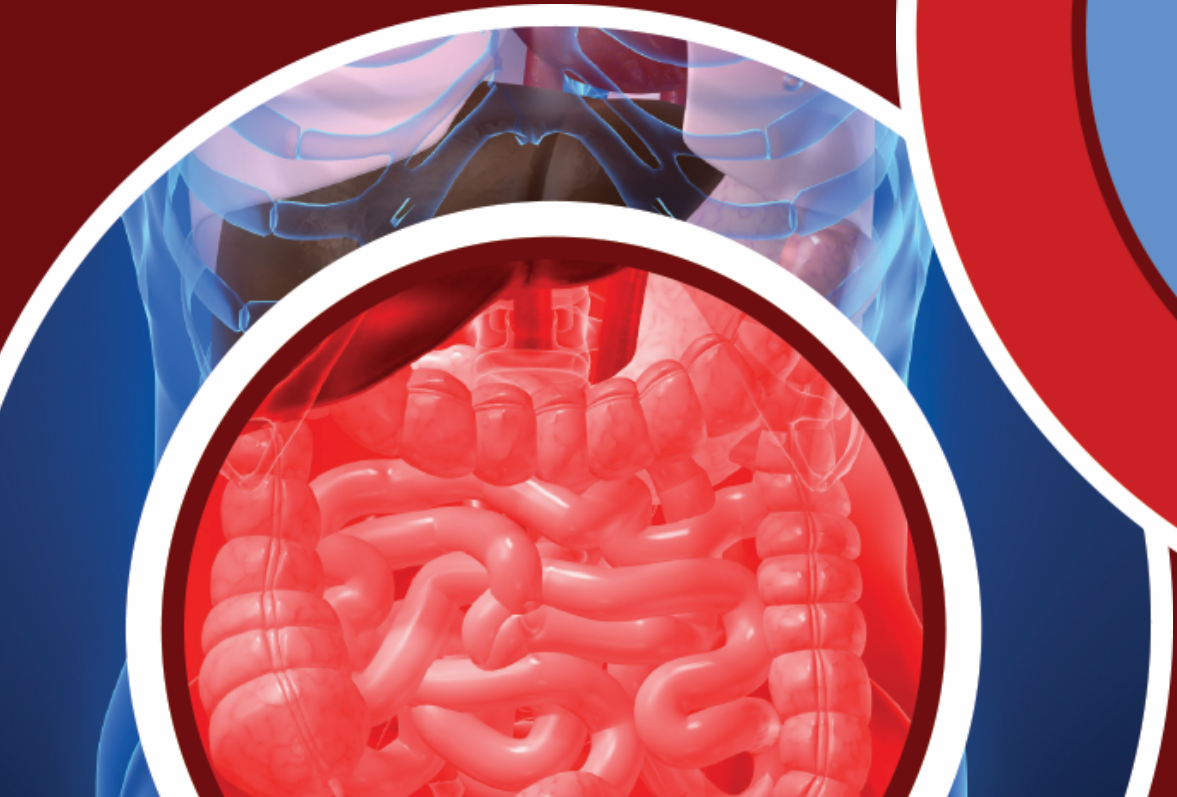
This program is not affiliated with the Crohn's and Colitis Congress®

Friday, February 8, 2019



MIPS Improvement Activity +
Earn ABIM MOC Credit

2019 Management of Ulcerative Colitis

Where, When, Who, and What Now?

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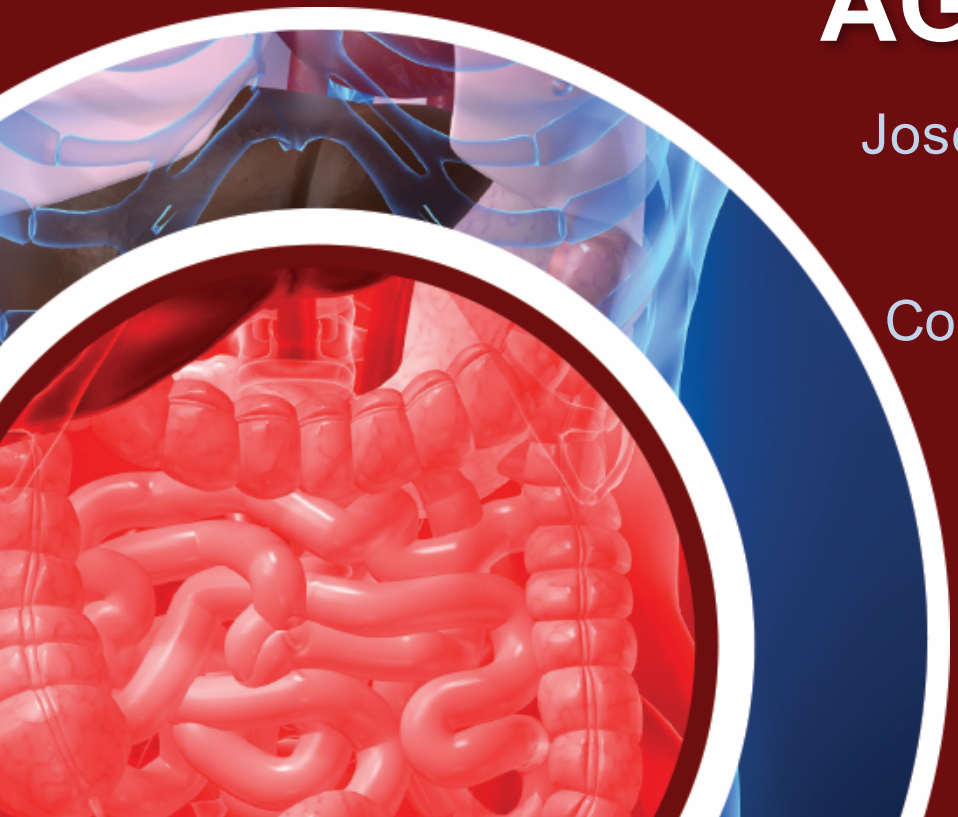
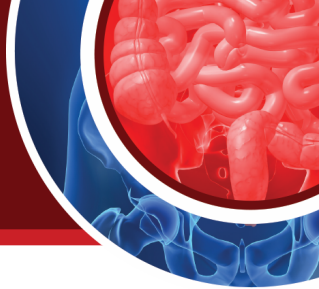


David T. Rubin, MD, FACG, AGAF, FACP, FASGE

Joseph B. Kirsner Professor of Medicine
Section Chief, Gastroenterology, Hepatology and Nutrition
Co-Director, Digestive Diseases Center
University of Chicago Medicine
Chicago, IL

David T. Rubin, MD, FACG, AGAF, FACP, FASGE
Disclosures



- **Grants:** AbbVie Inc.; Genentech, Inc./Roche; Janssen Pharmaceuticals, Inc.; Prometheus Laboratories Inc.; Shire; Takeda Pharmaceuticals U.S.A., Inc.
- **Consultant:** AbbVie Inc.; AbGenomics; Allergan; Arena Pharmaceuticals, Inc.; Biomica; Eli Lilly and Company; Genentech, Inc./Roche; Janssen Pharmaceuticals, Inc.; Medtronic; Merck & Co., Inc.; Napo Pharmaceuticals, Inc.; Pfizer Inc.; Shire; Takeda Pharmaceuticals U.S.A., Inc.; TARGET PharmaSolutions, Inc.
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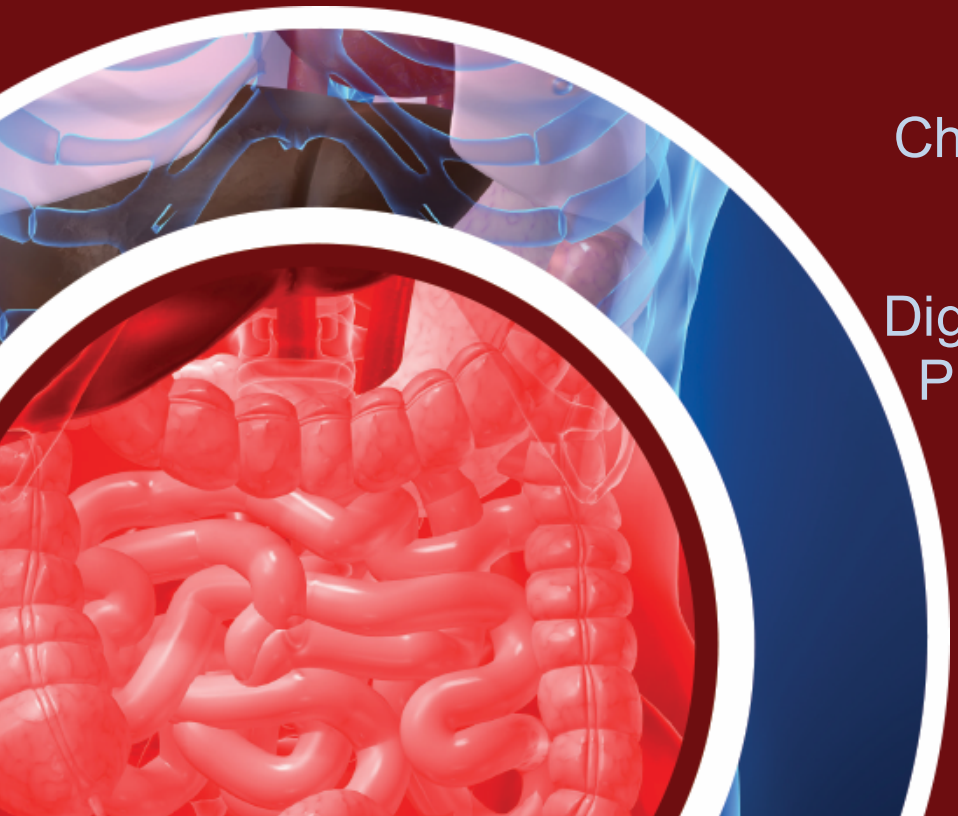
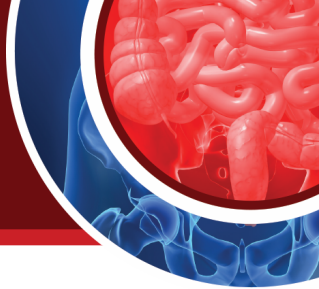


Miguel Regueiro, MD, AGAF, FACG, FACP

Chair, Department of Gastroenterology and Hepatology
Vice Chair,
Digestive Disease and Surgery Institute
Professor of Medicine, Lerner College of Medicine
Cleveland Clinic
Cleveland, OH

