Centre universitaire de santé McGill
McGill University Health Centre

Mentorat sur les MII:

Trois articles ayant marqué l'année 2023

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Centre universitaire de santé Mcgill , Montreal, Canada
13 Avril, 2024

Déclaration de conflits d’intérêts

X J’ai établi des relations avec une organisation à but lucratif ou sans but lucratif

Nature des relations	Nom de l’organisation à but lucratif ou sans but lucratif
Les paiements directs incluant les honoraires	Abbvie, Amgen, Avir, BMS, Celltion, Fresenius Kabi, Janssen, Innomar, Pfizer, Takeda
La participation à des comités consultatifs ou des bureaux de conférenciers	Abbvie, Amgen, Avir, BMS, Celltion, Fresenius Kabi, Janssen, Innomar, Pfizer, Takeda
Le financement de subventions ou d’essais cliniques	Abbvie, Janssen, Takeda
Les brevets sur un médicament, un produit ou un appareil	
Tout autre investissement ou toute autre relation qu’un participant raisonnable et bien informé pourrait considérer comme un facteur d’influence sur le contenu de l’activité éducative	

Compétences CanMEDS

X	**Expert médical** (En tant qu'experts médicaux, les médecins assument tous les rôles CanMEDS et s'appuient sur leur savoir médical, leurs compétences cliniques et leurs attitudes professionnelles pour dispenser des soins de grande qualité et sécuritaires centrés sur les besoins du patient. Pivot du référentiel CanMEDS, le rôle d'expert médical définit le champ de pratique clinique des médecins .)
	Communicateur (En tant que communicateurs, les médecins développent des relations professionnelles avec le patient et ses proches ce qui permet l'échange d'informations essentielles à la prestation de soins de qualité.)
X	**Collaborateur** (En tant que collaborateurs, les médecins travaillent efficacement avec d'autres professionnels de la santé pour prodiguer des soins sécuritaires et de grande qualité centrés sur les besoins du patient.)
	Leader (En tant que leaders, les médecins veillent à assurer l'excellence des soins, à titre de cliniciens, d'administrateurs, d'érudits ou d'enseignants et contribuent ainsi, avec d'autres intervenants, à l'évolution d'un système de santé de grande qualité.)
	Promoteur de santé (En tant que promoteurs de la santé, les médecins mettent à profit leur expertise et leur influence en oeuvrant avec des collectivités ou des populations de patients en vue d'améliorer la santé. Ils collaborent avec ceux qu'ils servent afin d'établir et de comprendre leurs besoins, d'être si nécessaire leur porte-parole, et de soutenir l'allocation des ressources permettant de procéder à un changement.)
X	**Érudit** (En tant qu'érudits, les médecins font preuve d'un engagement constant envers l'excellence dans la pratique médicale par un processus de formation continue, en enseignant à des tiers, en évaluant les données probantes et en contribuant à l'avancement de la science.)
	Professionnel (En tant que professionnels, les médecins ont le devoir de promouvoir et de protéger la santé et le bien-être d'autrui, tant sur le plan individuel que collectif. Ils doivent exercer leur profession selon les normes médicales actuelles, en respectant les codes de conduite quant aux comportements qui sont exigés d'eux, tout en étant responsables envers la profession et la société. De plus, les médecins contribuent à l'autoréglementation de la profession et voient au maintien de leur santé.)

Learning Objectives

At the end of this presentations, participants will be able to:

- Evaluate data that was newly published, in scientific journals, throughout the year 2023
- Assess the impact these data could have within the Canadian IBD landscape
- Discuss how these advancements can impact the care of IBD patients

3 new ways to treat IBD in 2024

PRE-BIOLOGIC THERAPY

DUAL BIOLOGIC THERAPY

CHRONIC POUCHITIS

Early Ileocecal Resection for Crohn's Disease Is Associated With Improved Long-term Outcomes Compared With Anti-Tumor Necrosis Factor Therapy: A Population-Based Cohort Study

Manasi Agrawal,[1,2] Anthony C. Ebert,[1] Gry Poulsen,[1] Ryan C. Ungaro,[2] Adam S. Faye,[3] Tine Jess,[1,4] Jean-Frederic Colombel,[2] and Kristine H. Allin[1,4]

Gastroenterology 2023;165:976–985

Early ileocecal resection for Crohn's disease

Early effective therapy is important for improving long-term outcomes. Generally, this has meant early effective medical therapy.

Surgery is traditionally reserved for the management of CD complications.

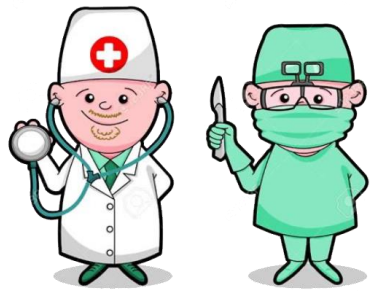
LIR!C Open Label RCT; ICR vs IFX as a first-line treatment for inflammatory ileocecal CD:

- Comparable QOL at 1 year[1]
- Lower direct healthcare cost at 1 year[2]
- Lower use of advanced therapy[3]:
  - ICR: 0% repeat ICR, 26% initiated anti-TNF, 32% initiated another therapy, **42% no additional therapy**
  - IFX: 48% required ICR, 52% continued IFX/switched/escalated*

GETAID ECCO 2023[4]

Retrospective French nationwide study of 592 patients undergoing ICR.

