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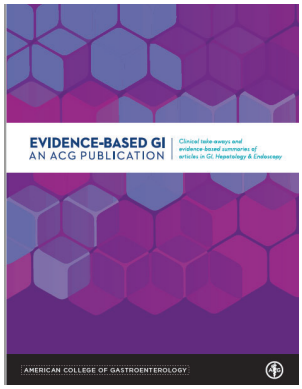

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Bridging the Gap: Impact of Gender-Affirming Care on IBD Flare Rates

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IBD

This summary reviews Bennett A, Field J, Newman KL, et al. Gender-Affirming Hormone Therapy and Risk of IBD Flare in Transgender and Gender Diverse Adults. Am J Gastroenterol. 2025 May 16. doi: 10.14309/ajg.0000000000003543.

Correspondence to Nikki Duong, MD. Associate Editor. Email: EBGI@gi.org

Keywords: transgender, gender non-binary, gender-affirming hormones, inflammatory bowel disease, ulcerative colitis, Crohn's disease, biologic medication

STRUCTURED ABSTRACT

Question: What is the impact of gender-affirming hormone therapy (GAHT) on rates of inflammatory bowel disease (IBD) flares in transgender and gender-diverse adults?

Design: This was a retrospective cohort study of adult patients diagnosed with IBD who were prescribed GAHT. Patients were stratified based on disease activity at the time of hormone initiation (active disease vs remission) and the type of hormone initiated (estrogen vs testosterone). Clinical data were reviewed for 12 months before and after the initiation of GAHT.

Setting: Five tertiary care centers across the United States. Data were collected for the 12 months preceding and following GAHT initiation.

Patients: Patients were identified using *ICD-10* codes and keyword searches

including "Crohn's disease," "ulcerative colitis," "transgender," and "gender dysphoria." Inclusion criteria required a diagnosis of IBD prior to GAHT initiation, with available clinical data both pre- and post-hormone therapy.

Intervention: Initiation of GAHT.

Outcome: Rate of IBD flares following GAHT initiation.

Data analysis: Statistical analyses included univariate comparisons using Pearson's chi-square test and multivariable logistic regression. The Wilcoxon rank-sum test for patients with available C-reactive protein and fecal calprotectin data.

Funding: This research was made possible in part by the Mayo Clinic Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery to Victor Chedid.

Results: A total of 85 transgender and gender-diverse adults with IBD who initiated GAHT were included. The cohort was predominantly White (95.3%) with a median age of 23.5 years. Slightly more than half were diagnosed with Crohn's disease (55.3%), while the remainder had ulcerative colitis (44.7%). At the time of GAHT initiation, 52.9% of participants were in clinical remission.

Overall, the proportion of patients experiencing an IBD flare decreased from 49% before GAHT initiation to 32% after ($P = 0.06$). However, when stratified by hormone type, patients receiving testosterone experienced a significantly higher flare rate post-GAHT (53%) compared to pre-GAHT (26%, $P = 0.01$). Similarly, individuals with active disease prior to GAHT initiation had significantly more flares post-treatment (58%) compared to those in remission at baseline (26%, $P = 0.003$). These findings remained significant in multivariable logistic regression: testosterone use (odds ratio [OR] 3.1, 95% confidence interval [CI] 1.2–8.1; $P = 0.015$) and active disease at baseline (OR 5.1, 95% CI 1.7–15.2; $P= 0.002$) were independently associated with increased flare risk (**Figure 1**).

COMMENTARY

Why Is This Important?

Approximately 1.6% of the US population identify as transgender, with the prevalence rising to 5.1% among young adults.[1] As this population ages, clinicians are increasingly likely to encounter transgender individuals in routine clinical practice. Limited studies suggest that the prevalence of

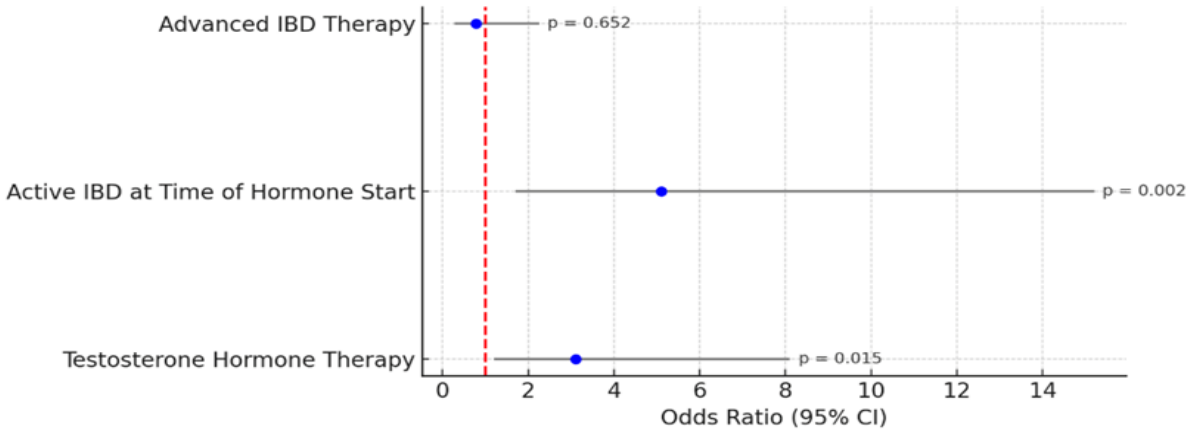

Figure 1. Factors associated with inflammatory bowel disease flares after gender-affirming hormone treatment.

