. Klotz U, Teml A, Schwab M. Clinical pharmacokinetics and use of infliximab. Clin Pharmacokinet 2007;46:645–60. [PubMed: 17655372]
20. Adedokun OJ, Xu Z, Marano CW, et al. Pharmacokinetics and Exposure-response Relationship of Golimumab in Patients with Moderately-to-Severely Active Ulcerative Colitis: Results from Phase 2/3 PURSUIT Induction and Maintenance Studies. J Crohns Colitis 2017;11:35–46. [PubMed: 27440869]
21. Lobo ED, Hansen RJ, Balthasar JP. Antibody pharmacokinetics and pharmacodynamics. J Pharm Sci 2004;93:2645–68. [PubMed: 15389672]
22. Colombel JF, Keir ME, Scherl A, et al. Discrepancies between patient-reported outcomes, and endoscopic and histological appearance in UC. Gut 2017;66:2063–2068. [PubMed: 27590995]
23. Narula N, Alshahrani AA, Yuan Y, et al. Patient-Reported Outcomes and Endoscopic Appearance of Ulcerative Colitis-a Systematic Review and Meta-Analysis. Clin Gastroenterol Hepatol 2019;17:411–8. [PubMed: 29913273]
24. Feagan BG, Lasch K, Lissoos T, et al. Rapid response to vedolizumab therapy in biologic-naive patients with inflammatory bowel diseases. Clin Gastroenterol Hepatol 2019;17:130–38 [PubMed: 29857145]
25. Hanauer S, Panaccione R, Danese S, et al. Tofacitinib Induction Therapy Reduces Symptoms Within 3 Days for Patients with Ulcerative Colitis. Clin Gastroenterol Hepatol 2019;17:139–47. [PubMed: 30012431]
26. Ma C, Beilman CL, Huang VW, et al. Similar Clinical and Surgical Outcomes Achieved with Early Compared to Late Anti-TNF Induction in Mild-to-Moderate Ulcerative Colitis: A Retrospective Cohort Study. Can J Gastroenterol Hepatol 2016;2016:2079582. [PubMed: 27478817]
27. Mandel MD, Balint A, Golovics PA, et al. Decreasing trends in hospitalizations during anti-TNF therapy are associated with time to anti-TNF therapy: Results from two referral centres. Dig Liver Dis 2014;46:985–90. [PubMed: 25156871]

WHAT YOU NEED TO KNOW

Background:

We compared the efficacy and speed of onset of action of infliximab vs golimumab induction therapy using patient-level data from phase 3 trials (ACT-1, ACT2, and PURSUIT-SC).

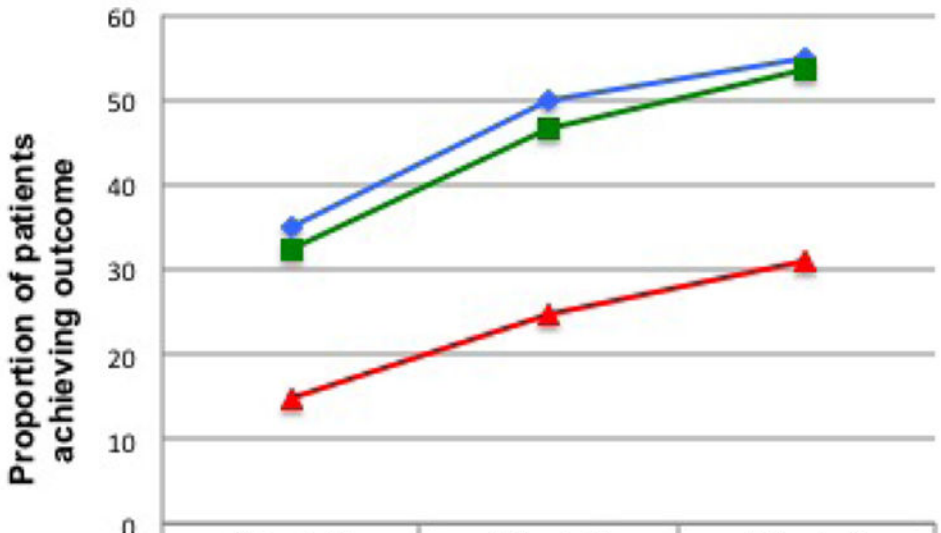
Findings:

Infliximab resolved symptoms more rapidly and had greater efficacy for inducing remission than golimumab in patients with moderate–severe UC.

Implications for Patient Care:

Infliximab may be preferred over golimumab in patients with moderate-severe UC.