~ **40% of patients with medically refractory inflammatory ileal CD who undergo ICR achieve durable remission** (Rutgeerts ≤ i1) ≥36 months.



1. Ponsioen CY, et al. Lancet Gastroenterol Hepatol. 2017 Nov;2(11):785-792
2. de Groof EJ, et al. Gut. 2019 Oct;68(10):1774-1780
3. Stevens TW et al. Lancet Gastroenterol Hepatol 2020;5:900-7
4. Abdalla S et al. ECCO 2023 Abstract DOP77

Early ileocecal resection for Crohn's disease

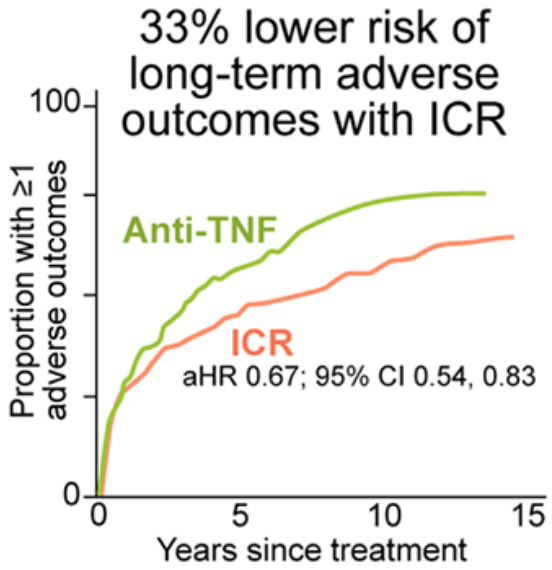
- **Aims**
- To compare long-term outcomes of ICR and anti-TNF therapy as primary treatment for ileal or ileocecal CD, initiated within 1 year of diagnosis, within the population based the Danish nationwide cohort.

- **Methods**
- Population-based cohort study from Denmark, comparing ICR vs anti-TNF as index treatment for ileocecal CD within 1 year of diagnosis (2003-2018)
- 15 years (2003 – 2018)

- **Primary outcome (composite):**
- **CD related hospitalization, systemic corticosteroid exposure, CD-related surgery, perianal CD.**

Results – primary composite outcome

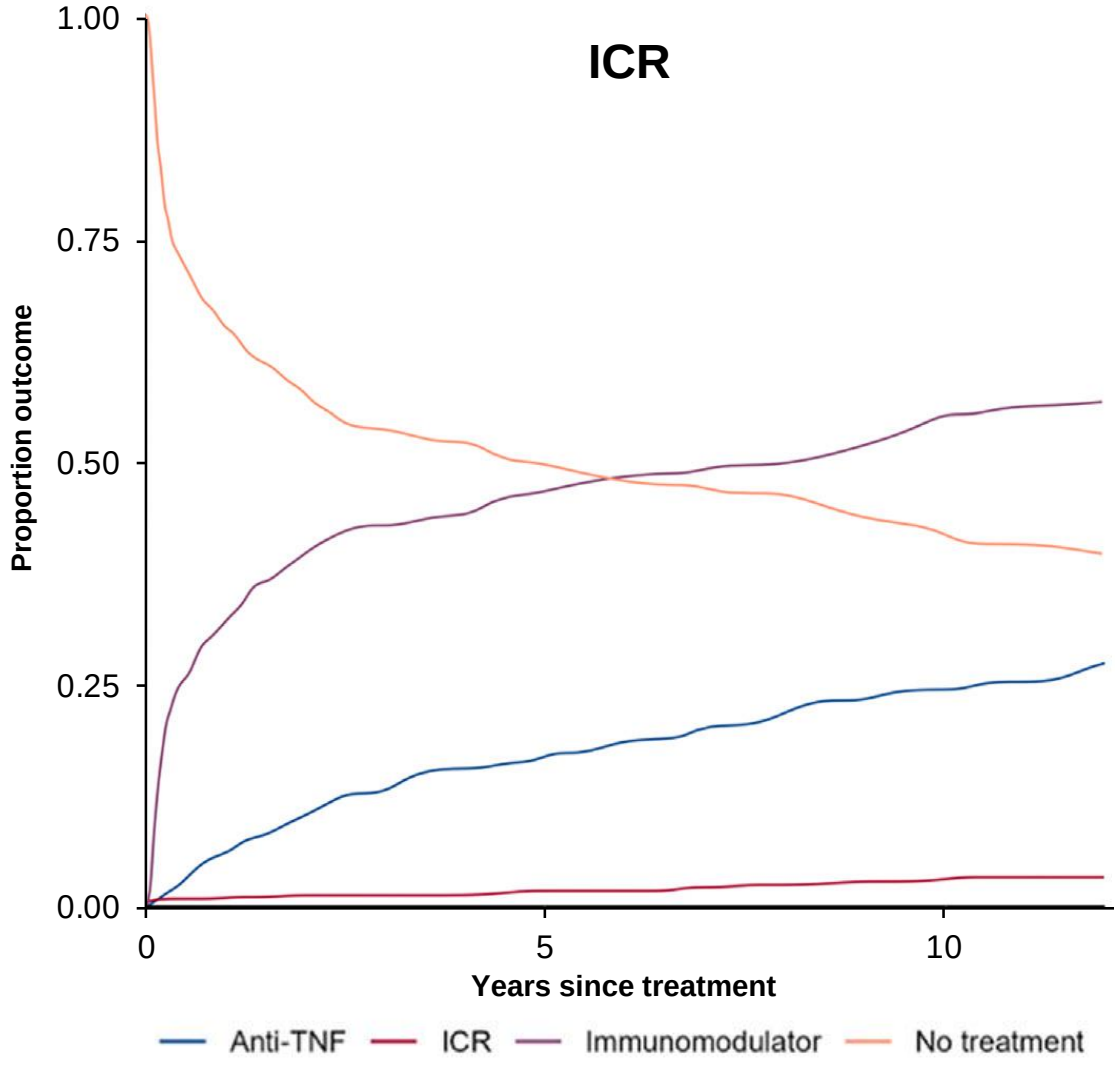
- 16,443 individuals diagnosed with CD between 2003 and 2018
- 1279 with ileocolonic or ileal CD and no prior surgery or biologic therapy; anti-TNF n=698, ICR n=581