inflammatory bowel disease is similar between transgender and cisgender individuals.[2]

There is limited evidence on the impact of gender-affirming hormone therapy on the clinical course of IBD. Most available data relate to hormone replacement therapy in older, cisgender populations, often at different dosages and risk profiles.[3,4] Sexual and gender minorities remain underrepresented in IBD research, despite facing unique clinical and psychosocial challenges. GAHT is a medically necessary and often life-saving intervention; thus, understanding its implications for chronic inflammatory diseases such as IBD is essential for delivering inclusive, comprehensive, and patient-centered care.[5,6,7]

Key Study Findings

There was no overall significant increase in the risk of IBD flares following initiation of GAHT. However, patients with active IBD at the time of hormone initiation and those who received testosterone were significantly more likely to experience disease flares.

Caution

This study has several limitations. First, it lacked detailed information on GAHT dosing, which may influence both flare risk and treatment response. The specific years included in the chart review were also not reported, which could affect the interpretation of both GAHT and IBD therapies used, given evolving standards of care. Additionally, a key objective marker of IBD flare—endoscopic findings—was unavailable, and serum hormone levels were not reported to determine adequacy of GAHT dosing. Lastly, the absence of patient-reported outcomes limits the ability to assess disease activity beyond objective clinical measures.

My Practice

In patients with IBD who are initiating GAHT, it is important to recognize that GAHT is a life-saving treatment for transgender and gender nonconforming individuals. Therefore, the approach to managing IBD should be focused on planning treatment and monitoring of IBD around the initiation of GAHT. According to this study, it is

important to ensure that a patient with IBD is in remission at time of initiating GAHT, since the risk of flare one year after initiating GAHT is higher in patients with active IBD. This is similar to the practice for patients with IBD who are planning to conceive.

When initiating GAHT, a multidisciplinary approach involving both the GAHT prescribing provider and the IBD provider is essential to coordinate an appropriate IBD management plan at the time of hormone initiation. For patients starting testosterone, an individualized, non-invasive IBD monitoring strategy may be warranted. This could include fecal calprotectin testing every 3 months during the first year, with consideration of radiologic and/or endoscopic evaluation within 6 to 12 months of initiation of GAHT.

For Future Research

Future research should include prospective studies that comprehensively capture IBD outcomes, including both objective clinical markers and patient-reported symptoms, as well as detailed data on GAHT dosing and duration. Further investigation is also needed to determine whether proactive monitoring of IBD patients initiating GAHT is warranted, particularly in those with active disease or those receiving testosterone. Such research will be essential to inform guidelines and optimize care for transgender and gender-diverse individuals living with IBD.

Conflicts of Interest

The authors have no reported conflicts of interest.

Acknowledgments

The authors thank Victor Chedid, MD, MS for his clinical input on the My Practice section of this summary.

Abbreviations

GAHT, gender-affirming hormone therapy; IBD, inflammatory bowel disease.

Happy Pride Month! Rainbows in Gastro is a group of physicians who aim to uplift the LGBTQIA+ community by increasing understanding of the unique digestive health needs of this population via research, advocate for patients on a national platform, and build community amongst our current and future LGBTQIA+ providers and our allies. Visit rainbowsingastro.org to learn more and support this organization as a participant or ally.

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Can Tacrolimus Tame Esophageal Lichen Planus?

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Associate Editor

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This summary reviews Kukreja K, Kumar A, Camisa C, Jacobs J, Richter JE. Esophageal lichen planus: The efficacy and safety of tacrolimus in reducing inflammation and need for dilation. *Clin Trans Gastroenterol*. 2024; 15(12): e00752.

Correspondence to Christopher Velez, MD. Associate Editor. Email: EBGI@gi.org

Keywords: Esophageal lichen planus, tacrolimus, immunosuppressive therapy, esophageal stricture, endoscopy

ESOPHAGEAL DISORDERS

STRUCTURED ABSTRACT

Question: Can low-dose oral tacrolimus effectively and safely reduce inflammation and the need for esophageal dilation in patients with esophageal lichen planus (ELP)?

Design: A retrospective cohort study.

Setting: Single tertiary care academic medical center: the University of South Florida and its affiliated Joy McCann Culverhouse Center for Swallowing Disorders.

Patients: Adults with confirmed ELP who underwent esophagogastroduodenoscopy (EGD) between 2011 and 2020 were included. All EGDs were performed by 1 of 2 esophagologists. Patients were identified via *International Classification of Diseases* and Current Procedural Terminology code review. Clinical, treatment, and endoscopic data were extracted from the electronic medical record.

Interventions: Patients were stratified into 2 cohorts: those treated with oral tacroli-

mus (1–2 mg twice daily) and those receiving alternative therapies (e.g., steroids, cyclosporine, or no treatment). Tacrolimus was prescribed by a dermatologist when standard treatments failed. All patients underwent baseline EGD with biopsy and bougie dilation, with repeat procedures as needed. Disease severity was assessed using the Esophageal Lichen Planus Severity Score (ELPSS), a novel endoscopic scoring tool capturing both inflammatory and fibrostenotic features (**Figure 1**).