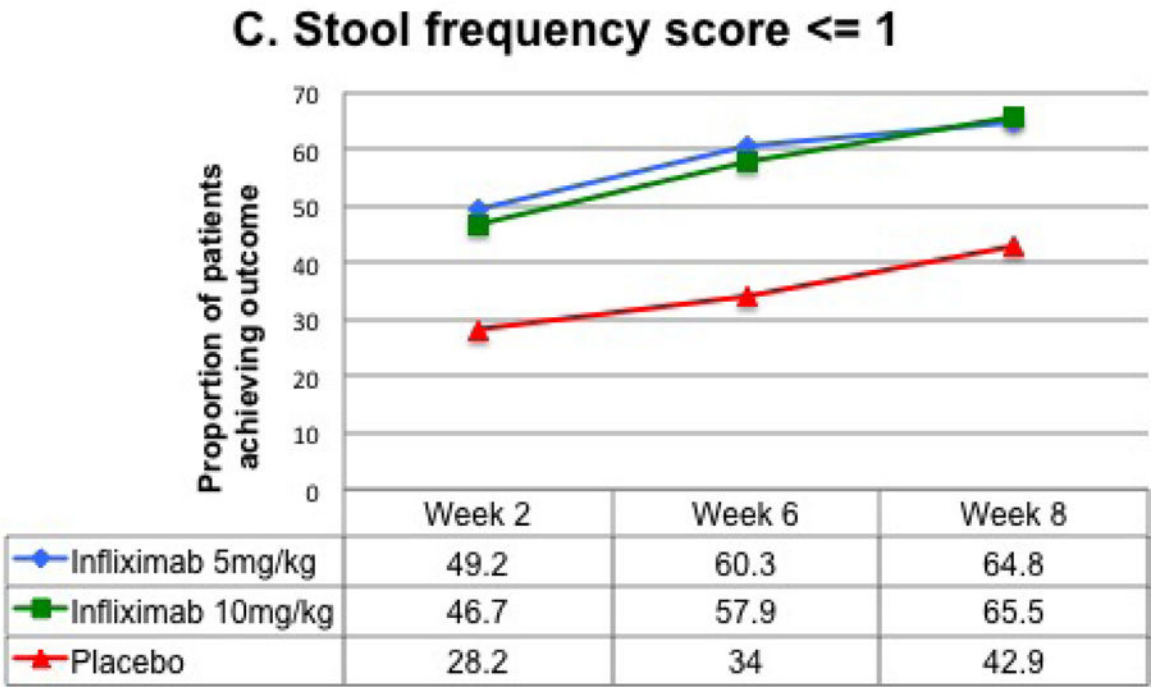
A. PRO-2 Remission



	Week 2	Week 6	Week 8
Infliximab 5mg/kg	35	50	54.8
Infliximab 10mg/kg	32.4	46.7	53.6
Placebo	14.8	24.6	30.9

B. Rectal bleeding score = 0

	Week 2	Week 6	Week 8
Infliximab 5mg/kg	53.3	62	68.7
Infliximab 10mg/kg	52.9	62.7	70.9
Placebo	33.2	41.5	51.3

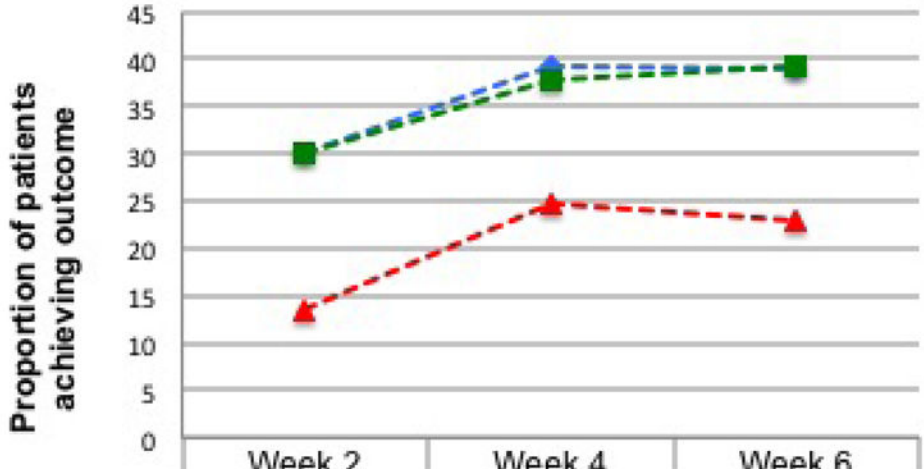


	Week 2	Week 6	Week 8
Infliximab 5mg/kg	49.2	60.3	64.8
Infliximab 10mg/kg	46.7	57.9	65.5
Placebo	28.2	34	42.9

Figure 1.