Miguel Regueiro, MD, AGAF, FACG, FACP

Disclosures



- **Research Support:** Abbvie Inc.; Janssen Pharmaceuticals, Inc.; Takeda Pharmaceuticals U.S.A., Inc.
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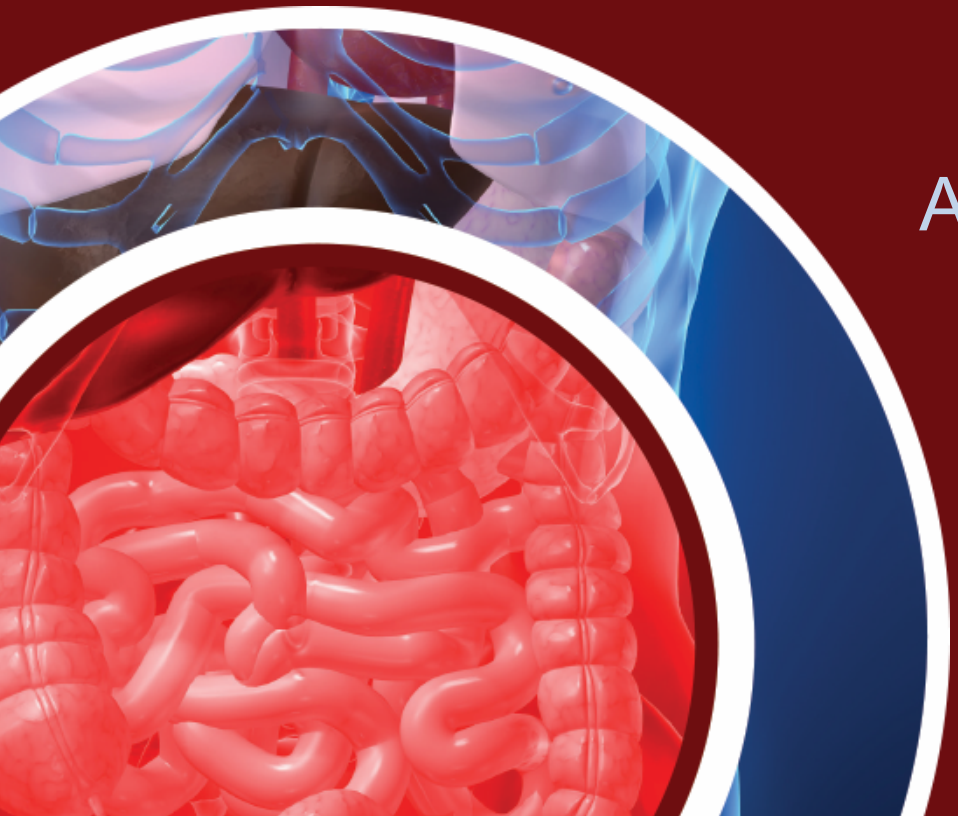
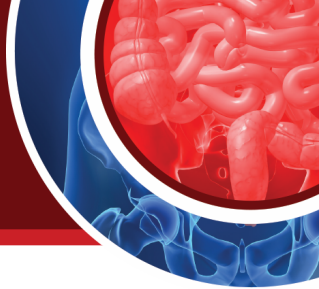


Learning Objective 1

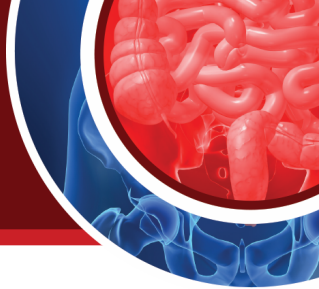
Apply approaches to identify moderate- to high-risk patients with UC in clinical practice.

Case: MG



- 30-year-old female
- 7 bloody stools per day
- Stool cultures negative
- Endoscopic findings: extensive colitis, deep ulcers

Audience Response



Which factor is most associated with poor prognosis in patients with ulcerative colitis (UC)?

A. Older age of onset
B. Early need for steroids
C. Low fecal calprotectin (FCP)
D. Family history of UC
E. Geboes score > 2
F. Not sure

Classification of UC Severity[1,2]

MILD
- < 4 stools/day ± blood
- Normal ESR
- No signs of toxicity

MODERATE
- ≥ 4 stools/day ± blood
- Minimal signs of toxicity

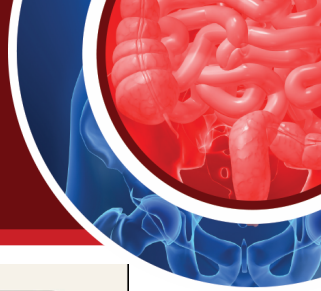
SEVERE
- > 6 bloody stools/day
- Fever
- Tachycardia
- Anemia or ↑ ESR

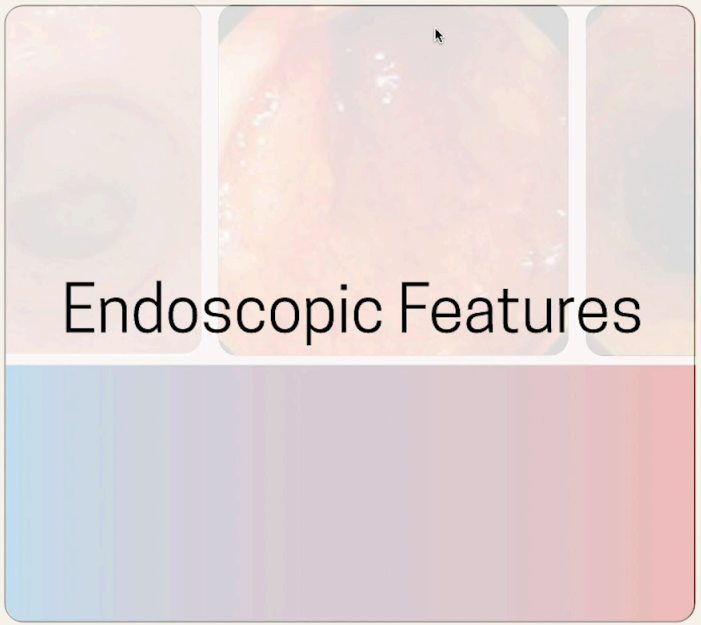
FULMINANT
- > 10 stools/day
- Continuous bleeding
- Toxicity
- Abdominal tenderness/distension
- Transfusion requirement
- Colonic dilation on x-ray

ESR = erythrocyte sedimentation rate.

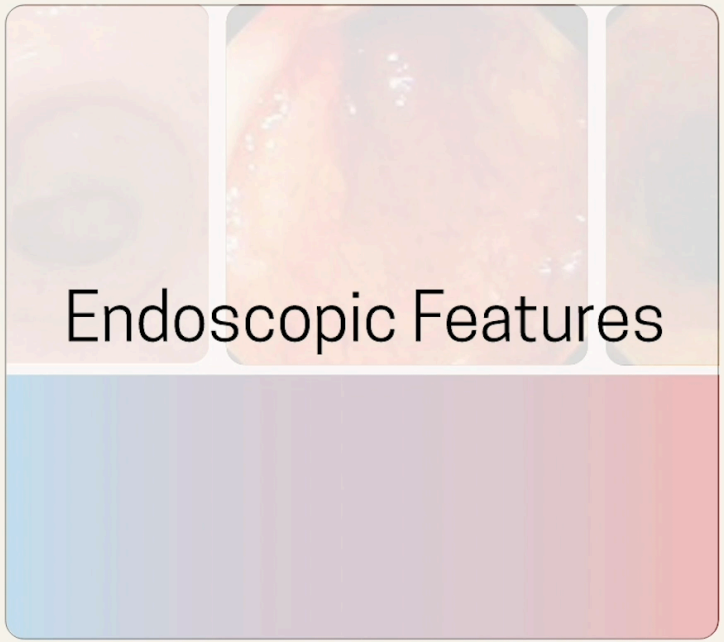
1. Truelove SC, Witts LJ. *Br Med J.* 1955;2:1041-1048. 2. Kornbluth A, Sachar DB. *Am J Gastroenterol*. 2010;105:501-523.

Endoscopic Activity





Histologic Activity



AGA Clinical Pathway for Ulcerative Colitis: Characterizing Colectomy Risk

Low Risk		Mod-High Risk
> 40 years	Age of diagnosis	< 40 years
Limited	Anatomic involvement	Extensive
Elevated	CRP, ESR, FCP levels	High
No	Steroid required	Yes
Mild	Ulcers	Deep
No	*Clostridium difficile* infection	Yes
No	History of hospitalization	Yes
No	CMV infection	Yes

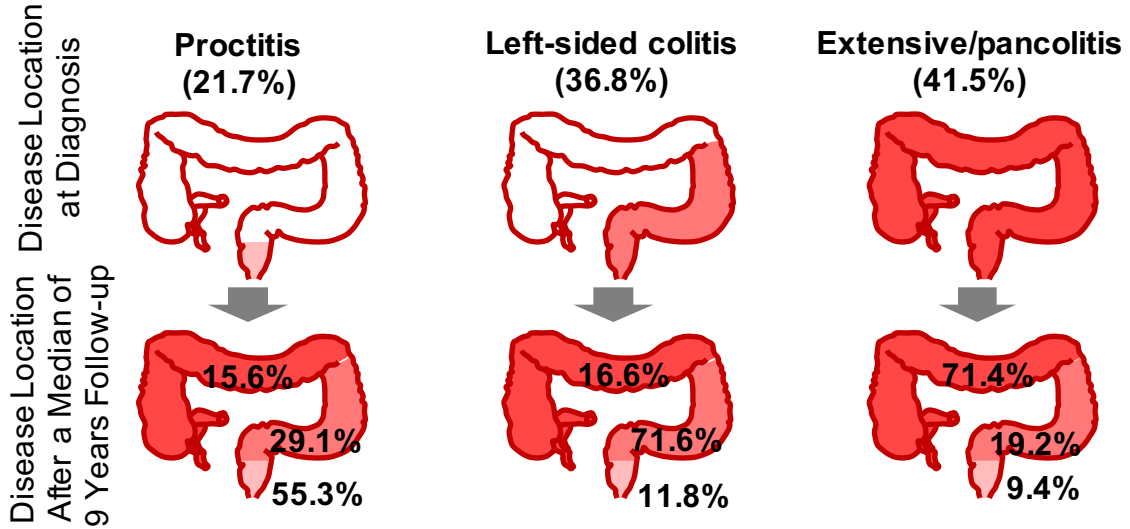
AGA = American Gastroenterological Association; CRP = C-reactive protein.

Dassopoulos T, et al. *Gastroenterology*. 2015;149:238-245.

Ulcerative Colitis Is a Progressive Disease: How Do We Measure Progression — Proximal Extension?