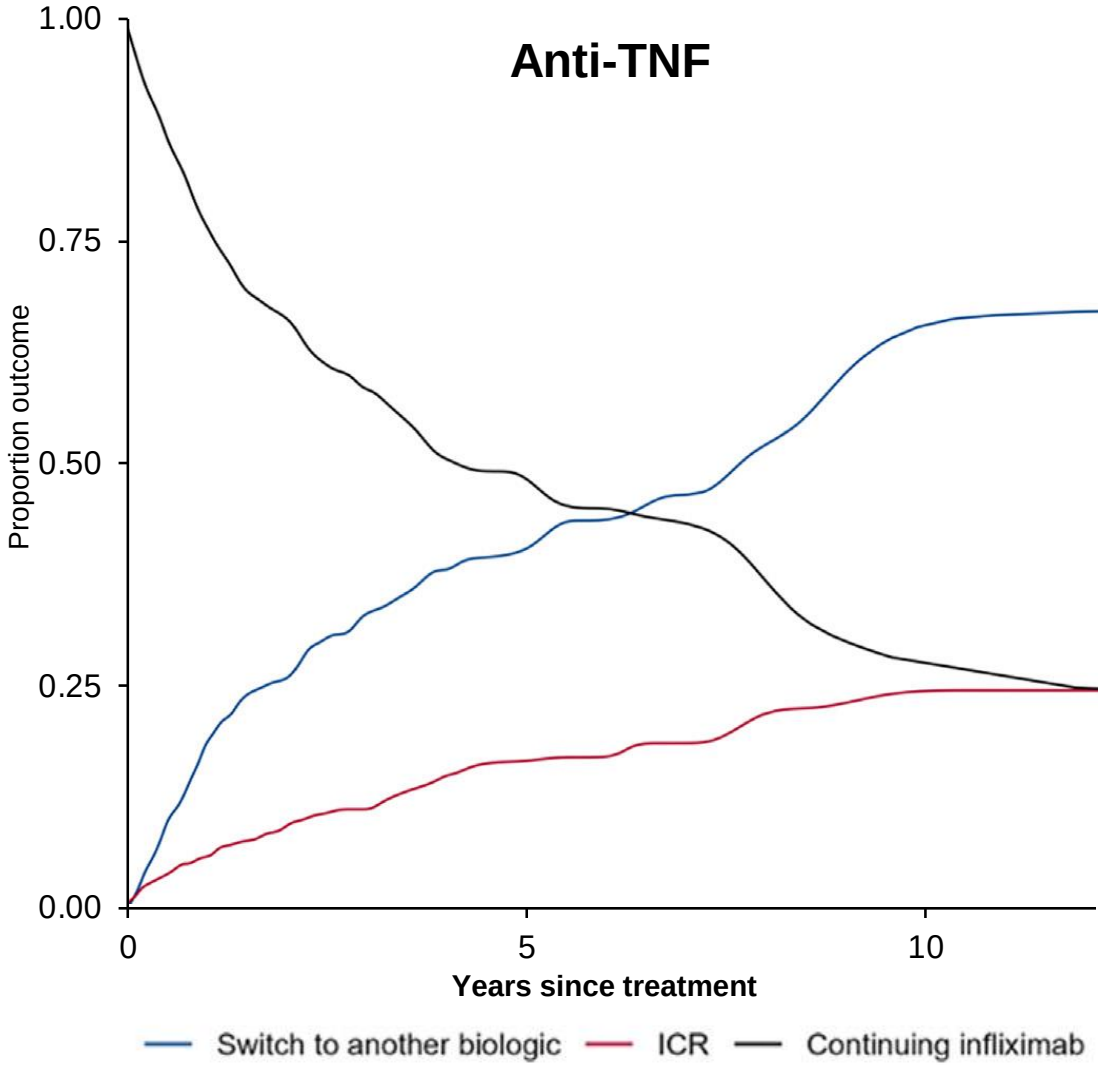


Secondary outcomes			
CD-related hospitalization	0.79	0.61	1.01
Systemic corticosteroids	0.71	0.54	0.92
CD-related surgery	0.56	0.39	0.80
Perianal CD	0.70	0.38	1.30

*Adjusted for age, sex, year, number of prior hospitalizations, number of unique prescription medications, corticosteroid, and IMM exposure