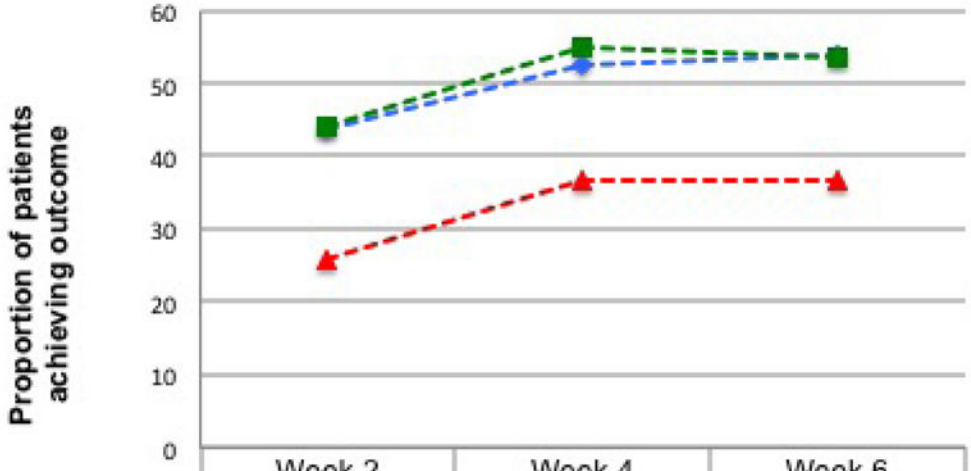
Rates of achieving (A) PRO2 remission, (B) rectal bleeding score = 0 and (C) stool frequency score ≤1 at weeks 2, 6 and 8, in infliximab vs. placebo-treated patients with moderate-severe ulcerative colitis

A. PRO-2 Remission

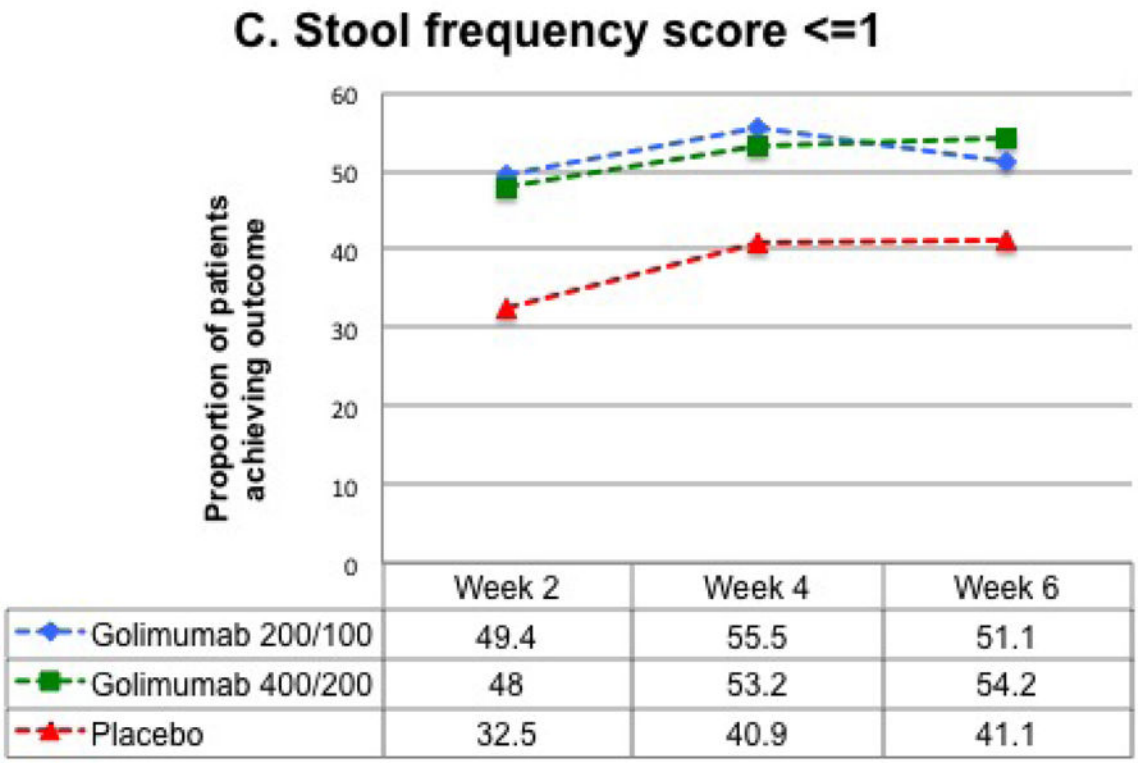


	Week 2	Week 4	Week 6
Golimumab 200/100	30	39.2	38.9
Golimumab 400/200	30	37.8	39.2
Placebo	13.5	24.6	23

B. Rectal bleeding score = 0



	Week 2	Week 4	Week 6
Golimumab 200/100	43.6	52.4	53.9
Golimumab 400/200	44	54.8	53.6
Placebo	25.8	36.6	36.6



	Week 2	Week 4	Week 6
Golimumab 200/100	49.4	55.5	51.1
Golimumab 400/200	48	53.2	54.2
Placebo	32.5	40.9	41.1

Figure 2.

Rates of achieving (A) PRO2 remission, (B) rectal bleeding score = 0 and (C) stool frequency score ≤1 at weeks 2, 4 and 6, in golimumab vs. placebo-treated patients with moderate-severe ulcerative colitis

Table 1.