Swiss irritable bowel disease (IBD) cohort study: Evolution of disease extent over a median disease duration of 9 years, from 2006 (N = 918)

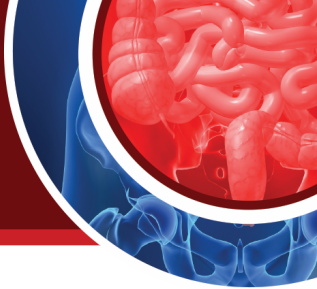
Disease duration at study inclusion: Median 6 years, interquartile range 2 - 13 years, range 0 - 46 years

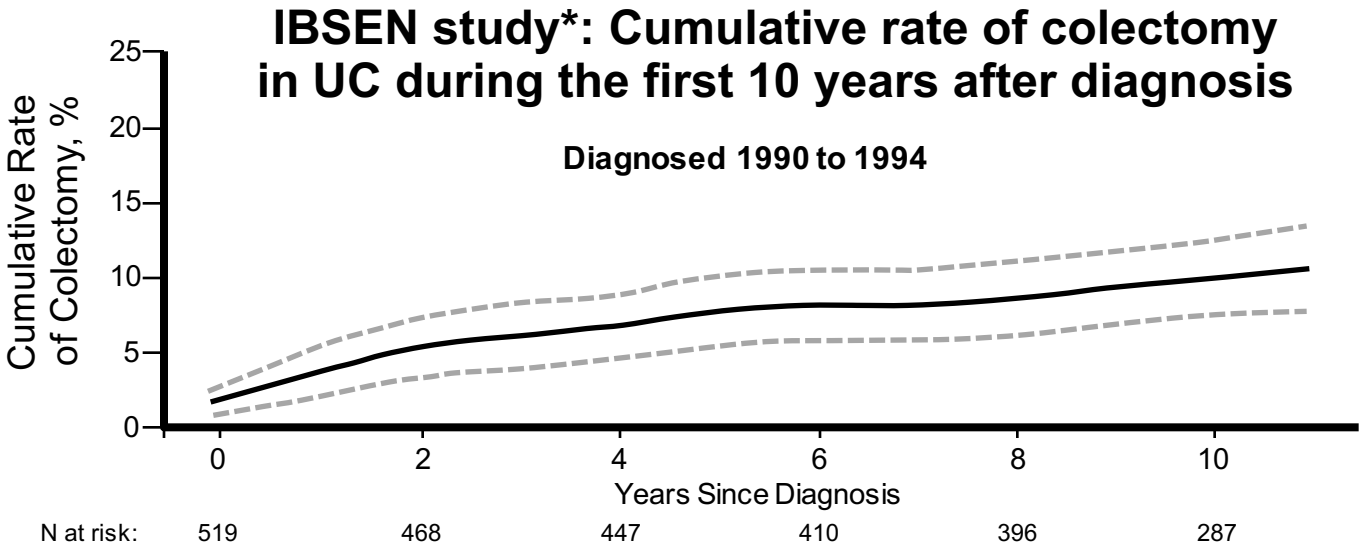


~15% of patients with UC experienced proximal disease extension over 9 years

Safroneeva E, et al. *Aliment Pharmacol Ther*. 2015;42:540-548.

Ulcerative Colitis Is a Progressive Disease: How Do We Measure Progression — Colectomy?



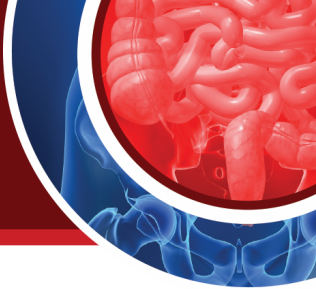


~10% of patients with UC required colectomy over 10 years

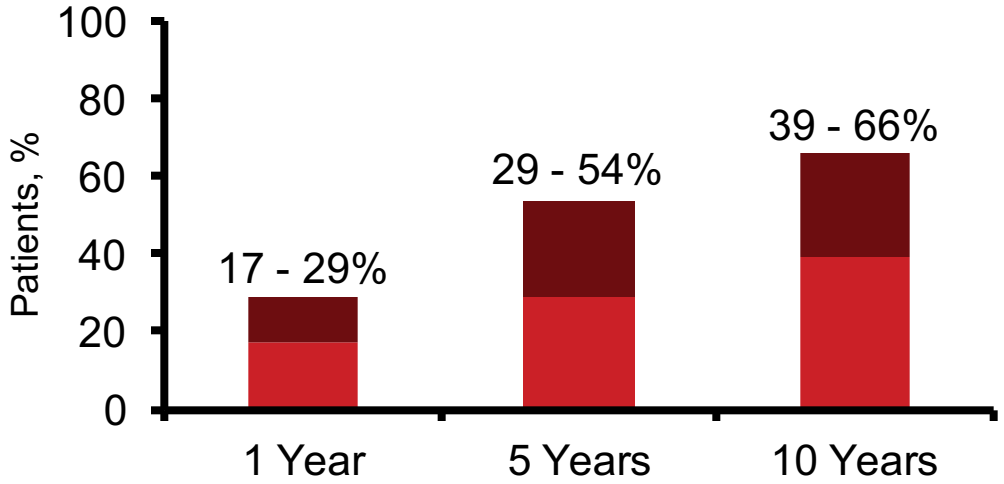
*From 1990 to 1994, patients with inflammatory bowel disease were enrolled in South-Eastern Norway and systematically followed-up for up to 10 years after diagnosis.

Solberg IC, et al. *Scand J Gastroenterol*. 2009;44:431-440.

Ulcerative Colitis Is a Progressive Disease: How Do We Measure Progression — Hospitalization?



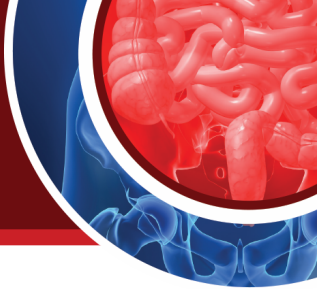
Cumulative probabilities of hospitalization in patients with UC



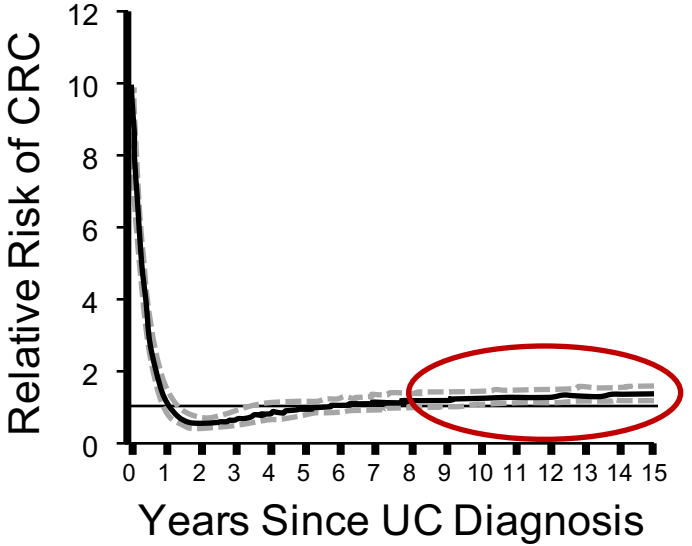
~50% of patients with UC required hospitalization at some point during disease course

Fumery M, et al. *Clin Gastroenterol Hepatol.* 2018;16(3):343-356.

Ulcerative Colitis Is a Progressive Disease: How Do We Measure Progression — Colorectal Cancer?



Risk of colorectal cancer in a nationwide cohort of Danish patients with UC over 30 years (N = 32,911)

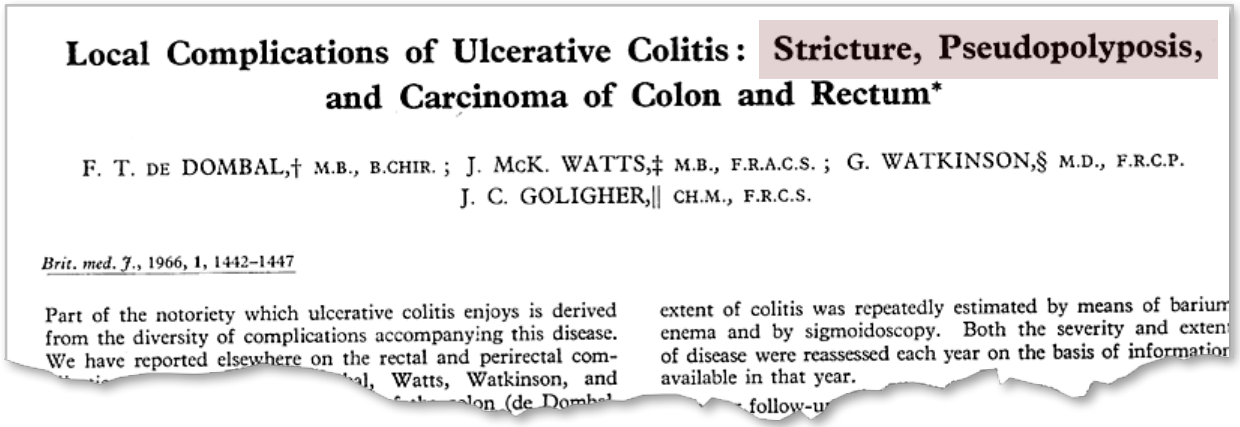


Relative risk adjusted for sex, age, calendar time.
Dotted lines indicated 95% confidence intervals.

Subgroups of patients with UC were at increased risk for colorectal cancer

Jess T, et al. *Gastroenterology*. 2012;143:375-381.

Ulcerative Colitis Is a Progressive Disease: How Do We Measure Progression — Bowel Damage?



Local Complications of Ulcerative Colitis: Stricture, Pseudopolyposis, and Carcinoma of Colon and Rectum*

F. T. DE DOMBAL,† M.B., B.CHIR.; J. McK. WATTS,‡ M.B., F.R.A.C.S.; G. WATKINSON,§ M.D., F.R.C.P.
J. C. GOLIGHER,‖ CH.M., F.R.C.S.

Brit. med. J., 1966, **1**, 1442–1447

Part of the notoriety which ulcerative colitis enjoys is derived from the diversity of complications accompanying this disease. We have reported elsewhere on the rectal and perirectal com-

…al, Watts, Watkinson, and …olon (de Dombal

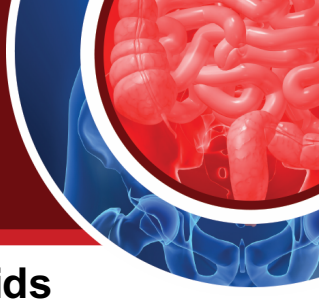
extent of colitis was repeatedly estimated by means of barium enema and by sigmoidoscopy. Both the severity and extent of disease were reassessed each year on the basis of information available in that year.