Outcomes: The primary outcome was change in ELPSS. Secondary outcomes included clinical response, frequency of dilations, and safety. The tacrolimus group showed a significant reduction in ELPSS (mean decrease of 2.2 points vs 0.3 in controls; $P = 0.02$) and a higher clinical response rate (89% vs 30%; $P = 0.04$). Both groups reached a maximal dilation diameter of 16 mm, though tacrolimus-treated patients required fewer dilations over time, a difference that did not reach statistical significance.

Data Analysis: Descriptive statistics summarized baseline characteristics. Group comparisons used the Mann-Whitney *U* test for continuous variables and chi-square or Fisher's exact test for categorical variables. Treatment effects were reported as mean differences with 95% confidence intervals. Kaplan-Meier analysis with log-rank testing compared response rates; dilation frequency was analyzed as a ratio over follow-up time. Significance was set at $P < 0.05$. Analyses were performed using SPSS v25 (IBM, Armonk, NY).

Funding: No external funding was reported.

Results: Twenty-two patients were included, evenly divided between tacrolimus (TAC) and non-tacrolimus (No-TAC) treatment groups. Baseline demographics and disease severity were comparable between groups. Tacrolimus therapy resulted in a significant reduction in disease severity, with mean ELPSS scores improving from 5.8 to 3.6, compared to a minimal change in the No-TAC group (5.9 to 5.6; $P = 0.02$). Clinical response was significantly higher in the TAC group (89% vs 30%; $P = 0.04$), and Kaplan-Meier analysis confirmed faster time-to-response (**Figure 2**).

All patients underwent bougie dilation, with a maximum diameter of 16 mm achieved in both groups. Although TAC-treated patients required fewer dilations over time, the difference was not statistically significant. Tacrolimus was generally well tolerated; 2 patients discontinued due to mild lab abnormalities. Minor procedural adverse events occurred in 1 patient per group.

These findings suggest that low-dose oral tacrolimus improves clinical and endoscopic outcomes in ELP with an acceptable safety profile.

ELP Severity Score	
Inflammation (Max 6)	**Fibrostenosis (Max 4)**
Pale, edematous, or lacy appearance (1)	None (0)
Sloughing or peeling (2)	Single stricture traversed with 10 mm scope (1)
Exudate (1-mild, 2-moderate, and 3-severe)	Multiple strictures or narrowing (2)
	**Additional points if narrowing required downsize to 5 mm scope (2)
Score range: 1-10. Interpretation: Mild (1-2), Moderate (3-4), Moderate-Severe (5-7), Severe (8-10)	