Baseline characteristics of patients with biologic-treated patients with ulcerative colitis, by exposure or nonexposure to concomitant 5-ASA

Characteristics	Golimumab (n= 734)	Infliximab (n=484)	Placebo (n=575)	p-value
Sex: Female	313 (42.6%)	190 (39.3%)	257 (44.7%)	0.20
Male	421 (57.4%)	294 (60.7%)	318 (55.3%)	
Disease extent				0.89
• Limited (up to splenic flexure)	427 (8.2%)	275 (7.5%)	324 (6.8%)	
• Extensive (extends beyond splenic flexure)	307 (41.8%)	203 (42.5%)	246 (43.2%)	
Disease activity				0.90
• Mayo Clinic Score, mean (SD)	8.5 (1.5)	8.4 (1.6)	8.4 (1.6)	
Concomitant Medications				
• Prednisone	349 (47.6%)	167 (34.5%)	243 (42.4%)	<0.01
• Immunosuppressives	239 (32.6%)	188 (38.8%)	199 (34.6%)	0.08
• 5-aminosalicylates	597 (81.4%)	352 (76.4%)	451 (80.2%)	0.10
Laboratory variables				
• Albumin (g/dL)				
○ Mean (SD)	4.19 (0.44)	4.07 (0.38)	4.14 (0.44)	<0.01
• C-reactive protein (mg/L)				
○ Mean (SD)	11.85 (20.46)	14.60 (21.42)	13.49 (1.9)	0.08

[Abbreviations: SD=Standard deviation; g=grams; mg=milligrams; dL=decilitre]

Table 2.

Rate of achieving clinical outcomes of interest at weeks 2 and 6 in patients treated with standard-dose infliximab vs. standard-dose golimumab. Odds ratios were derived from generalized estimating equations.

Outcome	Golimumab (Standard-dose)	Infliximab (Standard-dose)	p-value
Rectal bleeding score (RBS) = 0			
Week 2			
• Proportion (n/N)	144 / 330 (43.6%)	128 / 240 (53.3%)	
• Unadjusted OR (95% CI)	1.0	1.48 (1.06, 2.06)	0.02
• Adjusted OR (95% CI)	1.0	1.76 (1.21, 2.55)	<0.01
Week 6			
• Proportion (n/N)	173 / 321 (53.9%)	145 / 234 (62.0%)	
• Unadjusted OR (95% CI)	1.0	1.36 (0.97, 1.92)	0.07
• Adjusted OR (95% CI)	1.0	1.73 (1.20, 2.50)	<0.01
Stool Frequency Score (SFS) ≤1			
Week 2			
• Proportion (n/N)	163 / 330 (49.4%)	118 / 240 (49.2%)	
• Unadjusted OR (95% CI)	1.0	0.99 (0.71, 1.38)	0.96
• Adjusted OR (95% CI)	1.0	1.39 (0.95, 2.01)	0.09
Week 6			
• Proportion (n/N)	164 / 321 (51.1%)	141 / 234 (60.3%)	
• Unadjusted OR (95% CI)	1.0	1.41 (1.00, 1.97)	0.049
• Adjusted OR (95% CI)	1.0	1.77 (1.21, 2.57)	<0.01
PRO2 remission (RBS=0 AND SFS≤1)			
Week 2			
• Proportion (n/N)	99 / 330 (30.0%)	84 / 240 (35.0%)	
• Unadjusted OR (95% CI)	1.0	1.26 (0.88, 1.79)	0.21
• Adjusted OR (95% CI)	1.0	1.71 (1.15, 2.55)	<0.01
Week 6			
• Proportion (n/N)	125 / 321 (38.9%)	117 / 234 (50.0%)	
• Unadjusted OR (95% CI)	1.0	1.55 (1.10, 2.17)	0.01
• Adjusted OR (95% CI)	1.0	2.03 (1.40, 2.94)	<0.001

*Variables adjusted for include: sex, body weight, baseline disease activity, disease extent, concomitant corticosteroids, immunosuppressives and 5-aminosalicylates and baseline albumin and C-reactive protein

Table 3.

Rates of achieving overall clinical remission in patients treated with standard-dose infliximab (week 8) vs. standard-dose golimumab (week 6). Odds ratios were derived from logistic regression at fixed time points.

Outcome	Golimumab (Standard-dose)	Infliximab (Standard-dose)	p-value
All patients			
Clinical Remission			
• Proportion (n/N)	66 / 318 (20.8%)	89 / 229 (38.9%)	
• Unadjusted OR (95% CI)	1.0	2.43 (1.66, 3.56)	<0.001
• Adjusted OR (95% CI)	1.0	3.01 (1.95, 4.70)	<0.001
Baseline moderate disease activity			
Clinical Remission			
• Proportion (n/N)	52 / 225 (23.1%)	70 / 164 (42.7%)	
• Unadjusted OR (95% CI)	1.0	2.48 (1.60, 3.85)	<0.001
• Adjusted OR (95% CI)	1.0	3.13 (1.90, 5.21)	<0.001
Baseline severe disease activity			
Clinical Remission			
• Proportion (n/N)	14 / 93 (15.1%)	19 / 63 (30.2%)	
• Unadjusted OR (95% CI)	1.0	2.44 (1.12, 5.42)	0.03
• Adjusted OR (95% CI)	1.0	2.69 (1.00, 7.56)	0.05

*Variables adjusted for include: sex, body weight, baseline disease activity, disease extent, concomitant corticosteroids, immunosuppressives and 5-aminosalicylates and baseline albumin and C-reactive protein

eTable 1.