… follow-up

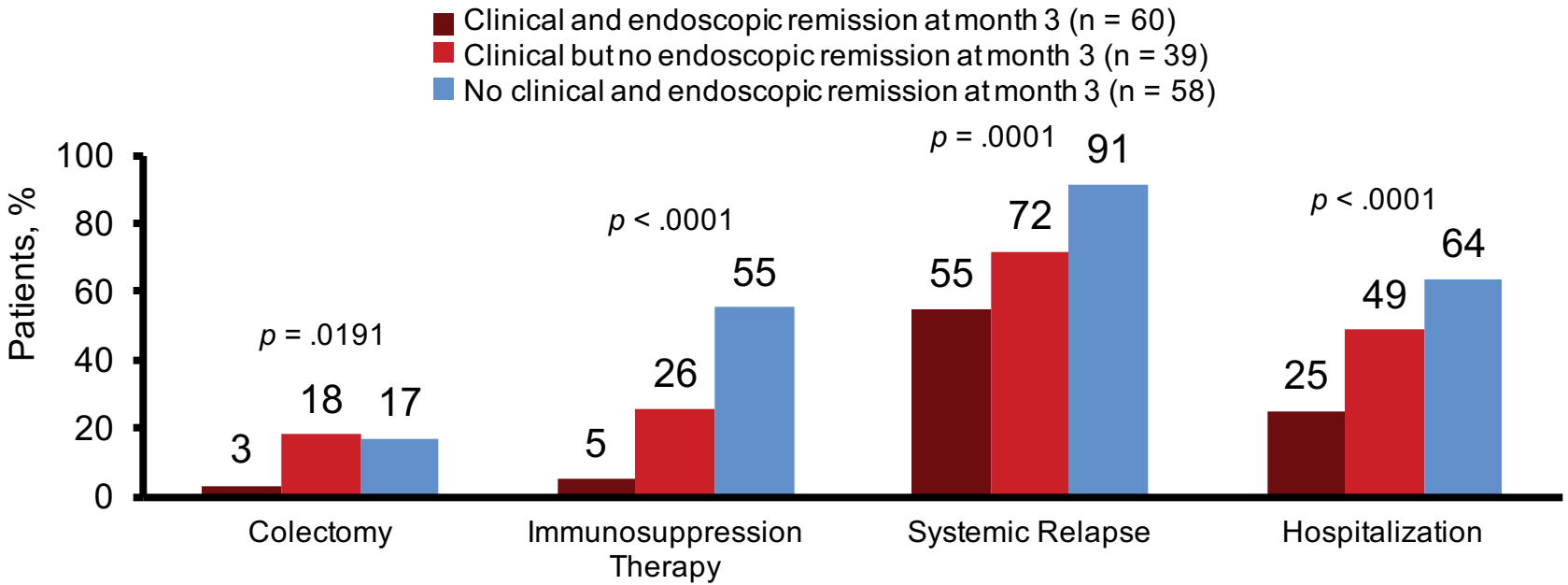
Other Damage		
Dysmotility	Anorectal dysfunction	Impaired permeability

Torres J, et al. *Inflamm Bowel Dis*. 2012;18:1356-1363.

Early, Lasting Clinical and Endoscopic Remission Predicts Better Long-Term Outcomes in UC



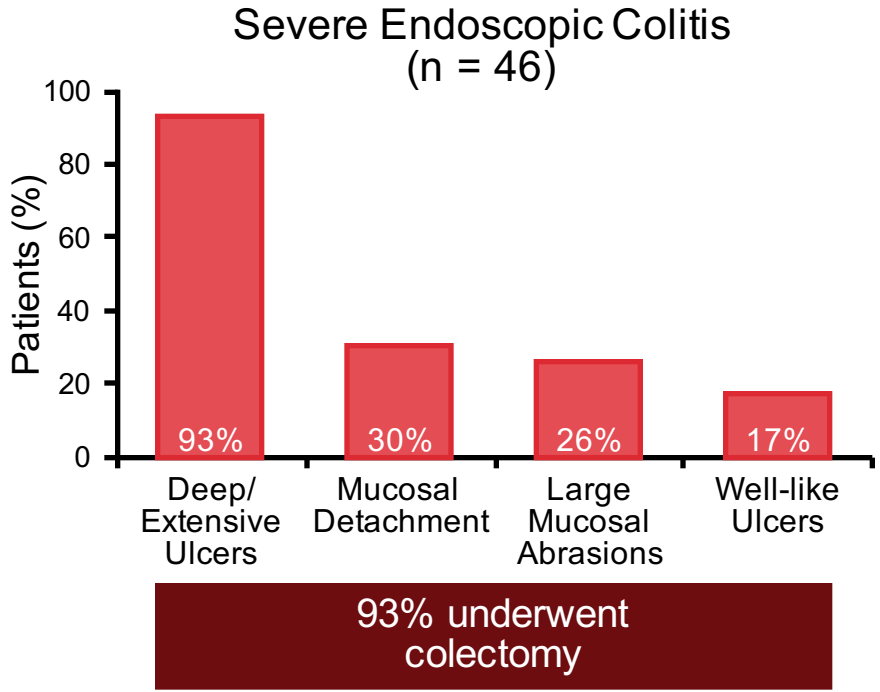
Outcome at 5-year follow-up according to early response to steroids

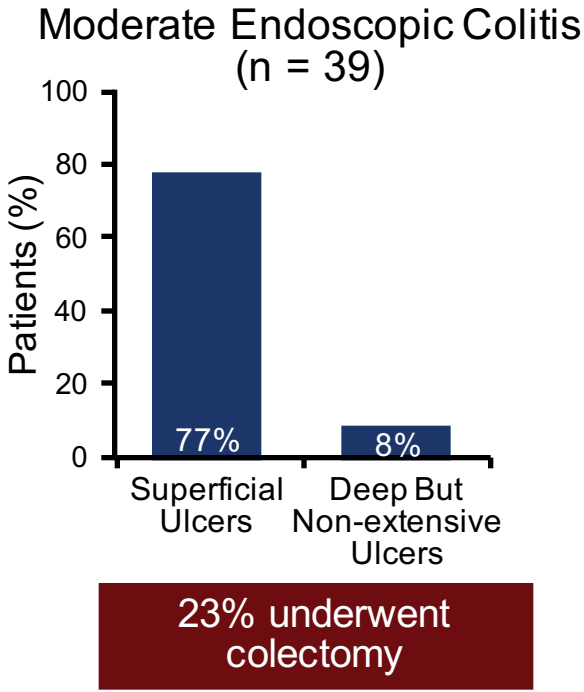


N = 157 patients with moderate-to-severe newly diagnosed UC; 5-year follow-up after first course of steroids; classified according to remission at 3 months; mean follow-up 51 (4 - 60) months.

Ardizzone S, et al. *Clin Gastroenterol Hepatol*. 2011;9:483-489.e3.

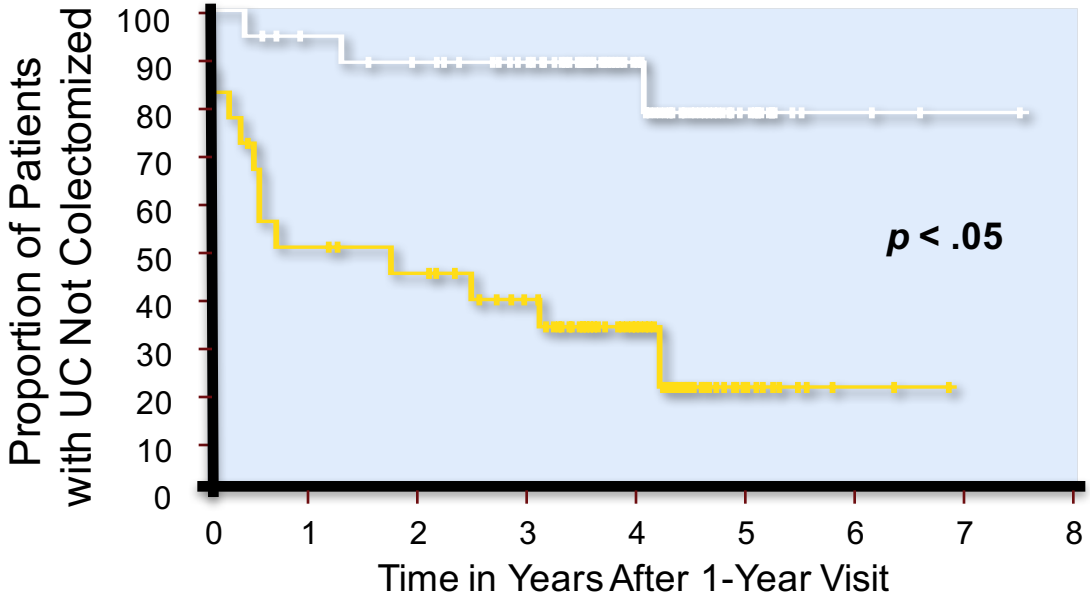
Severity of Endoscopic Disease in UC Correlates with Colectomy





Carbonnel F, et al. *Dig Dis Sci.* 1994;39(7):1550-1557.

Mucosal Healing at Year 1 Associated with Risk of Subsequent Colectomy in UC



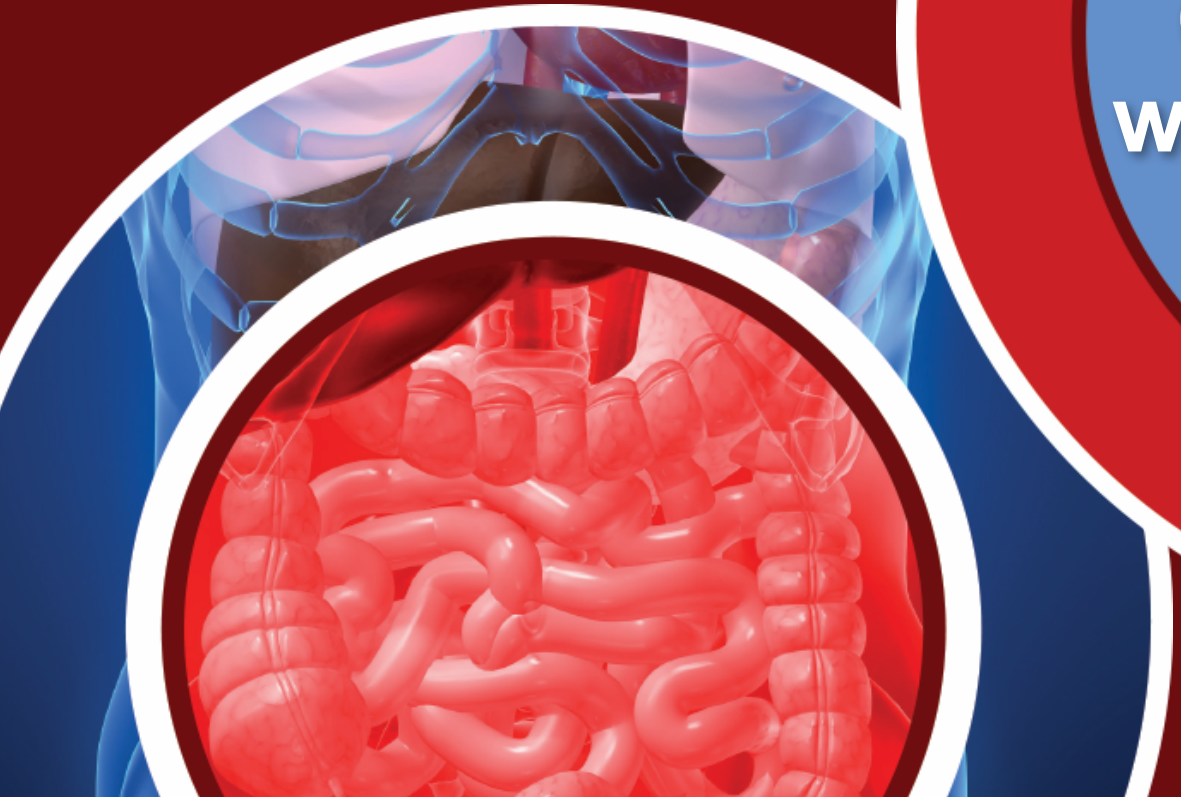
Patients without endoscopic activity at 1-year visit

Patients with endoscopic activity at 1-year visit

Patients with compromised mucosa 1 year after diagnosis showed a trend toward more surgeries.