ELPSS Examples

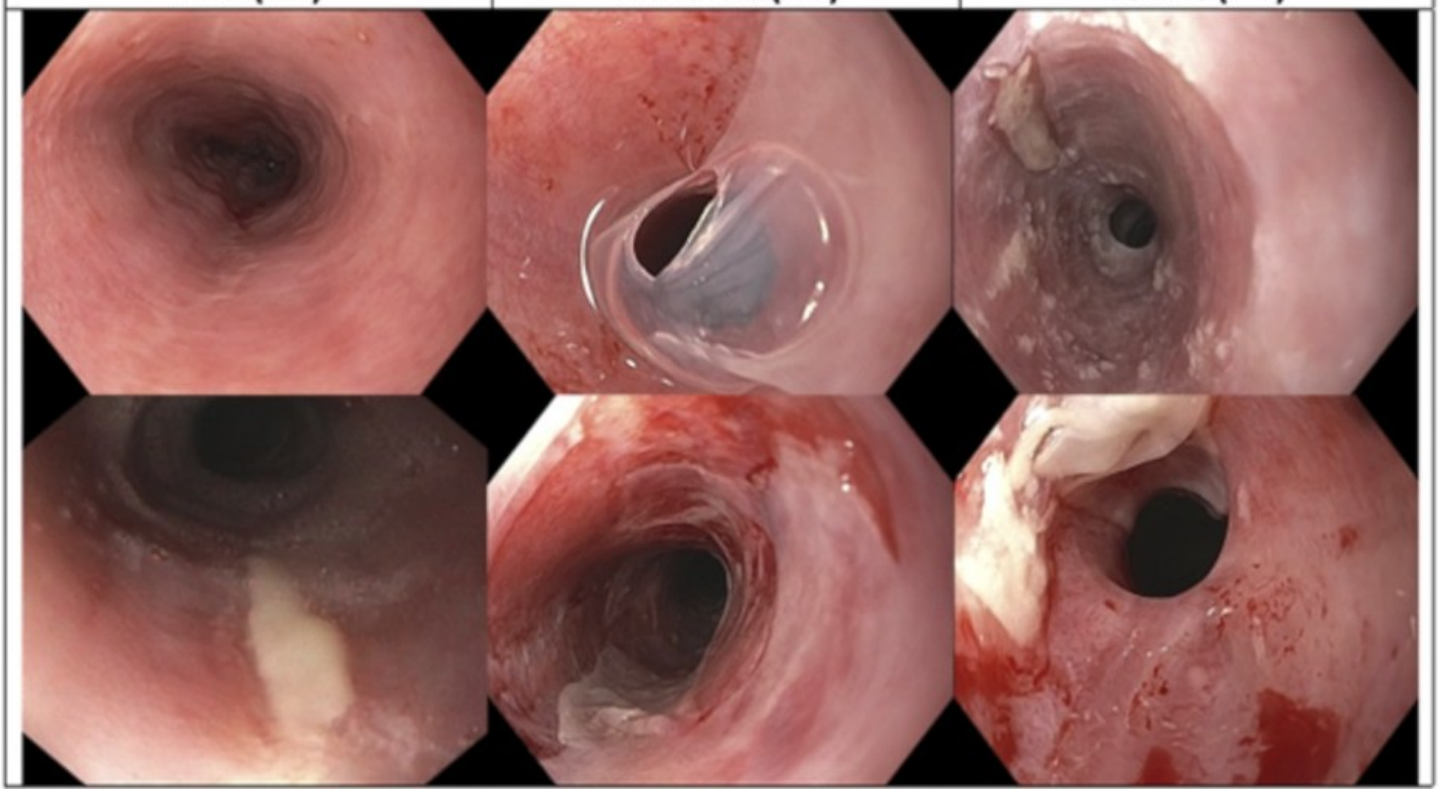

Figure 1. Illustration of the mild (left), moderate (middle), and severe (right) ELPSS. In the inflammatory component, sloughing or peeling occurs spontaneously or with the passage of scope only—not after dilatation. Exudate classification: mild—scattered punctate exudates; moderate—short serpiginous plaques; and severe—long, thick, serpiginous plaques. Within the fibrostenosis component, "multiple narrowing" describes more than one stricture or general narrowing involving more than one location in the esophagus. Adapted from ref. (1). ELP, esophageal lichen planus; ELPSS, Esophageal Lichen Planus Severity Score.

COMMENTARY

Why Is This Important?

ELP is a rare and under-recognized condition that presents significant diagnostic and therapeutic challenges, especially for gastroenterologists who often encounter these patients first. There is no consensus on diagnostic criteria or standard treatment, and existing histologic scoring systems are often impractical for routine use due to variability and nonspecific findings. This study introduces a visually based severity score (ELPSS) tailored for endoscopic use—similar to scoring tools in eosinophilic esophagitis—and highlights the potential of low-dose oral tacrolimus as a safe and effective treatment option for patients with moderate to severe ELP. Addressing this unmet need may improve disease recognition and long-term management.

Key Study Findings

Low-dose oral tacrolimus (1–2 mg twice daily) significantly reduced disease severity in ELP, as measured by ELPSS, compared to alternative therapies.

Patients treated with tacrolimus had a higher response rate (89% vs 30%) and required fewer dilations over time, suggesting both anti-inflammatory and antifibrotic benefits.

Tacrolimus was well tolerated, with only 2 discontinuations due to mild, manageable side effects.

The ELPSS showed good inter-rater reliability and may serve as a practical

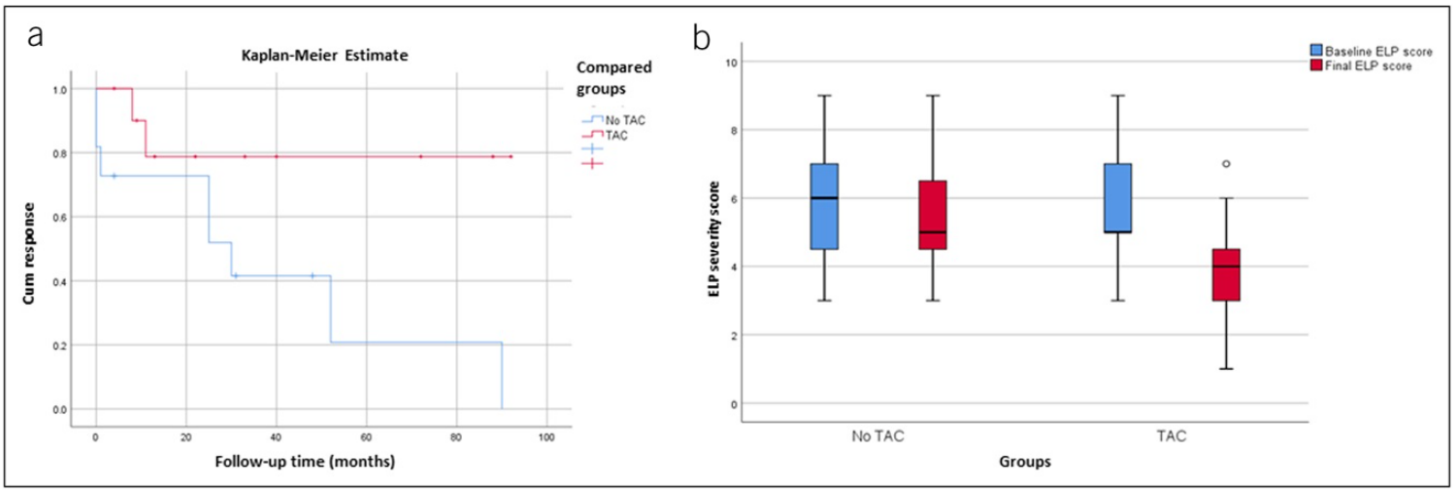

Figure 2. (a) Kaplan-Meier plot of response over time in patients undergoing tacrolimus treatment (TAC) vs no treatment; (b) box plot illustrating pre-post Esophageal Lichen Planus Severity Score in the TAC vs no-TAC group. The horizontal black lines denote median values, and the boxes extend from the 25th to the 75th percentile. The vertical extending lines represent adjacent values, and the dots represent the outliers.
ELP, esophageal lichen planus.

tool for clinicians to assess and monitor ELP severity in real time.

Caution

The principal causes for concern when interpreting this study include its design and sample size. Namely, while the authors did their best to standardize assessment of efficacy and rely upon reasonably objective metrics for success such as dilation practices, the sample size is too small to be definitive. Additionally, there could be long term risks for tacrolimus usage, particularly concerning immune suppression and potential nephrotoxicity (presumably less of a risk with the small doses needed to topical control). Shared decision making is critical prior to electing tacrolimus.