Characteristics of clinical trials of infliximab and golimumab included in the current study. Please note, for our study, we only focused on induction of remission.

Trial characteristics	Infliximab (ACT-1 and −2)	Golimumab (PURSUIT-SC)
Study Design; Sites, Time	Phase 3, multicenter, randomized, double-blind, placebo-controlled trial; 2002–05; Global trials; ACT-1 – 62 sites; ACT-2 – 55 sites • Central randomization with a dynamic treatment allocation stratified according to the investigational site and whether patients had ulcerative colitis that was refractory to corticosteroid therapy.	Phase 2 and 3, multicenter, randomized, double-blind, placebo-controlled trial; 2007–10; 217 sites in Eastern Europe (400 patients); North America (278 patients); Asia Pacific and South Africa (204 patients); and Western Europe and Israel (183 patients). • Only phase 3 data was included in our study • Allocation to treatment was performed using a central randomization center using an interactive voice-response system, using a permuted block randomization schema.
Inclusion criteria	Confirmed ulcerative colitis, with screening flexible sigmoidoscopy and biopsy • Mayo score of 6–12, with endoscopy subscore of 2–3, despite concurrent treatment with corticosteroids alone or in combination with azathioprine or mercaptopurine (ACT-1) or despite concurrent treatment with corticosteroids alone or in combination with azathioprine or mercaptopurine and medications containing 5-aminosalicylates	Confirmed ulcerative colitis, with screening flexible sigmoidoscopy and biopsy • Mayo score of 6–12, with endoscopy subscore of 2–3 • Inadequate response to, or had failed to tolerate, 1 or more of the following conventional therapies: oral mesalamine, oral corticosteroids, azathioprine, and/or 6mercaptopurine; or were corticosteroid dependent (ie, an inability to taper corticosteroids without recurrence of UC symptoms).
Exclusion criteria	• Indeterminate colitis • Crohn's disease • No prior anti-TNF agents • Positive PPD	• History of, or at imminent risk for, colectomy; who required gastrointestinal surgery within 2 months before screening; • Colitis limited to 20 cm of the colon (patients with ulcerative proctitis often have rectal bleeding as the primary clinical manifestation of the disease, thus, the utility of the Mayo score in this patient population is less clear); • History of colonic mucosal dysplasia or adenomatous colonic polyps that were not removed, were ineligible. • Patients were excluded if their screening stool study was positive for enteric pathogens or Clostridium difficile toxin. • Earlier use of the following medications also precluded study participation: biologic antiTNF agent(s) antagonists; natalizumab or other agents targeting the a-4 integrin, Bcell depleting agents (rituximab), or T-cell depleting agents (alemtuzumab, visilizumab) within 12 months of the first study-agent injection (or continued B- or Tcell depletion >12 months after completing therapy with lymphocyte depleting agents); oral orticosteroids at a dose >40 mg prednisone or its equivalent per day; receipt of cyclosporine, tacrolimus, sirolimus, or mycophenolate mofetil within 8 weeks before the first study agent injection; or use of an investigational agent within 5 half-lives of that agent before the first study agent injection.
Concurrent or prior medications	• Dose of concurrent medications remained constant except for corticosteroids, which were tapered by 5 mg weekly after week 8 until a dose of 20 mg per day was reached (corticosteroid dose stable during induction). Thereafter, the dose was reduced by 2.5 mg weekly until discontinuation • Rectally administered corticosteroids or medications containing 5aminosalicylates were not permitted within 2 weeks prior to screening	• Patients concurrently treated with oral mesalamine or corticosteroids were to receive a stable dose for at least 2 weeks before baseline, and patients receiving AZA and/or 6-mercaptopurine were to receive a stable dose for at least 4 weeks before baseline. • Patients were required to maintain stable doses of their concomitant UC medications during the study (corticosteroid dose stable during induction).
Follow-up visits	Week 0, 2, 6, 8 (for induction studies), 14, 22 and 30 (additional visits in ACT-1 at 38, 46 and 54) • Partial Mayo score at all visits • Full Mayo score at 0, 8, 30, and 54 (only for ACT-1) • For current study, only induction therapy was included (up to week 8)	Week 0, 2, 4, 6 (for induction study); maintenance study separate. • Partial Mayo score at all visits • Full Mayo score at 0, 6