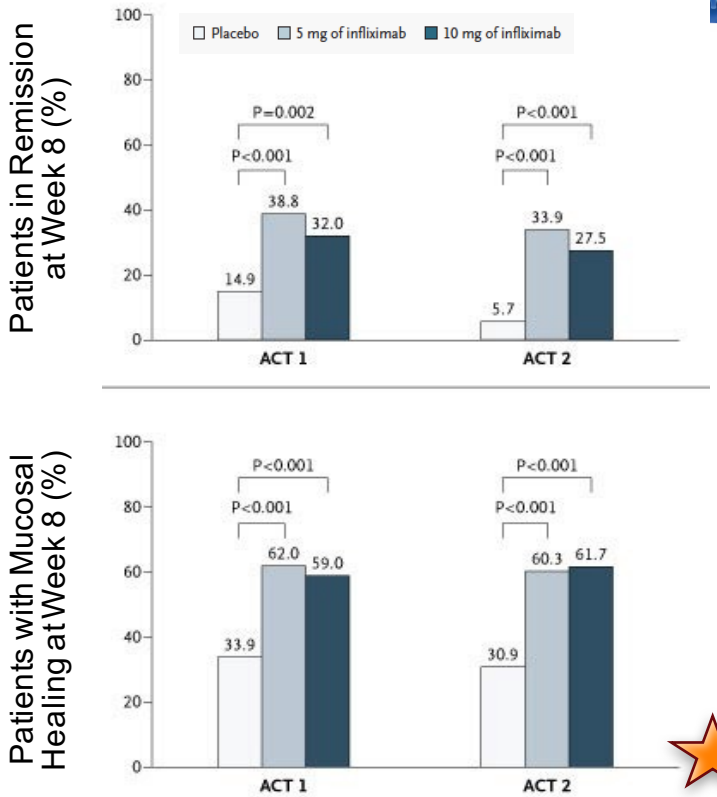
Frøslie KF, et al. *Gastroenterology*. 2007;133:412-422.

Symptoms Don't Often Correlate with Endoscopic Findings



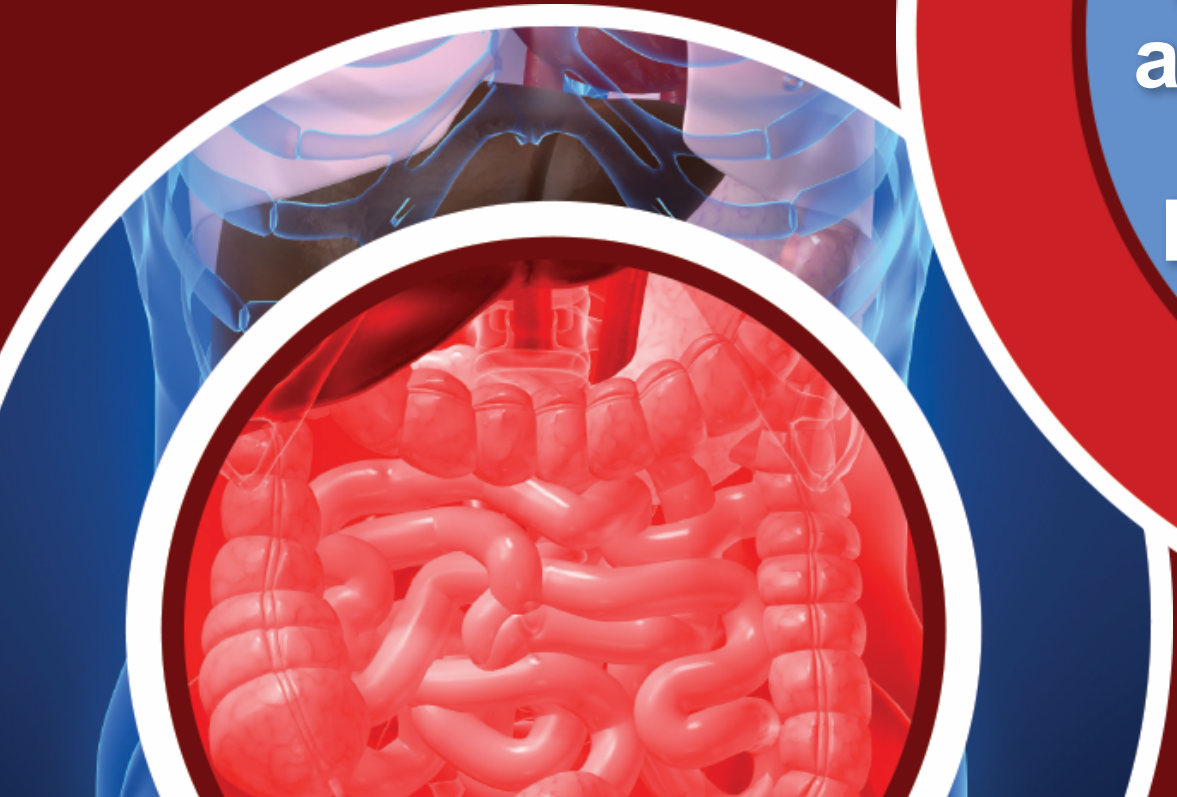
Symptoms Are Not a Reliable Indicator of Mucosal Healing in UC

- Meta-analysis of 13 studies found pooled prevalence of irritable bowel syndrome (IBS) at 36% [95% CI: 30.0 - 48.0%] in UC in remission[1]
- In ACT 1 and 2, at week 8 after infliximab induction, nearly twice as many patients had mucosal healing as had clinical remission[2]

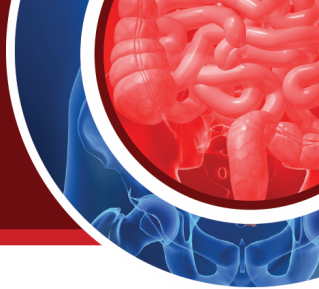


1. Halpin SJ, Ford AC. *Am J Gastroenterol.* 2012;107:1474-1482.
2. Rutgeerts P, et al. *N Engl J Med.* 2005;353:2462-2476.

What Do We Know About Measuring and Understanding Outcomes in Mucosal Healing?



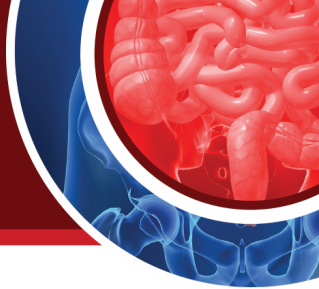
How Is Mucosal Healing Defined in UC?



- Return to normal vascular pattern[1]
- Absence of friability or ulcerations[1]
- Normal or near normal mucosal appearance, originally defined as with “slight hyperemia or slight granularity”[2]
- Histology
  - Geboes Score (GS)
  - Nancy Histology Index (NI)
  - Robarts Histology Index (RHI)

1. Pineton de Chambrun G, et al. *Nat Rev Gastroenterol Hepatol*. 2010;7(1):15-29. 2. Truelove SC, et al. *Br Med J*. 1955;2:1041-1048.

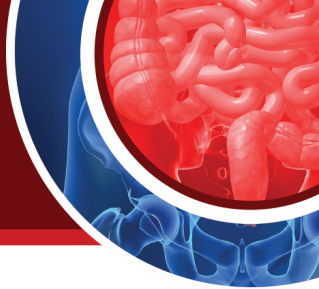
Role of FCP in IBD



- Diagnostic
- Assessing disease activity and response to treatment
- Prognostic
- Research

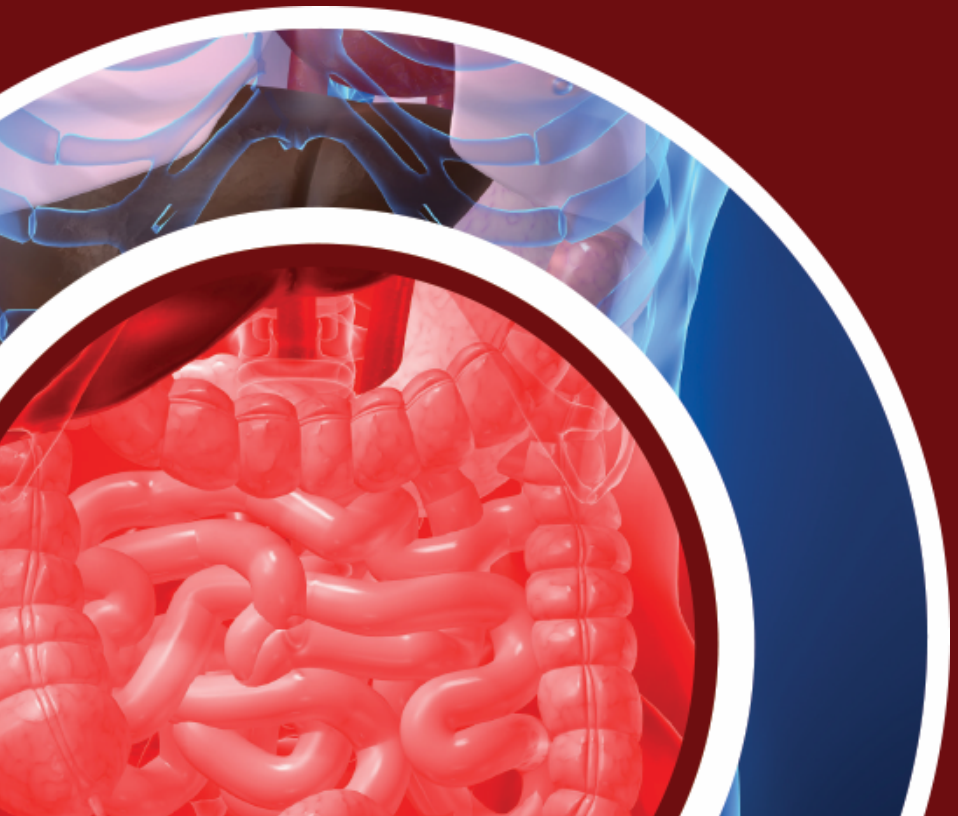
Walsham NE, et al. *Clin Exp Gastroenterol.* 2016;9:21-29.

Updated Goals of Management for IBD in 2018-2019[1,2]



- Clarify disease **type** and **severity**
- Induce remission rapidly – defined by both **patient-reported outcomes** and objective markers
  - Ulcerative colitis: Absence of rectal bleeding and diarrhea/altered bowel habits
- Maintain steroid-free remission
- Change the natural history of IBD
  - Avoid hospitalization and surgery
  - Avoid drug- and disease-related complications
  - Reduce costs of care

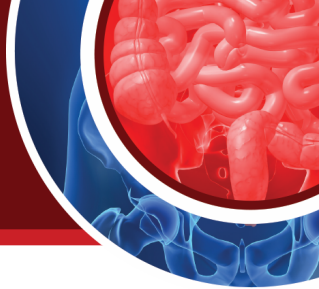
1. Rubin DT, et al. *Am J Gastroenterol Suppl*. 2016;3:4-7.
2. Peyrin-Biroulet L, et al. *Am J Gastroenterol*. 2015;110(9):1324-1338.