My Practice

Periodically when the EBGI Associate Editors convene, we review which recently published deserve to be summarized for our readership. This article spoke to me because it validated the care I offer a dear patient who I treat, who had been referred to me from a community practice for management of lichenoid esophagitis. Her thoughtful gastroenterologist had tried the usual immune suppressing regimens to no avail, and with good intention recommended gastrostomy tube placement to ensure nutritional status. Ever the spitfire, the patient decided that this was not how she wanted to spend her golden years and sought my opinion. I was initially flummoxed. Faced with dilations every 8-12 weeks with swallowed proton pump inhibitors combined with swallowed steroids, this was not sustainable for either of us. My colleague recommended tacrolimus; as a neuromotilist, I called upon my hepatology colleagues to help with dosing. We settled on a slurry of tacrolimus. Dilations are now spaced to every 6-months, with bougie dilation with a Savary. No more impactions and able to continue a generally normal *per os* intake, the patient is thankful. This article justifies my approach. Tacrolimus is not a first line agent I reach to, as people can be nervous about the immune suppression and the potential for tacrolimus-induced neurotoxicity and nephrotoxicity. But, with refractory strictures that are characteristic of this condition, I certainly would choose tacrolimus over a gastrostomy tube.

For Future Research

Fundamentally, this study is retrospective and small, making it unclear if the devised scoring system will be of utility. A larger data set would be needed for validation. Longer term data examining for possible sequelae of chronic tacrolimus use would be helpful, along with assessment for optimal formulation and dosing. Yet, given that this is a relatively rare condition, I doubt that such a study would be feasible. This study likely will be the best guess as to the role tacrolimus can play in successful management for this disease.

Conflicts of Interest

Dr. Syed reports and Dr. Vélez report no relevant conflicts.

Abbreviations

EGD, esophagogastroduodenoscopy; ELP, esophageal lichen planus; ELPSS, Esophageal Lichen Planus Severity Score; TAC, tacrolimus.

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EVIDENCE-BASED GI
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Surveillance Endoscopy in Barrett's Esophagus: Does It Work?

Dr Margaret J. Zhou
Associate Editor

Margaret J. Zhou, MD, MS

Clinical Assistant Professor of Medicine, Division of Gastroenterology & Hepatology, Stanford University, Stanford, CA

ENDOSCOPY

This summary reviews Old O, Jankowski J, Attwood S, et al; BOSS Trial Team. Barrett's Oesophagus Surveillance Versus Endoscopy at Need Study (BOSS): A Randomized Controlled Trial. Gastroenterology. 2025 Apr 1:S0016-5085(25)00587-6.

Correspondence to Margaret Zhou, MD, MS. Associate Editor. Email: EBGI@gi.org

Keywords: Barrett's esophagus; endoscopy; esophageal adenocarcinoma; RCT

STRUCTURED ABSTRACT

Question: In patients with Barrett's esophagus (BE), does scheduled surveillance endoscopy improve overall survival compared to endoscopy at-need?

Design: Randomized controlled trial (RCT).

Setting: One hundred nine centers in the United Kingdom.

Patients: Individuals ages 18 years or older with non-dysplastic BE (NDBE) or BE with low-grade dysplasia (LGD) diagnosed within 2 years of study recruitment. Patients with high-grade dysplasia (HGD), esophageal adenocarcinoma (EAC), or a history of upper gastrointestinal (GI) cancers were excluded.

Interventions: Patients were randomized to scheduled endoscopic surveillance every 2 years (+/- 3 months) with 4-quadrant biopsies taken every 2 cm or endoscopy at-need (performed for evaluation of symptoms). In both arms, patients were offered endoscopy if they developed dysphagia, unexplained weight loss of >7 lb. iron-deficiency anemia, recurrent vomiting, or worsening upper GI symptoms. Minimum follow-up time was 10 years.

Patients in the at-need endoscopy arm were offered an exit endoscopy, which was recommended by the Data and Safety Monitoring Committee after review of interim trial data. Patients, clinicians, and researchers were aware of the allocated study arm.

Outcomes: The primary outcome was overall survival from the time of randomization to death of any cause. Patients who did not have an event were censored at whichever was first of the date of complete study withdrawal or end of follow-up.

Secondary outcomes included 1) cancer-specific survival, defined as death from all cancers; 2) time to diagnosis of EAC; 3) stage of EAC at diagnosis; 4) serious adverse events related to endoscopy; and 5) frequency of endoscopy.

Data Analysis: Study design was specified for a superiority trial for the primary outcome of overall survival, estimating that 3,400 patients were needed to detect a hazard ratio (HR) of 1.3 at 93% power. All analyses used the intention-to-treat population.

Funding: Health Technology Assessment Programme, United Kingdom.

Results: The study recruited 3,453 patients from March 2009 – November 2011, with 1,733 patients randomized to scheduled surveillance endoscopy and 1,719 patients to endoscopy at-need. Median follow-up was 12.8 years, including 39,512 total patient-years of follow-up.

Mean age at randomization was 63 years, men comprised 71% of participants, and long-segment BE was found in 56%. LGD was present in 1% of patients before trial enrollment. Intestinal metaplasia was present in 75% of patients. Loss to

follow-up occurred in 5.2% of all participants (6.7% in the scheduled surveillance arm vs. 3.6% in the endoscopy at-need arm).