Results – secondary outcomes





Conclusions

1. Early ICR in patients select CD patient appears safe and associated with improved long-term outcomes
2. This study supports previous data and suggests some patients with inflammatory ileal CD can achieve a durable remission following early ICR
3. Ileocecal resection may not need to be reserved for patients with complications of Crohn’s disease

Guselkumab plus golimumab combination therapy versus guselkumab or golimumab monotherapy in patients with ulcerative colitis (VEGA): a randomised, double-blind, controlled, phase 2, proof-of-concept trial

Prof Brian G Feagan MD [a], Prof Bruce E Sands MD [b], Prof William J Sandborn MD [c], Matthew Germinaro MD [d], Marion Vetter MD [d], Jie Shao PhD [d], Shihong Sheng PhD [d], Jewel Johanns PhD [d], Prof Julián Panés MD [e]
VEGA Study Group†

The Lancet Gastroenterology & Hepatology Volume 8, Issue 4, April 2023, Pages 307-320

Introduction

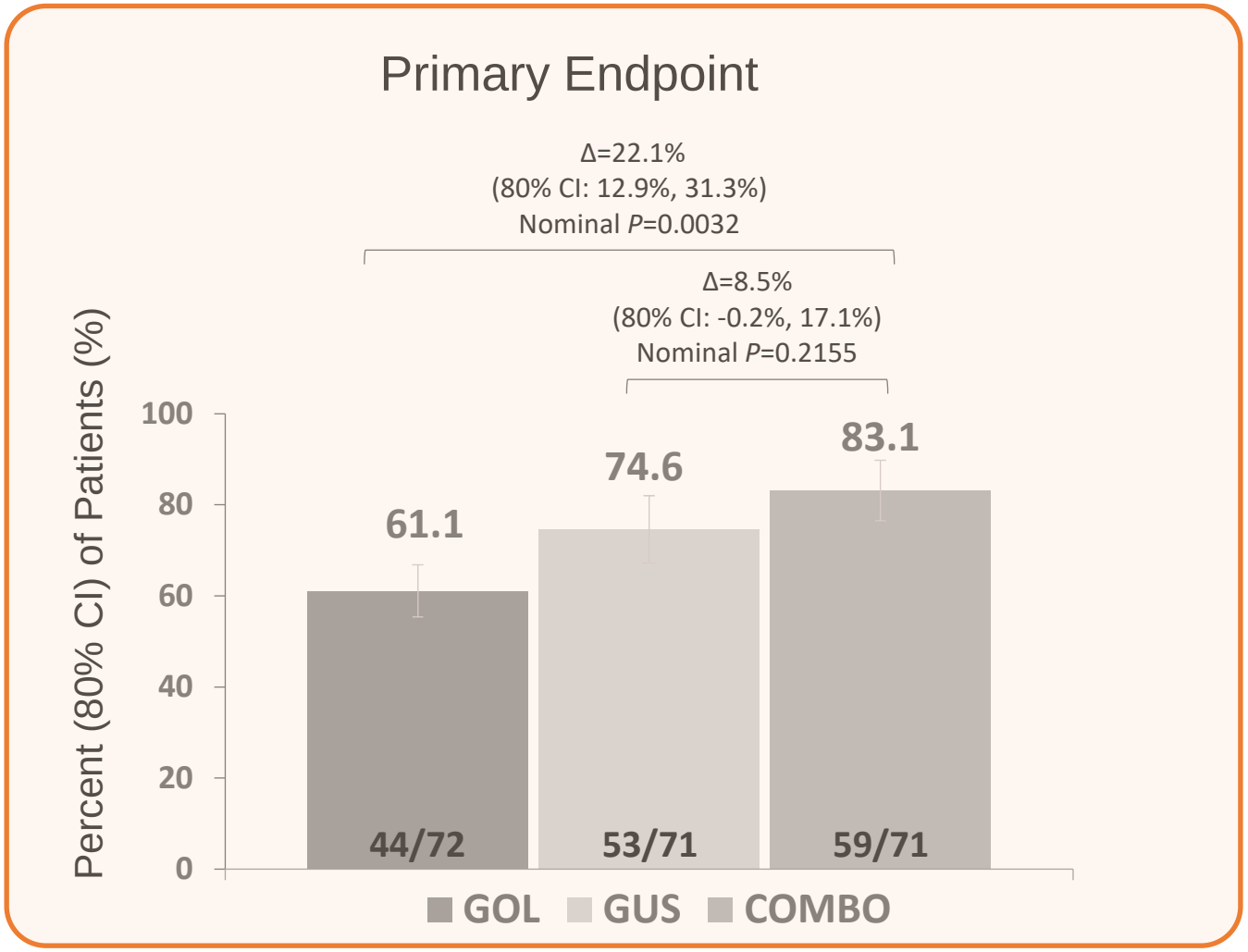
- Despite multiple new biologics to treat UC, clinical remission rates remain quite low (30-40%)
- Dual biologic therapy is being used in the clinic for refractory IBD patients with moderate success
- Can the use of dual biologics in bio-naïve UC patients during induction improve clinical remission rates