Learning Objective 2

Integrate evidence-based guidelines and findings from real-world studies into management plans for patients with UC that factor in treatment goals, initial therapy, continuous monitoring, and medication adjustments as needed.

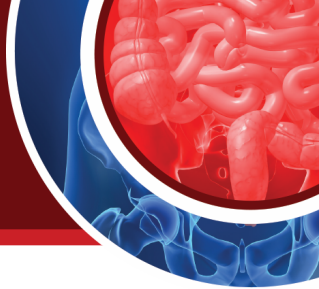
AGA UC Care Pathway



- Risk assessment of UC
  - Inflammation
  - Comorbidities
  - Colectomy risk
- Initial therapy
- Exacerbation treatment options
- Clinical decision support tool

Dassopoulos T, et al. *Gastroenterology*. 2015;149(1):238-245.

UC Care Pathway



Make diagnosis and assess inflammatory status (1)

Assess comorbidities and disease- and therapy-related complications (2)

Stratify according to colectomy risk (3)

High-Risk Patient

Identify patient requiring hospitalization

Low-Risk Patient

Inductive and maintenance therapy (low-risk) (4)

Outpatient

Inpatient

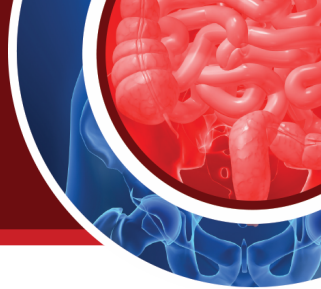
Inductive and maintenance therapy (high-risk, outpatient) (5)

Inductive and maintenance therapy (high-risk, inpatient) (7)

Therapy for high-risk outpatient not in remission (6)

Dassopoulos T, et al. *Gastroenterology*. 2015;149(1):238-245.

UC Care Pathway



Make diagnosis and assess inflammatory status (1)

Stratify according to colectomy risk (3)

Low-Risk Patient

Inductive and maintenance therapy (low-risk) (4)

As… comorbidities and dise…

…d therapy-related complications (2)

High-Risk Patient

Identify patient requiring hospitalization

Outpatient

Induct… and maintenance therapy (hig…risk, outpatient) (5)

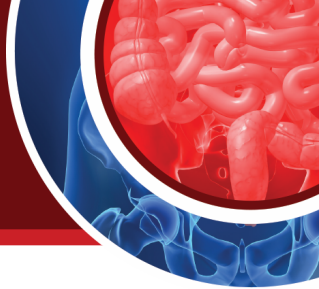
Therapy for hig…isk outpatient not in remis… (6)

Inpatient

Inductive and mainten…ce therapy (high-risk, inpa…nt) (7)

Dassopoulos T, et al. *Gastroenterology*. 2015;149(1):238-245.

Case: MG



- 30-year-old female
- 7 bloody stools per day
- Stool cultures negative
- Endoscopic findings: extensive colitis, deep ulcers

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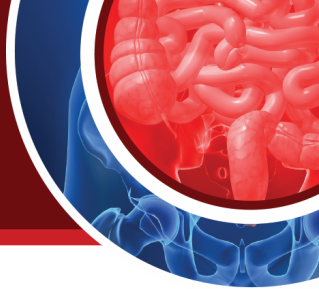
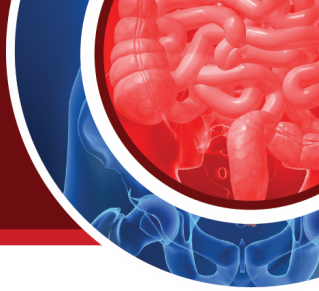


What would be your first step in treating MG?

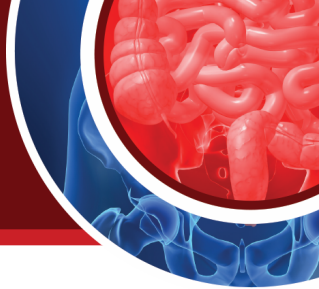
A. Short course of steroids with initiation of thiopurine
B. Tumor necrosis factor (TNF) inhibitor
C. Vedolizumab (VDZ) +/- immunosupressants
D. Tofacitinib
E. Not sure

When to Introduce Biologics in Patients with UC



- Steroid-refractory UC
- Steroid-dependent UC
- Immunomodulator-refractory UC
- Immunomodulator-intolerant UC
- Clinical predictors of a poor outcome at diagnosis?

Approved Therapies for Moderate-to-Severe Ulcerative Colitis

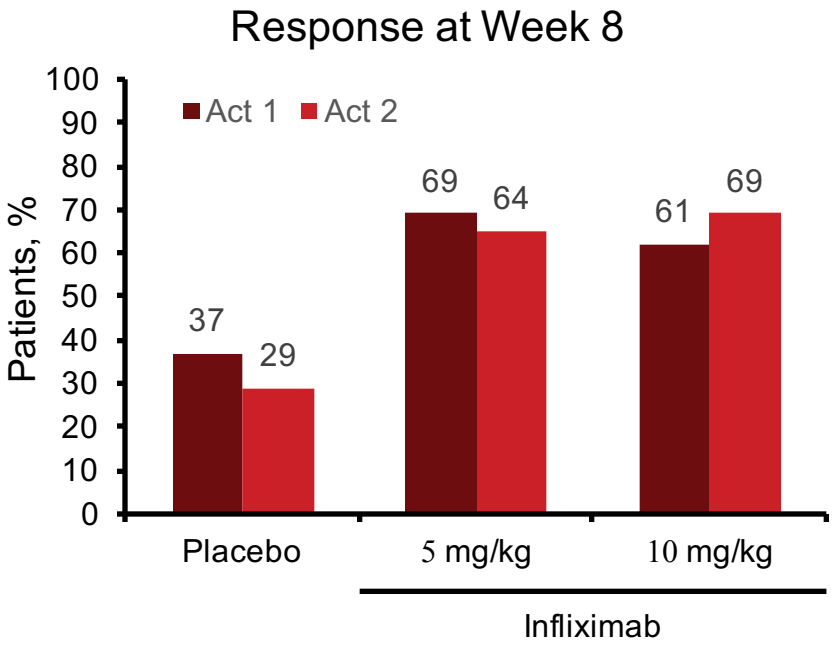


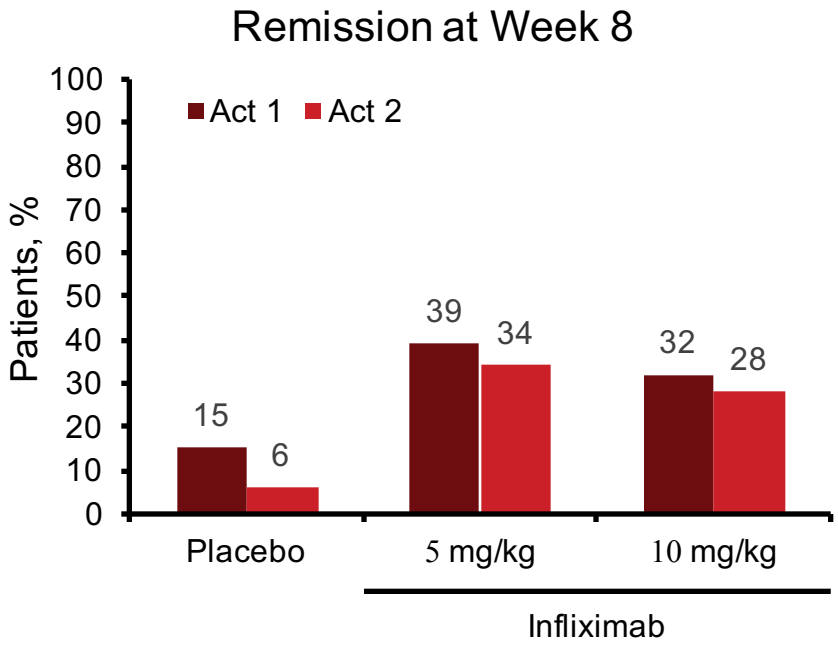
	Mechanism	Induction of Clinical Response and Remission	Adverse Events*
Infliximab	Anti-TNF	ACT[1]	Serious infections, opportunistic infections. Need to test for tuberculosis (TB) and hepatitis B virus (HBV) prior to initiation of therapy.
Adalimumab	Anti-TNF	ULTRA[2]	
Golimumab	Anti-TNF	PURSUIT-SC[3]	
VDZ	Selective α4β7 integrin antagonist	GEMINI[4]	Nasopharyngitis
Tofacitinib	JAK-inhibitor	OCTAVE Induction[5]	Serious infections, opportunistic infections. Need to test for TB and HBV prior to initiation of therapy. (Increased risk of herpes zoster)

**See prescribing information for full listing of warnings, precautions, and adverse events.*

1. Rutgeerts P, et al. *N Engl J Med.* 2005;353(23):2462-2476. 2. Sandborn WJ, et al. *Gastroenterology*. 2012;142(2):257-265.
3. Sandborn WJ, et al. *Gastroenterology*. 2014;146(1):96-109. 4. Feagan BG, et al. *N Engl J Med*. 2013;369(8):699-710.
5. Sandborn WJ et al. *N Engl J Med*. 2017;376:1723-1736.

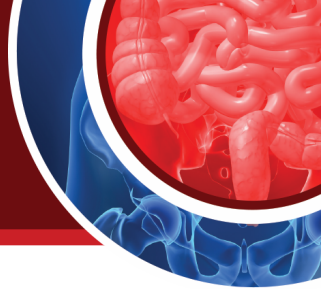
Induction Treatment with Anti-TNFα in UC



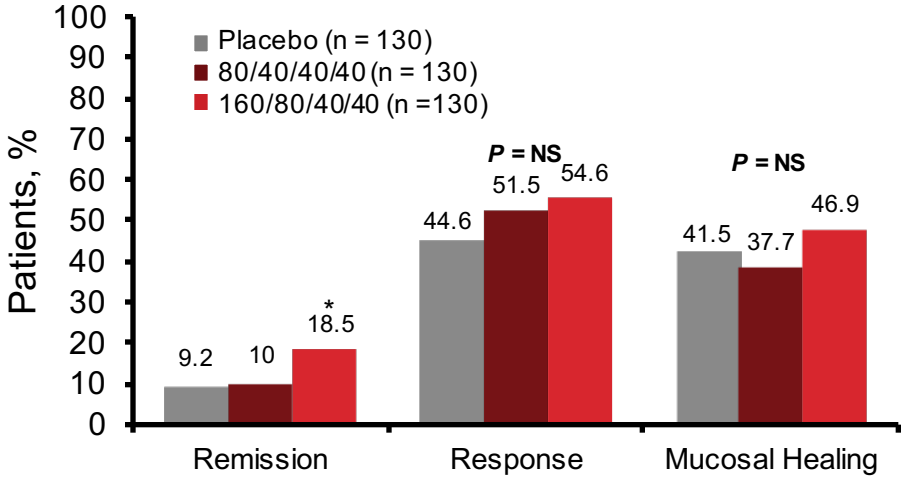


Rutgeerts P, et al. *N Engl J Med*. 2005;353(23):2462-2476.