In total, 333 deaths (19.2%) occurred in the scheduled surveillance arm vs 356 deaths (20.7%) in the endoscopy at-need arm, corresponding to a HR for overall survival (OS) of 0.95 (95% confidence interval [CI] 0.82-1.10; log-rank $P = 0.52$) (**Table 1**). Deaths from any cancer occurred in 108 patients in the scheduled surveillance arm (32.4%) vs 106 patients in the at-need endoscopy arm (29.8%) (HR 1.01; 95% CI 0.77-1.33, log-rank $P = 0.76$). Death from esophageal cancer occurred in 22 patients in the scheduled surveillance arm (1.2%) vs 19 patients in the endoscopy at-need arm (1.1%).

Forty patients (2.3%) in the surveillance arm were diagnosed with EAC vs 31 patients (1.8%) in the at-need arm (HR 1.32; 95% CI 0.82-2.11, log-rank $P = 0.210$). This included 18 patients in the surveillance arm vs 12 patients in the at-need arm with T1, T1a, or T1b cancers. Few patients were diagnosed with nodal or metastatic disease, but these proportions were similar between the 2 groups.

In the surveillance arm, 1,606 patients (93%) underwent at least 1 endoscopy during the study period compared to 1,006 (59%) of patients in the at-need arm. Median interval between endoscopies was 24.8 months in the surveillance arm vs 25.7 months in the at-need arm.

	Adjusted HR (95% CI)	Log-rank P-value
Overall survival	0.95 (0.82-1.10)	0.520
Cancer-specific mortality	1.01 (0.77-1.33)	0.761
EAC diagnosis	1.32 (0.82-2.11)	0.210

Table 1. Results from adjusted Cox regression models comparing scheduled surveillance endoscopy vs at-need endoscopy.[a]

[a] Adjusted models included all randomization factors as well as prognostic factors including sex, indefinite or low-grade dysplasia, obesity, and time from BE diagnosis to trial entry.

COMMENTARY

Why Is This Important?

This is the first RCT to study endoscopic surveillance in BE and the largest existing RCT of patients with BE.

Key Study Findings

Among 3,453 patients with BE, this study found no difference in overall survival in patients randomized to surveillance endoscopy every 2 years vs at-need endoscopy offered for symptoms (19.2% vs 20.7%; 95% CI 0.82-1.10; log-rank $P = 0.52$).

Caution

This is an important and needed study to understand the impact of endoscopic surveillance in BE. However, the study conclusion that there was no statistically significant difference in outcomes, specifically overall survival, between patients in the scheduled surveillance vs. at-need endoscopy arms should be interpreted cautiously due to several limitations.

This study was likely underpowered to detect a difference in all-cause mortality due to the sample size calculation being based on a relatively large HR of 1.3. The authors acknowledge that at the time the trial began in 2009, the risk of progression of BE to EAC was estimated to be closer to 1% per year, whereas progression based on more recent data is estimated to be closer to 0.2% per year.[1, 2] Thus, the sample size needed to detect a difference between groups is likely much larger than was calculated and recruited for this study. Furthermore, the study did not address the important question of whether surveillance endoscopy impacted EAC-related mortality. The study did report on esophageal cancer-related mortality but did not specify whether these were cases of EAC or esophageal squamous cell carcinoma, which is important to differentiate in a BE cohort.

There was significant cross-contamination between treatment arms, as a large proportion of patients (59%) in the endoscopy at-need arm underwent at least 1 endoscopy during the study period. Patients in the at-need arm underwent endoscopy at almost the same surveillance interval as the scheduled surveillance arm (25.7 months in the at-need arm vs 24.8 months in the scheduled surveillance arm). This likely biased the study results towards the null.

Of note, 25% of patients did not have intestinal metaplasia (IM) on pathology, which may make extrapolation to US-based BE cohorts challenging as IM is required for diagnosis of BE based on American guidelines. This may have further biased the study towards the null given that progression rates of columnar-lined mucosa without pathologically confirmed IM to EAC is lower than that of IM.[1]

Lastly, the study did not provide data on the quality of surveillance endoscopy, such as adherence to Seattle protocol biopsies or use of advanced imaging techniques. The high proportion of T2 cancers in the scheduled surveillance arm (35% of EACs) was similar to the at-need arm (32% of EACs).[3, 4] These proportions are higher than reported in other BE cohorts, which raises the question of possible missed lesions or endoscopic quality in the surveillance arm.

My Practice

Current guidelines recommend surveillance endoscopy every 3-5 years for patients with NDBE.[5] Based on this study, it is difficult to conclude that there was no benefit with scheduled surveillance endoscopy, and I do not plan to change my approach to endoscopic surveillance. In my patients with NDBE, I generally perform endoscopic surveillance every 3 years and discuss with patients the option of surveillance every 5 years if they have short-segment BE without any other significant risk factors for EAC (i.e., family history of EAC, tobacco use, obesity). During surveillance endoscopy, I perform a high-quality endoscopy using a distal attachment cap with both white-light and virtual chromoendoscopy (most frequently, narrow band imaging in my practice). I also aim to spend adequate time inspecting the BE segment (approximately 1 minute per centimeter of BE) and adhere to Seattle protocol biopsies (4-quadrant biopsies every 2 cm for NDBE or every 1 cm for patients with a history of dysplasia) with separate biopsies taken for visible lesions. The quality of endoscopy has been associated with improved neoplasia detection in BE cohorts and likely has a significant impact on the efficacy of surveillance programs.