Baseline Patient Characteristics

	GOL	GUS	COMBO → GUS
Number of Patients	72	71	71
Mean age (SD), years	38.1 (10.47)	39.1 (13.67)	37.8 (11.69)
Male, n (%)	42 (58.3)	40 (56.3)	34 (47.9)
UC duration, years, mean (SD)	**4.7 (4.48)**	**5.4 (5.70)**	**4.6 (4.61)**
Disease limited to left side of colon, n (%)	38 (52.8)	36 (50.7)	50 (70.4)
Full Mayo score (0-12), mean (SD)	8.7 (1.44)	8.9 (1.33)	8.8 (1.37)
Endoscopy subscore (0-3), n (%)			
Subscore of 2 (moderate)	35 (48.6)	24 (33.8)	28 (39.4)
Subscore of 3 (severe)	**37 (51.4)**	**47 (66.2)**	**43 (60.6)**
Patients receiving CS at baseline, n (%)	31 (43.1)	28 (39.4)	29 (40.8)
CRP (mg/L), median (IQR)*	2.5 (1.2; 7.7)	3.4 (1.0; 12.1)	3.9 (1.1; 13.5)
FCal (mg/kg), median (IQR)†	1588.0 (421.0; 3224.0)	1511.0 (495.0; 4166.0)	1577.0 (605.0; 3577.0)
UC Medication History, no. (%)			
Immunosuppressants‡	24 (33)	28 (39)	37 (52)
VDZ	0	3 (4)	5 (7)
TOFA	1 (1)	1 (1)	2 (3)

*Data for CRP concentrations were available for 213 patients: 71 receiving combination therapy, 72 receiving GOL monotherapy, and 70 receiving GUS monotherapy. †Data for FCal, concentrations were available for 203 patients: 67 receiving combination therapy, 69 receiving GOL monotherapy, and 67 receiving GUS monotherapy. ‡Immunosuppressants included AZA, 6-MP, or MTX. 6-MP, 6-mercaptopurine; AZA, azathioprine; CRP, C-reactive protein; CS, corticosteroid; FCal, fecal calprotectin; GOL, golimumab; GUS, guselkumab; IQR, interquartile range.; MTX, methotrexate; VDZ, vedolizumab. Feagan BG, et al. Lancet Gastroenterol Hepatol. 2023;8(4):307-320.