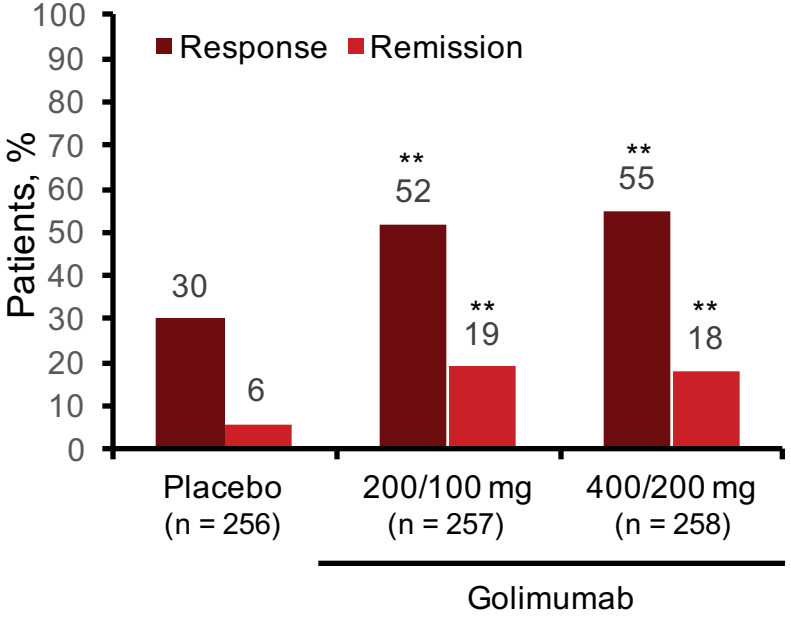
Induction Treatment with Anti-TNFα in UC



Adalimumab Outcomes at Week 8[1]



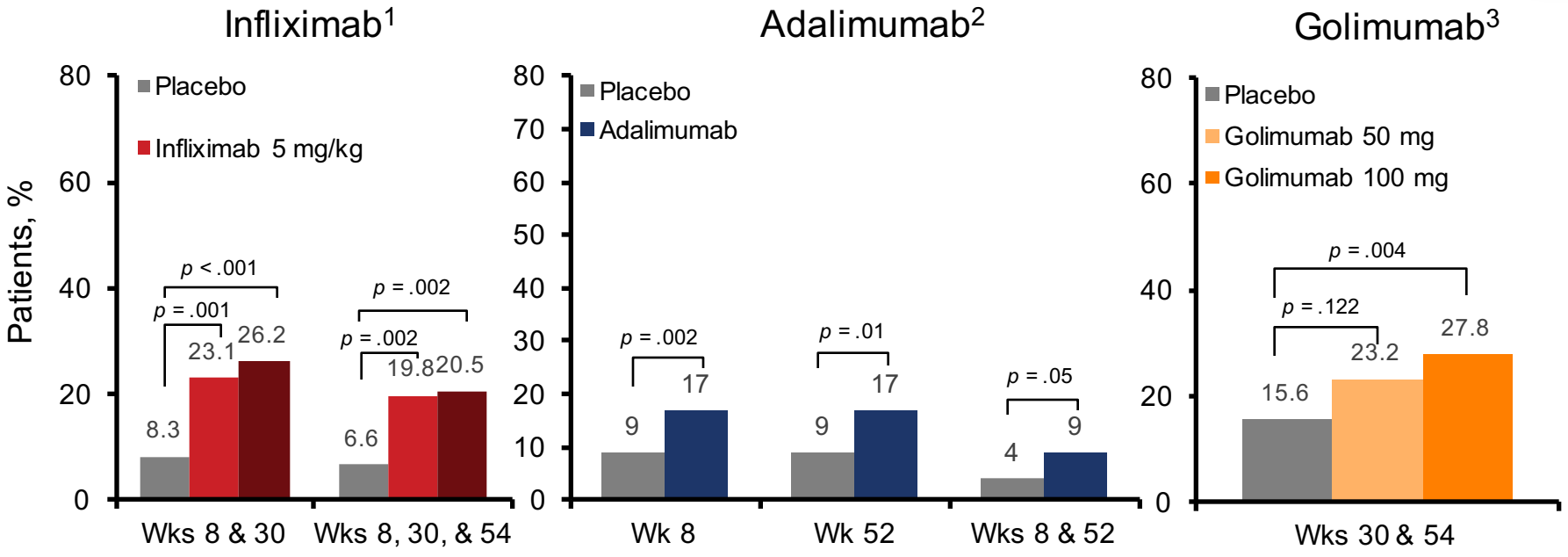
Golimumab Outcomes at Week 6[2]



* $p < .05$; **$p < .001$

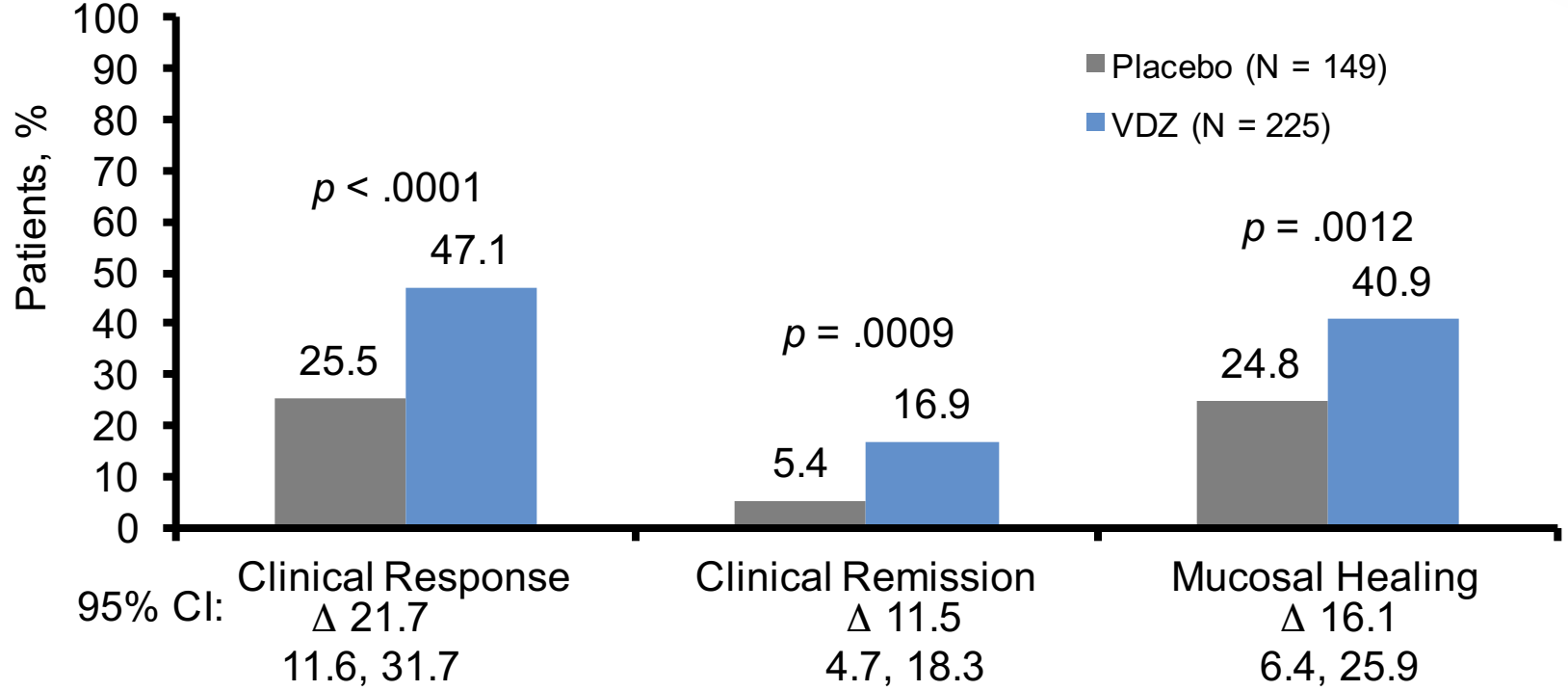
1. Reinisch W, et al. *Gut.* 2011;60(6):780-787. 2. Sandborn WJ, et al. *Gastroenterology.* 2014;146(1):85-95.

Maintenance Treatment with Anti-TNFα in UC



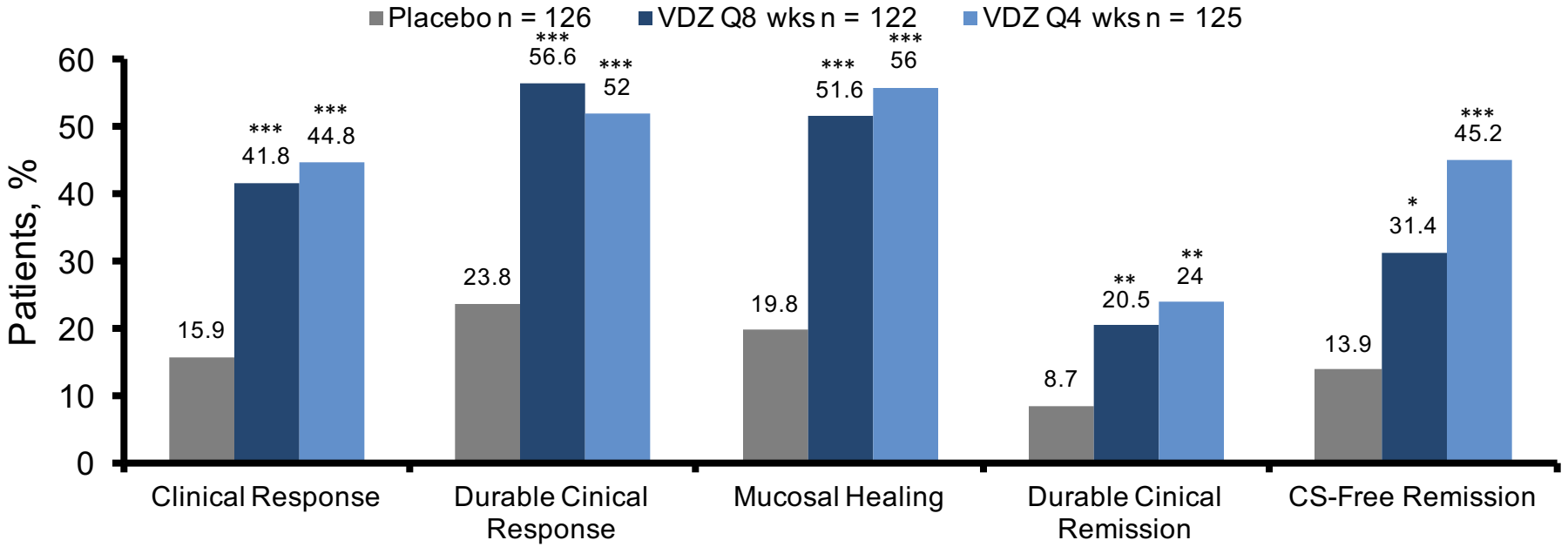
1. Rutgeerts P, et al. *N Engl J Med*. 2005;353(23):2462-2476. 2. Sandborn WJ, et al. *Gastroenterology*. 2012;142(2):257-265.
3. Sandborn WJ, et al. *Gastroenterology*. 2014;146(1):96-109.