For Future Research

While an additional RCT with a larger sample size may be helpful to address the limitations of this study, conducting another RCT on endoscopic surveillance in BE will be very challenging. Instead, further study on the use of risk stratification tools or biomarkers to help with predicting progression to HGD/EAC may provide more personalized surveillance strategies for patients with BE. Furthermore, additional research on quality metrics in endoscopy for BE is needed, as there are currently no widely established quality metrics to assess BE care.

Conflicts of Interest

Dr. Zhou reports no conflicts of interest related to this study.

Abbreviations

BE, Barrett's esophagus; CI, confidence interval; EAC, esophageal adenocarcinoma; HGD, high-grade dysplasia; HR, hazard ratio; IM, intestinal metaplasia; LGD, low-grade dysplasia; NDBE, non-dysplastic BE; OS, overall survival; RCT, Randomized controlled trial.

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EVIDENCE-BASED GI
AN ACG PUBLICATION

Subcutaneous Guselkumab Is Effective for Both Induction and Maintenance of Crohn's Disease

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IBD

This summary reviews Hart A, Panaccione R, Steinwurz F, et al. Efficacy and safety of guselkumab subcutaneous induction and maintenance in participants with moderately to severely active Crohn's disease: Results from the phase 3 GRAVITI Study. *Gastroenterology*. 2025:S0016-5085(25)00522-0.

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Keywords: Crohn's disease, guselkumab, placebo-controlled trial

STRUCTURED ABSTRACT

Question: Is subcutaneous (SC) guselkumab safe and effect for moderate-to-severe Crohn's disease (CD) for both induction and maintenance?

Design: Phase 3, randomized, double-blind, placebo-controlled treat-through trial.

Setting: One hundred forty-three centers across 23 countries or territories.

Patients: Three hundred forty-seven adults of age ≥18 years with moderately to severely active CD and prior exposure to one or more biologic or conventional therapies

Interventions: Patients were randomized in a 1:1:1 ratio to receive either a placebo, guselkumab 400 mg SC every 4 weeks (q4w) for induction followed by 100 mg SC q8w for maintenance (standard dose maintenance), or 400 mg SC q4w for induction followed by 200 mg SC q4w for maintenance (high dose maintenance).

Outcomes: Co-primary endpoints were the clinical remission (Crohn's Disease Activity Score <150) and endoscopic response (≥50% reduction of baseline Simple Endoscopic Score for Crohn's Disease) score), both at week 12. Other endpoints included Patient-Reported Outcome-2 remission (abdominal pain score ≤1 and stool frequency score ≤3) at week 12, clinical response at week 12, clinical remission at weeks 24 and 48, change in C-reactive protein and fecal calprotectin, and adverse events.

Data Analysis: Common Risk Differences were calculated using Mantel-Haenszel stratum weights at a significance level of 0.05. Efficacy analyses were performed for participants who received ≥1 dose of study agent.

Funding: Johnson & Johnson.

Results: At week 12, guselkumab was superior to placebo for clinical remission (56.1% vs 21.4%, $P < 0.01$) and endoscopic response (41.3% vs 21.4%, $P < 0.01$). Similar findings were observed at week 48 for clinical remission (60.0% standard dose, 66.1% high dose, 17.1% placebo, $P < 0.01$) and endoscopic response (44.3%, 51.3%, 6.8%, $P < 0.01$) (**Figure 1**). Guselkumab was effective for both bio-naïve and bio-exposed patients. Median C-reactive protein and fecal calprotectin concentrations decreased through week 48 with guselkumab compared to placebo. Adverse events were similar between guselkumab (327.2 per 100 participant years [PY] high dose maintenance, 307.2 per 100 PYs standard dose maintenance) and placebo (413.0 per 100 PYs).

COMMENTARY

Why Is This Important?

The GALAXI trials have previously established the efficacy of guselkumab for induction and maintenance of moderate-to-severe CD.[1,2] Guselkumab is now the third approved anti-interleukin (IL) 23 therapy approved for this indication.[3,4] However, the GRAVITI trial is the first to evaluate an IL-23 therapy with a SC induction option. Efficacy results for both induction and maintenance in GRAVITI were overall similar to the findings from the GALAXI trials, which only included IV induction of guselkumab. Importantly, both trials utilized treat-through designs to better represent real-world clinical practice. SC induction offers patients greater convenience and less resource utilization but without sacrificing clinical efficacy through at least 48 weeks of therapy.