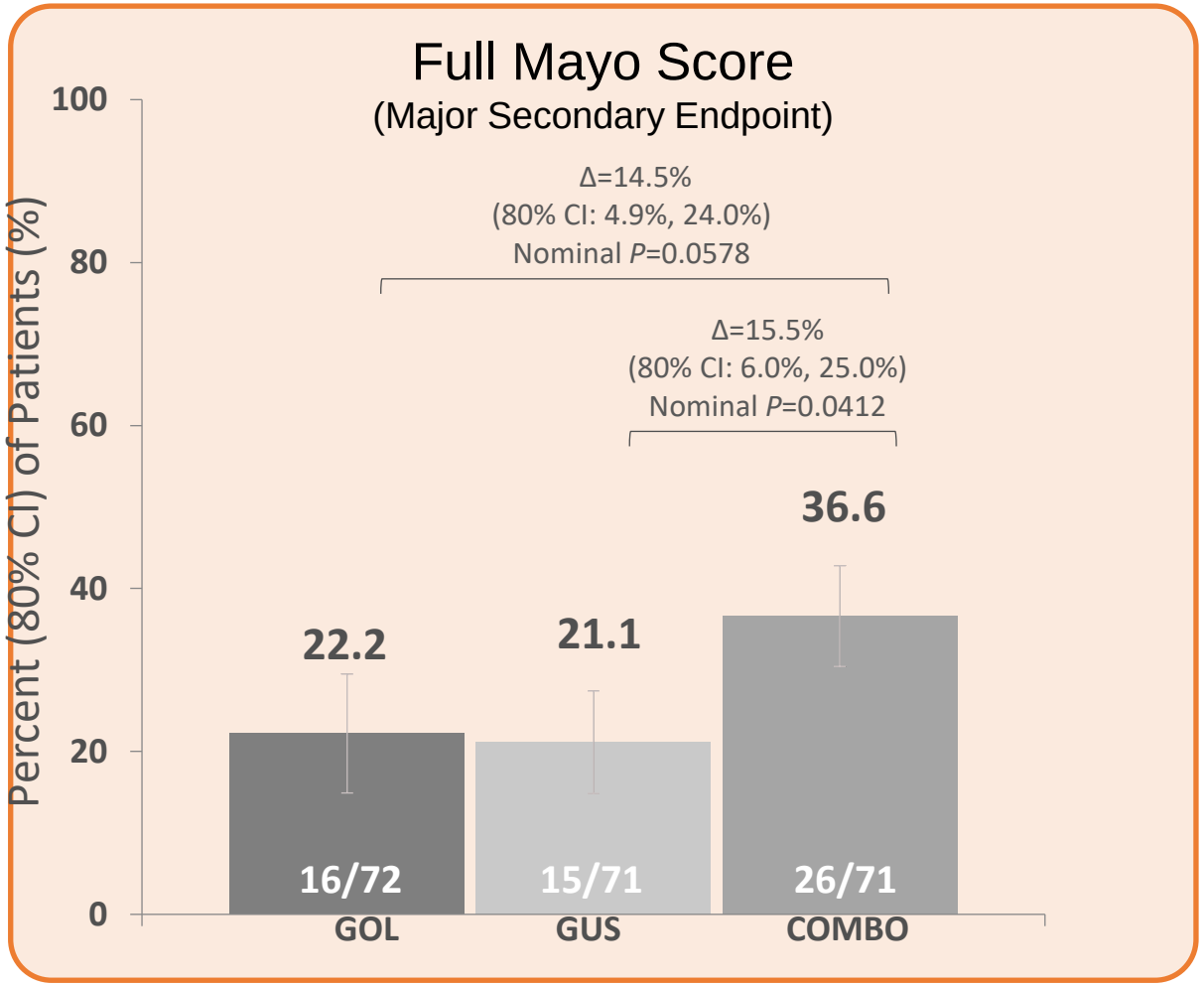
Clinical Response at Week 12



Statistical significance was not achieved between the combination therapy group and both monotherapy groups, thus the primary efficacy endpoint was not met. Clinical Response (Full Mayo Score): Decrease from Baseline in the Mayo Score ≥30% and ≥3 Points with either a Decrease in RBS≥1 or a RBS= 0/1.

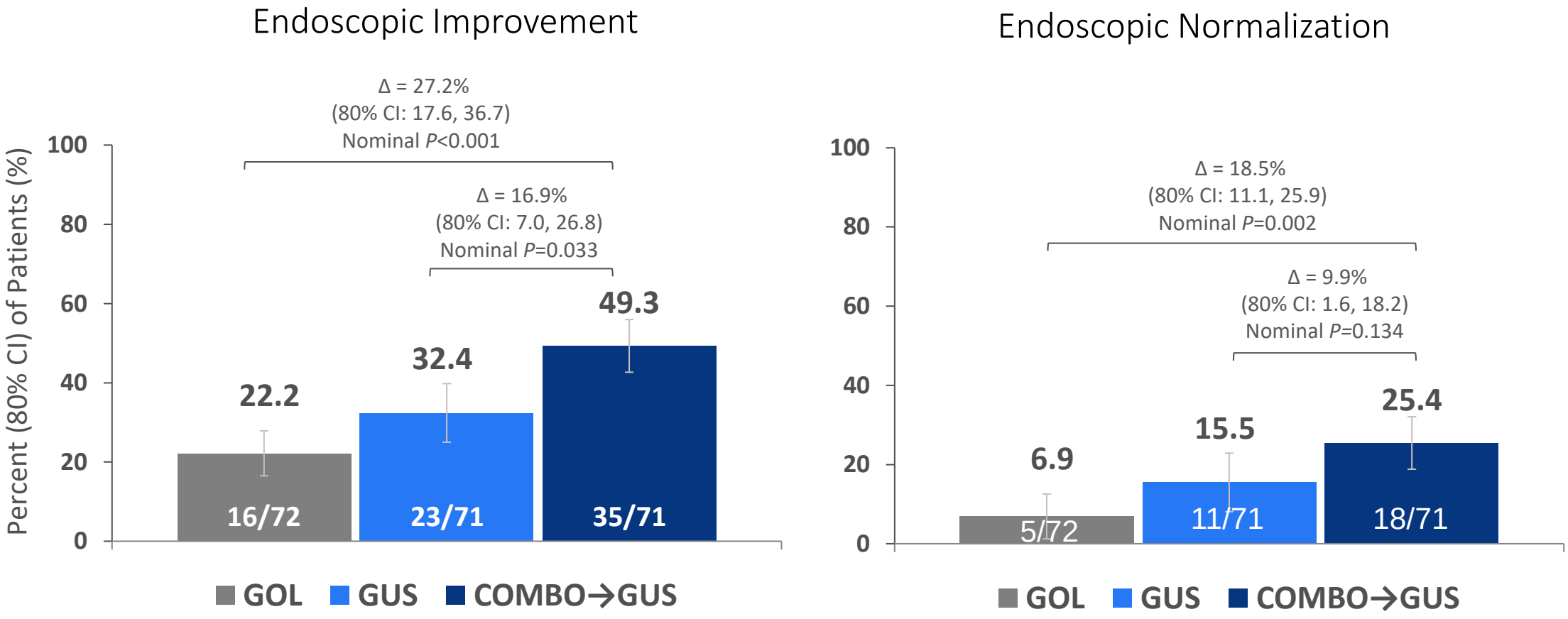
1. Feagan BG, et al. DDW 2022. Oral Presentation #886. 2. Feagan BG, et al. Lancet Gastroenterol Hepatol. 2023;8(4):307-320.