Trial characteristics	Infliximab (ACT-1 and −2)	Golimumab (PURSUIT-SC)
Outcome measure	Mayo score and partial Mayo score (from this PRO2 remission was derived for current study); locally read sigmoidoscopy	Mayo score and partial Mayo score (from this PRO2 remission was derived for current study); locally read sigmoidoscopy; For scoring of rectal bleeding and stool frequency subscores, the average score from the most recent consecutive 3 days before the study visit was used.
Outcome definition	• Clinical response was defined as a decrease from baseline in the total Mayo score of at least 3 points and at least 30 percent, with an accompanying decrease in the subscore for rectal bleeding of at least 1 point or an absolute subscore for rectal bleeding of 0 or 1 • Clinical remission was defined as a total Mayo score of 2 points or lower, with no individual subscore exceeding 1 point. • Mucosal healing was defined as an absolute subscore for endoscopy of 0 or 1. • For our study, PRO2 remission was derived from partial Mayo score	• Clinical response decrease from baseline in the Mayo score ≥30% and ≥3 points, accompanied by either a rectal bleeding subscore of 0 or 1 or a decrease from baseline in the rectal bleeding subscore ≥1 • Clinical remission was defined as a total Mayo score of 2 points or lower, with no individual subscore exceeding 1 point. • Mucosal healing was defined as an absolute subscore for endoscopy of 0 or 1. • For our study, PRO2 remission was derived from partial Mayo score

eTable 2.

Rates of achieving clinical outcomes of interest at weeks 2, 6, and 8 in patients treated with infliximab and corresponding placebo. Odds ratios were derived from generalized estimating equations.

Outcome	Placebo	Infliximab 5mg/kg (Standard-dose)	Infliximab 10mg/kg (High-dose)
Rectal bleeding score (RBS) = 0			
Week 2			
• Proportion (n/N)	79 / 238 (33.2%)	128 / 240 (53.3%)	128 / 242 (52.9%)
• Unadjusted OR (95% CI)	1.0	2.30 (1.59, 3.33)	2.26 (1.56, 3.27)
• Adjusted OR (95% CI)	1.0	2.35 (1.57, 3.51) *	2.35 (1.58, 3.51) *
Week 6			
• Proportion (n/N)	88 / 212 (41.5%)	145 / 234 (62.0%)	143 / 228 (62.7%)
• Unadjusted OR (95% CI)	1.0	2.28 (1.57, 3.32)	2.29 (1.57, 3.33)
• Adjusted OR (95% CI)	1.0	2.41 (1.62, 3.60)	2.33 (1.56, 3.49)
Week 8			
• Proportion (n/N)	97 / 189 (51.3%)	158 / 230 (68.7%)	158 / 223 (70.9%)
• Unadjusted OR (95% CI)	1.0	2.16 (1.46, 3.19)	2.29 (1.55, 3.39)
• Adjusted OR (95% CI)	1.0	2.24 (1.47, 3.40)	2.27 (1.49, 3.47)
Stool Frequency Score (SFS) ≤1			
Week 2			
• Proportion (n/N)	67 / 238 (28.2%)	240 (49.2%)	113 / 242 (46.7%)
• Unadjusted OR (95% CI)	1.0	2.47 (1.69, 3.61)	2.24 (1.53, 3.27)
• Adjusted OR (95% CI)	1.0	2.63 (1.75, 3.95)	2.20 (1.46, 3.30)
Week 6			
• Proportion (n/N)	72 / 212 (34.0%)	141 / 234 (60.3%)	132 / 228 (57.9%)
• Unadjusted OR (95% CI)	1.0	2.93 (2.00, 4.30)	2.63 (1.79, 3.86)
• Adjusted OR (95% CI)	1.0	3.01 (1.99, 4.55)	2.55 (1.69, 3.84)
Week 8			
• Proportion (n/N)	81 / 189 (42.9%)	230 (64.8%)	146 / 223 (65.5%)
• Unadjusted OR (95% CI)	1.0	2.50 (1.71, 3.66)	2.54 (1.73, 3.74)
• Adjusted OR (95% CI)	1.0	2.68 (1.78, 4.02)	2.38 (1.58, 3.59)
PRO 2 remission (RBS =0 AND SFS≤1)			
Week 2			
• Proportion (n/N)	35 / 237 (14.8%)	84 / 240 (35.0%)	78 / 241 (32.4%)
• Unadjusted OR (95% CI)	1.0	3.11 (1.99, 4.86)	2.76 (1.76, 4.33)
• Adjusted OR (95% CI)	1.0	3.22 (2.01, 5.16)	2.74 (1.70, 4.41)
Week 6			
• Proportion (n/N)	52 / 211 (24.6%)	117 / 234 (50.0%)	106 / 227 (46.7%)

Outcome	Placebo	Infliximab 5mg/kg (Standard-dose)	Infliximab 10mg/kg (High-dose)
• Unadjusted OR (95% CI)	1.0	3.03 (2.02, 4.52)	2.59 (1.73, 3.88)
• Adjusted OR (95% CI)	1.0	3.15 (2.06, 4.83)	2.51 (1.64, 3.85)
Week 8			
• Proportion (n/N)	58 / 188 (30.9%)	126 / 230 (54.8%)	145 / 222 (53.6%)
• Unadjusted OR (95% CI)	1.0	2.77 (1.86, 4.12)	2.62 (1.76, 3.90)
• Adjusted OR (95% CI)	1.0	2.99 (1.96, 4.57)	2.41 (1.58, 3.68)

*Variables adjusted for include: sex, body weight, baseline disease activity, disease extent, concomitant corticosteroids, immunosuppressives and 5-aminosalicylates and baseline albumin and C-reactive protein

eTable 3.