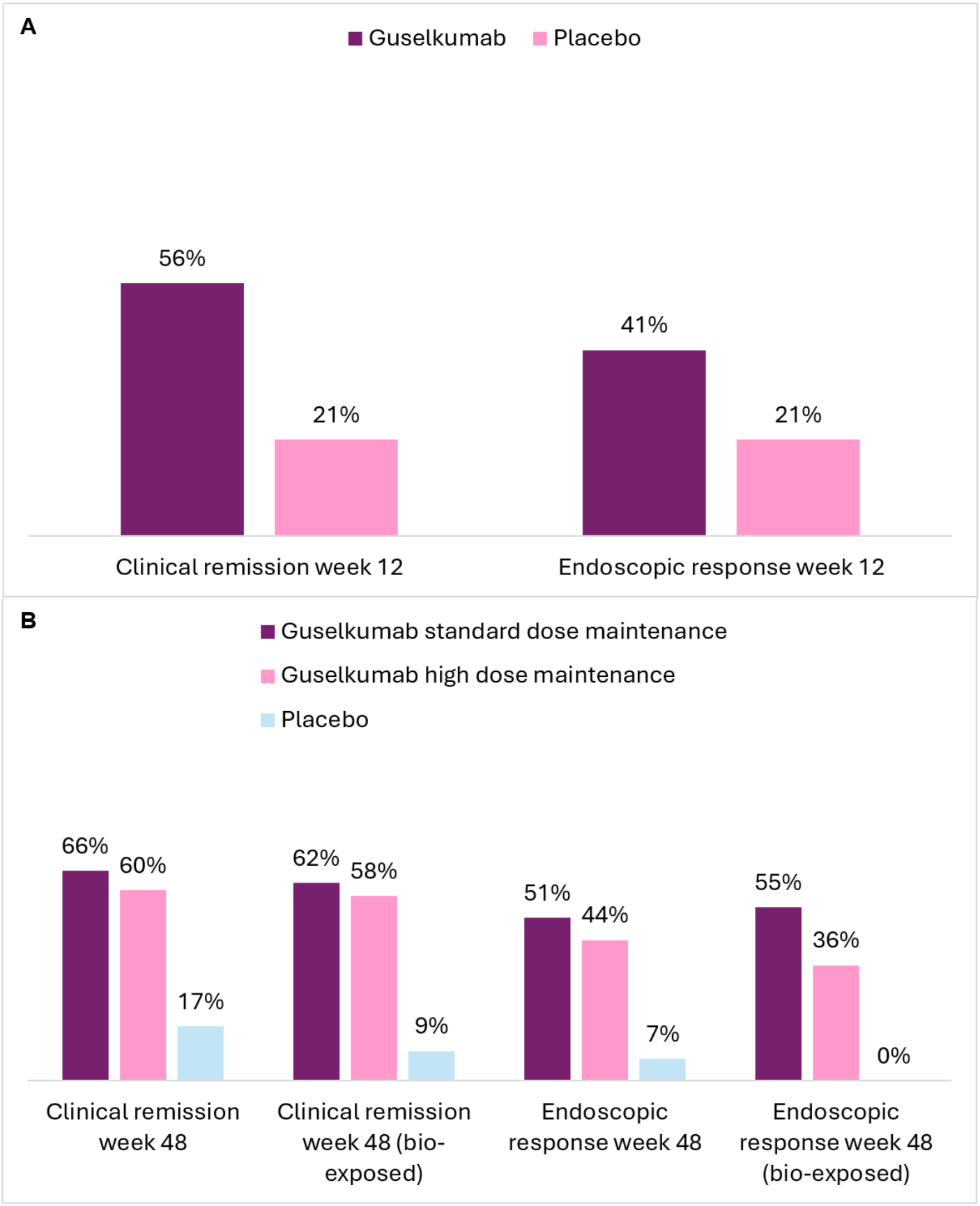

Figure 1. **A**. Coprimary endpoints for subcutaneous guselkumab vs placebo. **B**. Selected 48-week endpoints. All comparisons vs placebo are statistically significant at $P = 0.05$.

Key Study Findings

The study found that SC guselkumab for both induction and maintenance resulted in superior clinical and endoscopic outcomes through 48 weeks compared to placebo.

Efficacy was maintained for both bio-naïve and bio-exposed populations. These findings were consistent with results from the GALAXI trials that utilized IV guselkumab induction. Adverse events were similar between both dosing regimens of SC guselkumab maintenance and placebo, and the most commonly reported AEs being upper respiratory tract infections, abdominal pain, and COVID-19. No new safety signals were identified in this study when compared to other indications for guselkumab, including ulcerative colitis. Anti-guselkumab antibodies were detected in 8.8% of participants, however there was no impact on serum guselkumab concentrations, efficacy, or safety.

Caution

The study was not designed to detect differences in efficacy and safety between SC maintenance regimens, nor were there statistical comparisons to intravenous induction regimens. Maintenance dose escalation from 100 mg q8w to 200 mg q4w was not assessed in cases of loss of response, which should be the subject of future research. The long-term efficacy, safety, and durability of SC guselkumab maintenance therapy are also unknown.

My Practice

In my practice, I commonly prescribe IL-23 antagonists as both first and second-line therapies for both CD and ulcerative colitis. Now with a SC induction option, I will likely utilize guselkumab therapy more often than other IL-23 antagonists for Crohn's disease. The majority of my patients appreciate and prefer the convenience of SC therapies over intravenous infusions for both induction and maintenance. Furthermore, the option of having 2 maintenance dosing regimens allows me to tailor my therapy to a patient's disease severity.

For Future Research

Because of the rapid growth of advanced therapies for inflammatory bowel disease, there is an increasing need for head-to-head trials and comparative effectiveness studies to guide therapy selection. Additionally, we require large, prospective studies to evaluate and compare the effectiveness of IL-23 antagonists across the various disease locations and phenotypes of CD (e.g. ileal and fistulizing disease).

Conflict of Interest

Dr. Dalal has research grant support from Janssen and Pfizer and has served as a consultant for Janssen, Takeda, and Centaur Labs.

Abbreviations

CD, Crohn's disease; COVID-19, coronavirus disease-2019; q4w, Every 4 weeks; q8w, every 8 weeks; PY, participant year; SC, subcutaneous.

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