Clinical Remission at Week 12



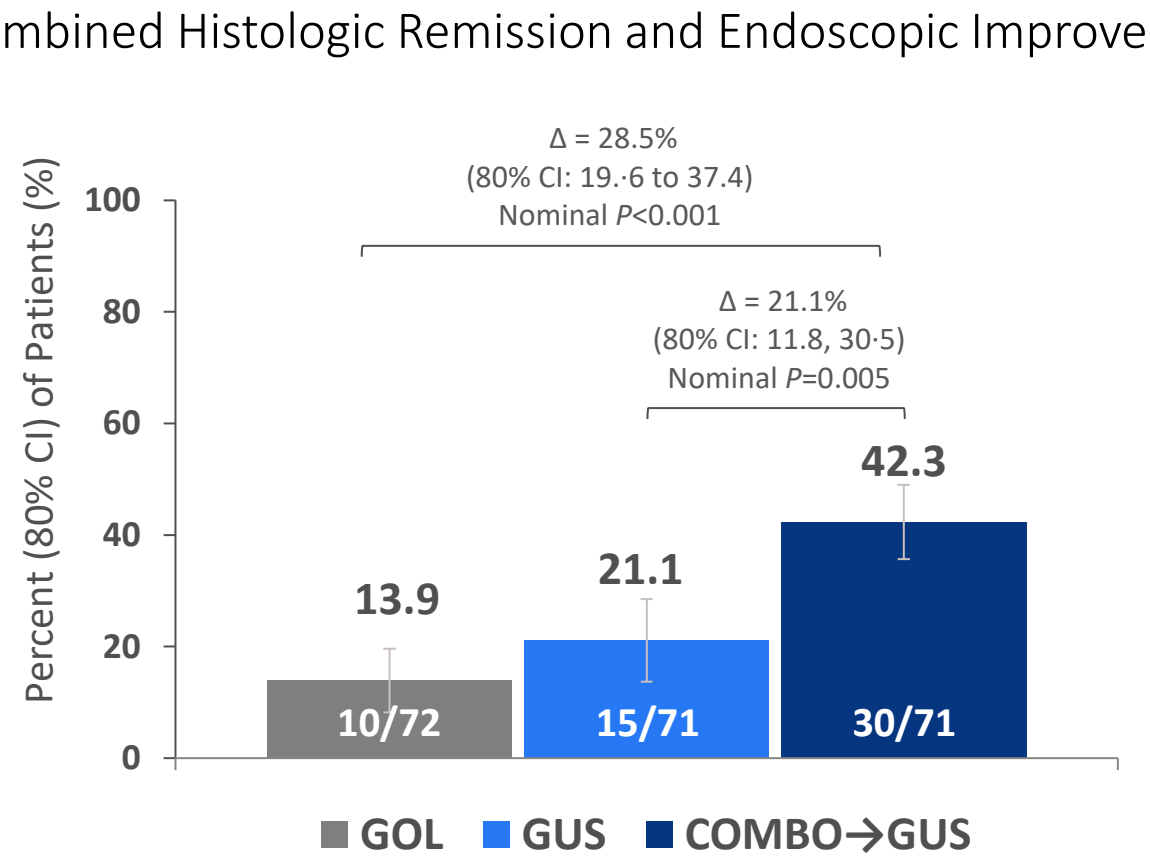
Clinical Remission (Full Mayo Score): Mayo Score ≤2 with No Individual Subscore >1; (Modified Mayo Score): Mayo SFS=0/1 and Not Increased from Baseline, a RBS=0, and an ES=0/1 with No Friability. 1. Feagan BG, et al. DDW 2022. Oral Presentation #886. 2. Feagan BG, et al. Lancet Gastroenterol Hepatol. 2023;8(4):307-320.

Endoscopic Outcomes at Week 38



Endoscopic Improvement: Endoscopy Subscore of 0 or 1 with No Friability Present on the Endoscopy. Endoscopic Normalization: Endoscopy Subscore of 0 with No Friability Present on the Endoscopy. 1. Feagan BG, et al. ACG 2022. Oral Presentation #40. 2. Feagan BG, et al. Lancet Gastroenterol Hepatol. 2023;8(4):307-320.

Histologic Remission and Endoscopic Improvement at Week 38



Histologic Remission: Absence of Neutrophils from the Mucosa (Both Lamina Propria and Epithelium), No Crypt Destruction, and No Erosions, Ulcerations or Granulation Tissue According to the Geboes Grading System. Endoscopic Improvement: Endoscopy Subscore of 0 or 1 with No Friability Present on the Endoscopy.

1. Feagan BG, et al. ACG 2022. Oral Presentation #40. 2. Feagan BG, et al. Lancet Gastroenterol Hepatol. 2023;8(4):307-320.

Conclusions

1. Patients treated with GUS and GOLI, followed by GUS monotherapy achieved higher rates of clinical/endoscopic remission Week 38 compared to GUS or GOL alone (no safety findings)

2. Important landmark RCT study that demonstrates that dual biologic therapy during induction improves overall outcomes and may help to break the current therapeutic treatment ceiling
   - Continued maintenance with dual biologics may be even more beneficial and ongoing Phase 3 studies with anti-TNF/IL-23 (single injection) will address this question (DUET CD/UC)
   - Ideal combination therapy (biologics/small molecules) not yet known → studies are ongoing
   - Reimbursement for two different biologics/small molecules will be challenging

ORIGINAL ARTICLE

Vedolizumab for the Treatment of Chronic Pouchitis

S. Travis, M.S. Silverberg, S. Danese, P. Gionchetti, M. Löwenberg, V. Jairath, B.G. Feagan, B. Bressler, M. Ferrante, A. Hart, D. Lindner, A. Escher, S. Jones, and B. Shen, for the EARNEST Study Group*

N Engl J Med 388;13 nejm.org March 30, 2023

Vedolizumab for the treatment of chronic pouchitis: The EARNEST trial

- Chronic pouchitis is common and significantly affects QoL in individuals with an ileal pouch anal anastomosis (IPAA)
- Research question – Does vedolizumab lead to clinical and endoscopic remission in individuals with an IPAA?
- Study design – Double - blind RCT vedolizumab vs. placebo
  (All received ciprofloxacin for the first 4 weeks)

Travis S et al, N Engl J Med 2023;388:1191-200

Study design

- Cohort (n=102)
  >= 3 episodes of pouchitis (past year)