Rate of achieving clinical outcomes of interest at weeks 2, 4, and 6 in patients treated with golimumab and corresponding placebo. Odds ratios were derived from generalized estimating equations.

Outcome	Placebo	Golimumab 200/100 (Standard-dose)	Golimumab (400/200) (High-dose)
Rectal bleeding score (RBS) = 0			
Week 2			
• Proportion (n/N)	84 / 326 (25.8%)	144 / 330 (43.6%)	144 / 327 (44.0%)
• Unadjusted OR (95% CI)	1.0	2.20 (1.58, 3.06)	2.24 (1.61, 3.11)
• Adjusted OR (95% CI)	1.0	2.24 (1.59, 3.16)	2.32 (1.64, 3.28)
Week 4			
• Proportion (n/N)	116 / 317 (36.6%)	167 / 319 (52.4%)	178 / 325 (54.8%)
• Unadjusted OR (95% CI)	1.0	1.91 (1.40, 2.62)	2.11 (1.54, 2.89)
• Adjusted OR (95% CI)	1.0	1.94 (1.39, 2.69)	2.21 (1.59, 3.08)
Week 6			
• Proportion (n/N)	113 / 309 (36.6%)	173 / 321 (53.9%)	171 / 319 (53.6%)
• Unadjusted OR (95% CI)	1.0	2.07 (1.51, 2.85)	2.01 (1.46, 2.76)
• Adjusted OR (95% CI)	1.0	2.05 (1.47, 2.85)	2.11 (1.52, 2.95)
Stool Frequency Score (SFS) ≤1			
Week 2			
• Proportion (n/N)	106 / 326 (32.5%)	163 / 330 (49.4%)	157 / 327 (48.0%)
• Unadjusted OR (95% CI)	1.0	2.02 (1.47, 2.77)	1.91 (1.39, 2.63)
• Adjusted OR (95% CI)	1.0	2.02 (1.44, 2.82)	2.10 (1.50, 2.94)
Week 4			
• Proportion (n/N)	130 / 318 (40.9%)	177 / 319 (55.5%)	173 / 325 (53.2%)
• Unadjusted OR (95% CI)	1.0	1.83 (1.34, 2.50)	1.67 (1.22, 2.27)
• Adjusted OR (95% CI)	1.0	1.98 (1.41, 2.76)	1.90 (1.36, 2.64)
Week 6			
• Proportion (n/N)	127 / 309 (41.1%)	164 / 321 (51.1%)	173 / 319 (54.2%)
• Unadjusted OR (95% CI)	1.0	1.55 (1.13, 2.11)	1.69 (1.24, 2.31)
• Adjusted OR (95% CI)	1.0	1.66 (1.19, 2.31)	1.98 (1.42, 2.76)
PR O2 remission (RBS=0 AND SFS≤1)			
Week 2			
• Proportion (n/N)	44 / 326 (13.5%)	99 / 330 (30.0%)	98 / 327 (30.0%)
• Unadjusted OR (95% CI)	1.0	2.72 (1.84, 4.04)	2.72 (1.83, 4.04)
• Adjusted OR (95% CI)	1.0	2.69 (1.78, 4.07)	2.96 (1.96, 4.46)
Week 4			
• Proportion (n/N)	78 / 317 (24.6%)	125 / 319 (39.2%)	123 / 325 (37.8%)

Outcome	Placebo	Golimumab 200/100 (Standard-dose)	Golimumab (400/200) (High-dose)
• Unadjusted OR (95% CI)	1.0	1.98 (1.41, 2.78)	1.88 (1.34, 2.64)
• Adjusted OR (95% CI)	1.0	2.07 (1.45, 2.97)	2.12 (1.48, 3.03)
Week 6			
• Proportion (n/N)	71 / 309 (23.0%)	125 / 321 (38.9%)	125 / 319 (39.2%)
• Unadjusted OR (95% CI)	1.0	2.19 (1.55, 3.11)	2.18 (1.54, 3.09)
• Adjusted OR (95% CI)	1.0	2.20 (1.53, 3.17)	2.38 (1.66, 3.43)

*Variables adjusted for include: sex, body weight, baseline disease activity, disease extent, concomitant corticosteroids, immunosuppressives and 5-aminosalicylates and baseline albumin and C-reactive protein

eTable 4.

Rates of achieving clinical outcomes of interest at weeks 2 and 6 in placebo arms of trials of infliximab vs. golimumab

Outcome	Placebo – Golimumab	Placebo – Infliximab	p-value
Rectal bleeding score (RBS) = 0			
Week 2			
• Proportion (n/N)	84 / 326 (25.8%)	79 / 238 (33.2%)	
• Unadjusted OR (95% CI)	1.0	1.42 (0.99, 2.05)	0.06
• Adjusted OR (95% CI)	1.0	1.52 (1.03, 2.24)	0.03
Week 6			
• Proportion (n/N)	113 / 309 (36.6%)	88 / 212 (41.5%)	
• Unadjusted OR (95% CI)	1.0	1.23 (0.86, 1.75)	0.26
• Adjusted OR (95% CI)	1.0	1.36 (0.94, 1.99)	0.11
Stool Frequency Score (SFS) ≤1			
Week 2			
• Proportion (n/N)	106 / 326 (32.5%)	67 / 238 (28.2%)	
• Unadjusted OR (95% CI)	1.0	0.81 (0.56, 1.17)	0.26
• Adjusted OR (95% CI)	1.0	1.10 (0.75, 1.63)	0.63
Week 6			
• Proportion (n/N)	127 / 309 (41.1%)	72 / 212 (34.0%)	
• Unadjusted OR (95% CI)	1.0	0.73 (0.51, 1.05)	0.09
• Adjusted OR (95% CI)	1.0	1.04 (0.70, 1.53)	0.86
PRO2 remission (RBS=0 AND SFS≤1)			
Week 2			
• Proportion (n/N)	44 / 326 (13.5%)	35 / 238 (14.7%)	
• Unadjusted OR (95% CI)	1.0	1.10 (0.68, 1.77)	0.70
• Adjusted OR (95% CI)	1.0	1.35 (0.82, 2.22)	0.23
Week 6			
• Proportion (n/N)	71 / 309 (23.0%)	52 / 212 (24.5%)	
• Unadjusted OR (95% CI)	1.0	1.11 (0.73, 1.66)	0.63
• Adjusted OR (95% CI)	1.0	1.40 (0.90, 2.16)	0.14

*Variables adjusted for include: sex, body weight, baseline disease activity, disease extent, concomitant corticosteroids, immunosuppressives and 5-aminosalicylates and baseline albumin and C-reactive protein

eTable 5.

Rates of achieving clinical outcomes of interest at weeks 2 and 6 with high-dose infliximab vs. high-dose golimumab

Outcome	Golimumab 400/200 (High-dose)	Infliximab 10mg/kg (High-dose)	p-value
Rectal bleeding score (RBS) = 0			
Week 2			
• Proportion (n/N)	144 / 327 (44.0%)	128 / 240 (53.3%)	
• Unadjusted OR (95% CI)	1.0	1.48 (1.06, 2.06)	0.04
• Adjusted OR (95% CI)	1.0	1.68 (1.17, 2.41)	<0.01
Week 6			
• Proportion (n/N)	171 / 319 (53.6%)	143 / 228 (62.7%)	
• Unadjusted OR (95% CI)	1.0	1.36 (0.99, 1.96)	0.06
• Adjusted OR (95% CI)	1.0	1.60 (1.11, 2.31)	0.01
Stool Frequency Score (SFS) ≤1			
Week 2			
• Proportion (n/N)	157 / 327 (48.0%)	113 / 242 (46.7%)	
• Unadjusted OR (95% CI)	1.0	0.95 (0.68, 1.32)	0.76
• Adjusted OR (95% CI)	1.0	1.14 (0.79, 1.64)	0.50
Week 6			
• Proportion (n/N)	173 / 319 (54.2%)	132 / 228 (57.9%)	
• Unadjusted OR (95% CI)	1.0	1.14 (0.81, 1.60)	0.45
• Adjusted OR (95% CI)	1.0	1.32 (0.91, 1.92)	0.14
PRO2 remission (RBS=0 AND SFS≤1)			
Week 2			
• Proportion (n/N)	98 / 327 (30.0%)	79 / 242 (32.6%)	
• Unadjusted OR (95% CI)	1.0	1.13 (0.79, 1.62)	0.50
• Adjusted OR (95% CI)	1.0	1.35 (0.91, 1.98)	0.13
Week 6			
• Proportion (n/N)	125 / 321 (38.9%)	107 / 228 (46.9%)	
• Unadjusted OR (95% CI)	1.0	1.33 (0.95, 1.88)	0.10
• Adjusted OR (95% CI)	1.0	1.56 (1.08, 2.25)	0.02

*Variables adjusted for include: sex, body weight, baseline disease activity, disease extent, concomitant corticosteroids, immunosuppressives and 5-aminosalicylates and baseline albumin and C-reactive protein

eTable 6.

Mean percentage change in partial Mayo Clinic Score between standard-dose infliximab and golimumab using generalized estimating equation (note: negative score indicates greater magnitude of decline in partial mayo score as compared to baseline)

Time point (infliximab vs. golimumab)	Estimate (mean percentage difference)	95% CI	p-value
Unadjusted Analysis			
Week 2	−4.5	(−9.5 to +0.4)	0.07
Week 6	−6.9	(−13.0 to −0.9)	0.2
Adjusted Analysis*			
Week 2	−8.8	(−14.0 to −3.5)	0.001
Week 6	−10.9	(−17.1 to −4.7)	<0.001

*Variables adjusted for include: sex, body weight, baseline disease activity, disease extent, concomitant corticosteroids, immunosuppressives and 5-aminosalicylates and baseline albumin and C-reactive protein