- Vedolizumab naïve
  +/- exposed to other therapies

Table 1. Demographic and Clinical Characteristics at Baseline (Full Analysis Set).*

Characteristic	Vedolizumab (N=51)	Placebo (N=51)
Median age (range) – yr	42.0 (19-67)	45.0 (19-68)
Male sex – no. (%)	32 (63)	38 (74)
Continuous use of antibiotics immediately before baseline – no. (%)	29 (57)	25 (49)
Time since IPAA – no. (%)		
<7 yr	16 (31)	21 (41)
≥7 yr	35 (69)	30 (59)
Previous use of a TNF antagonist after colectomy — no. (%)		
TNF antagonist not used	36 (71)	38 (74)
Treatment failure with a TNF antagonist	15 (29)	12 (24)

Primary outcome: mPDAI defined remission

Primary outcome
mPDAI remission at week 14

Secondary outcome
mPDAI remission at week 34

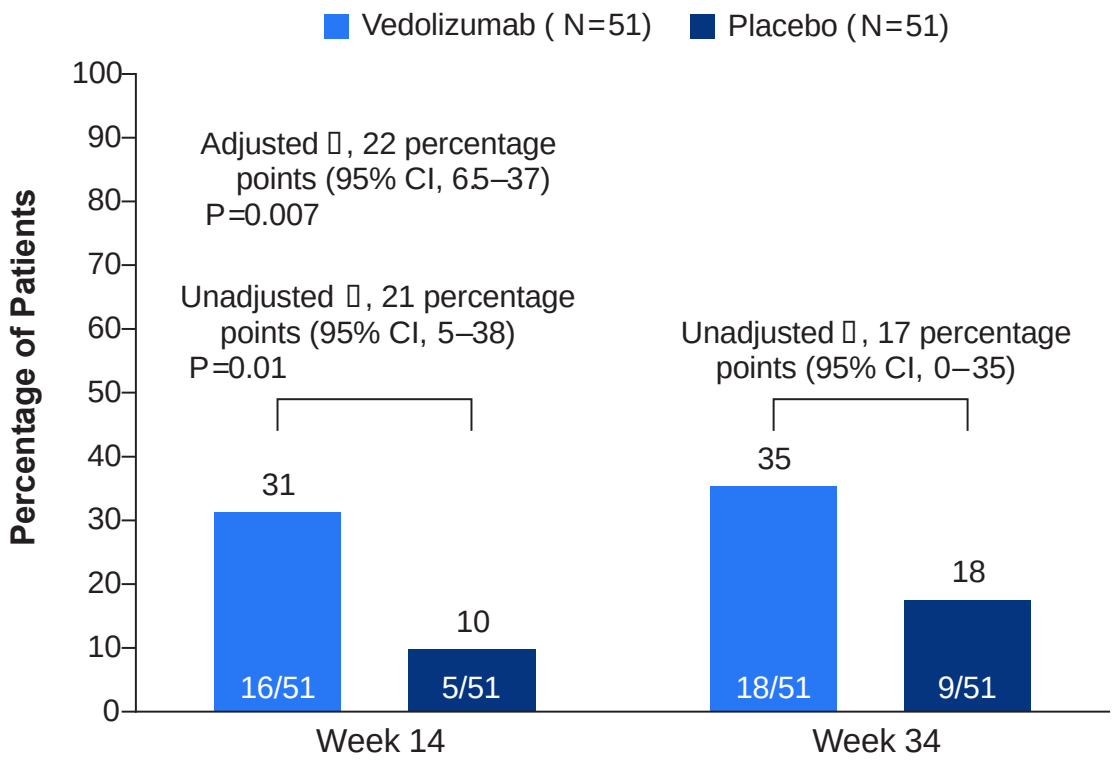


Figure 1.mPDAI-Defined Remission (Full Analysis Set).

** mPDAI clinical and endoscopic criteria*

*** PDAI clinical, endoscopic, histologic*

Secondary Outcomes

Secondary outcome
(mPDAI remission at week 34)
mPDAI response at weeks 14, 34
PDAI remission at weeks 14, 34
IBDQ &QoL

** mPDAI clinical and endoscopic criteria*

*** PDAI clinical, endoscopic, histologic*

Safety/Adverse effects:
Pouchitis (clinical definition only)
URTI/headache

Table 2. Secondary Efficacy End Points (Full Analysis Set).*

End Point	Vedolizumab (N=51)	Placebo (N=51)
mPDAI-defined remission at wk 34 – no. (%)	18 (35)	9 (18)
PDAI-defined remission – no. (%)		
Wk 14	18 (35)	5 (10)
Wk 34	19 (37)	9 (18)
mPDAI-defined response – no. (%)		
Wk 14	32 (63)	17 (33)
Wk 34	26 (51)	15 (29)

Conclusions

1. Treatment with vedolizumab was more effective than placebo in inducing remission in patients who had chronic pouchitis after undergoing IPAA for ulcerative colitis. C

2. Vedolizumab should be the treatment of choice for chronic pouchitis patients

Overall Conclusions

- Consider surgery in patients with limited ileal disease (prior to the use of biologics or after primary biologic failure)
- Otherwise, early treatment with biologics is best (PROFILE) and perhaps eventually with dual biologic therapy
- In patients with chronic pouchitis use vedolizumab

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Thank-you !

Questions/Comments ?

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