VDZ for Induction of Remission in UC (GEMINI I)



Feagan BG, et al. *N Engl J Med*. 2013;369:699-710.

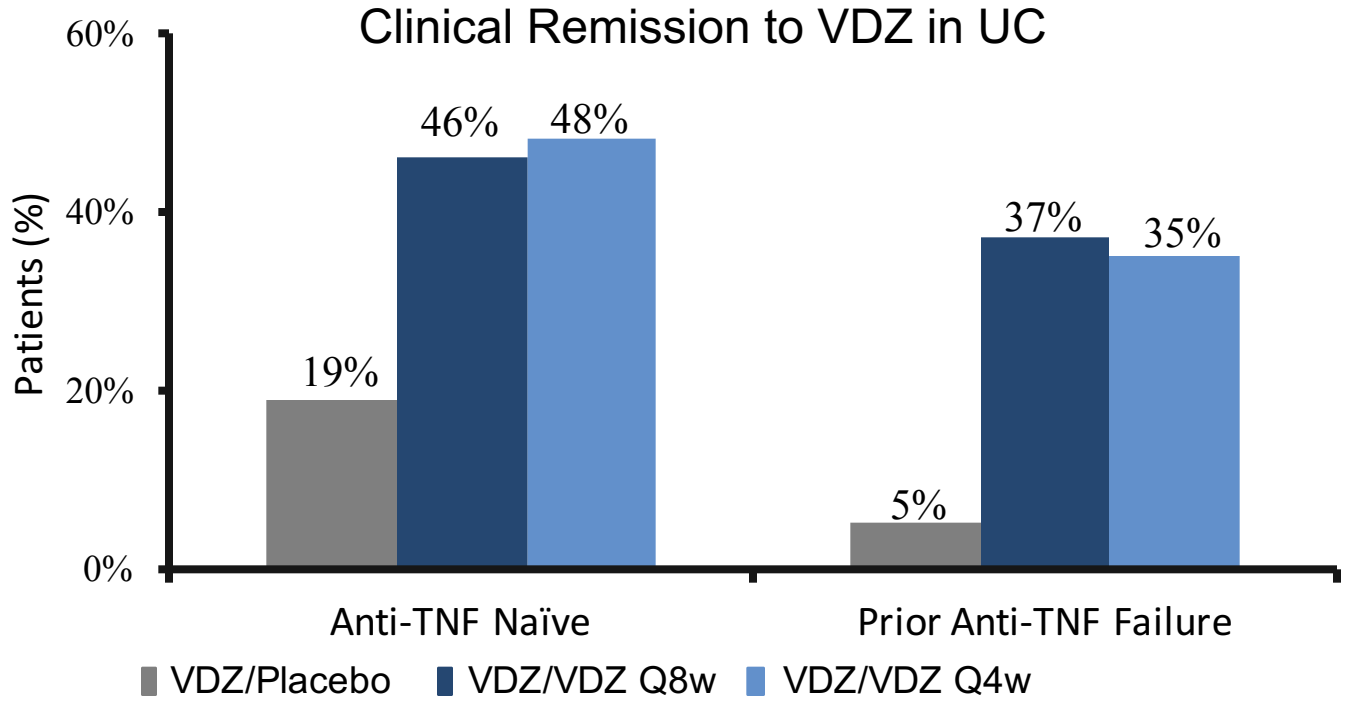
VDZ for Maintenance of Remission in UC (GEMINI I) at Week 52



*$p < .05$ **$p < .01$ ***$p < .001$

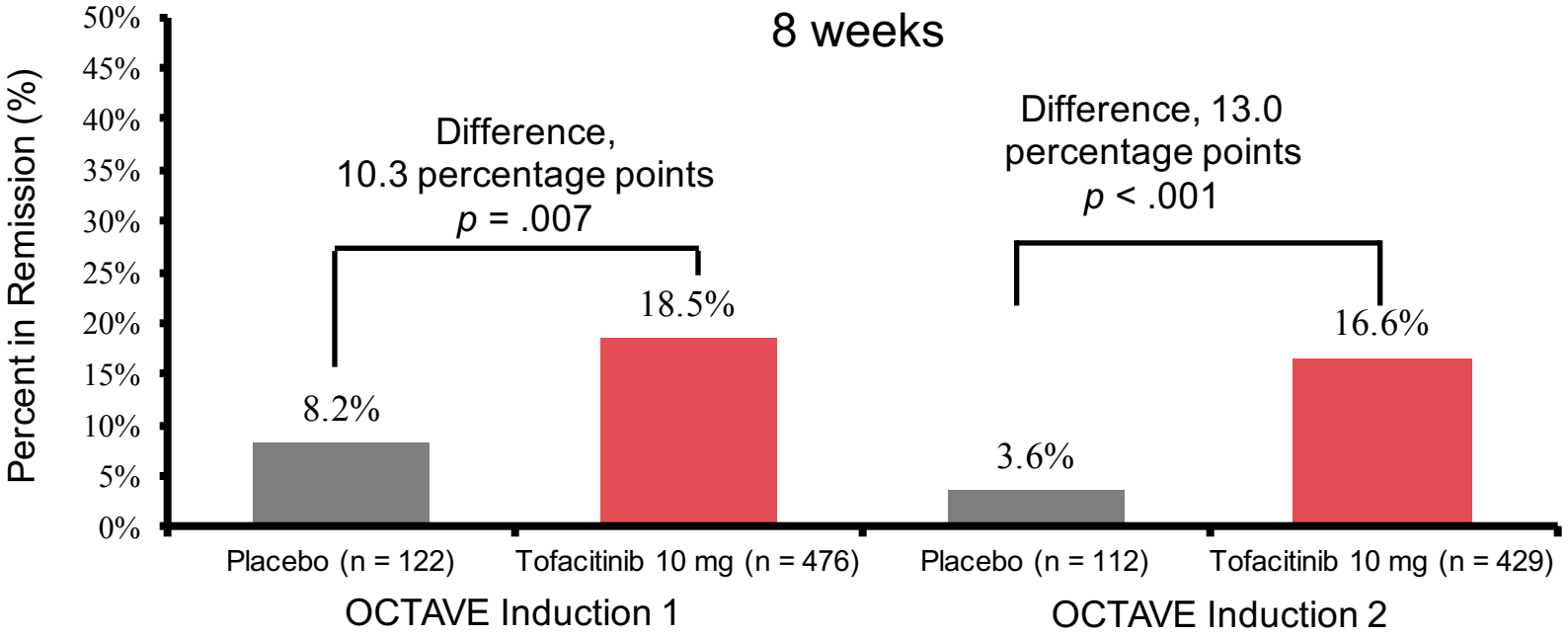
Feagan BG, et al. *N Engl J Med*. 2013;369:699-710.

Anti-TNF Naïve Patients Do Better with VDZ (GEMINI I)



Feagan BG, et al. *N Engl J Med*. 2013;369:699-710.

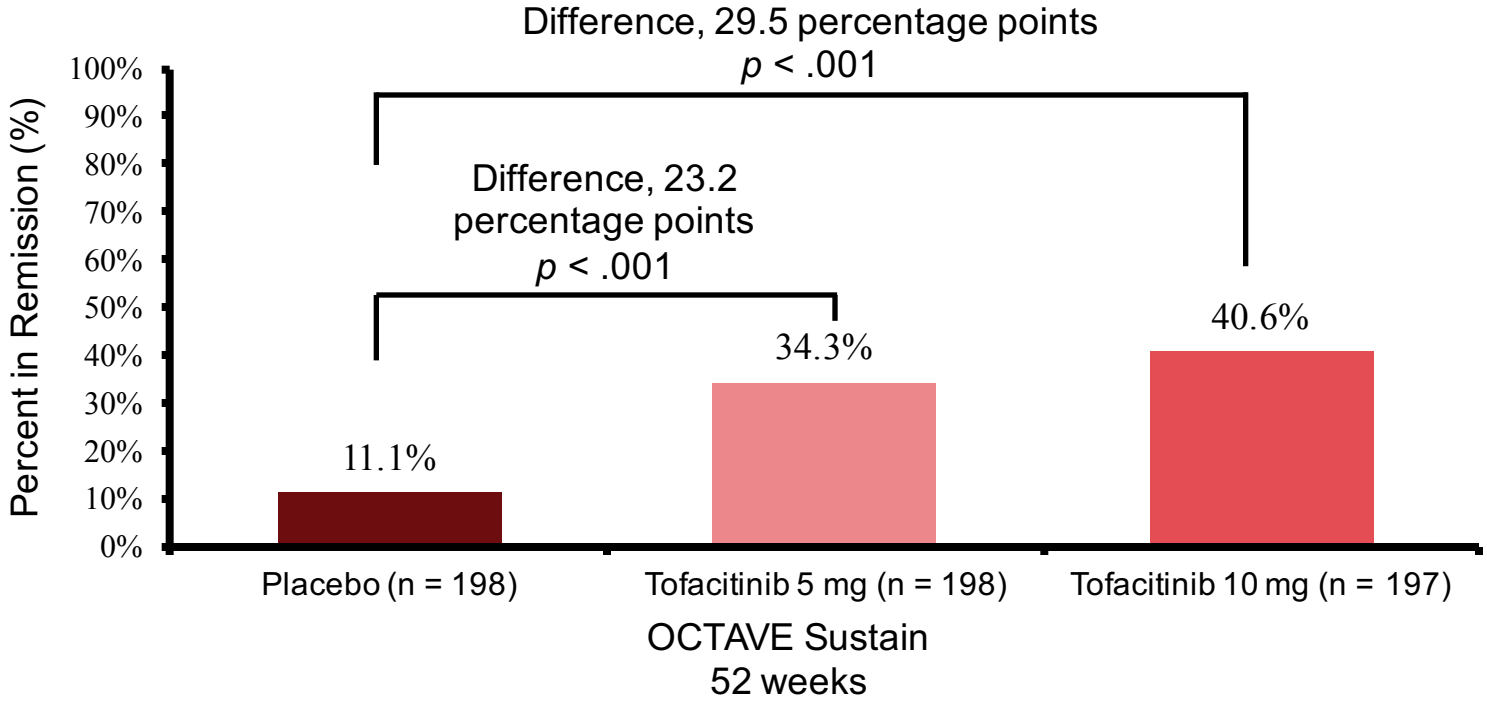
Tofacitinib for Induction of Remission in Patients with UC



Remission = total Mayo score of ≤ 2, with no subscore > 1 and a rectal bleeding subscore of 0.

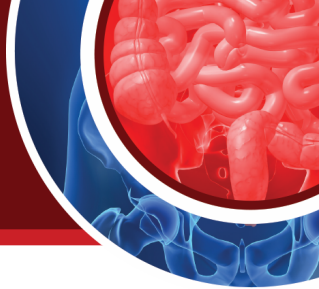
Sandborn WJ, et al. *N Engl J Med*. 2017;376:1723-1736.

Tofacitinib for Maintenance of Remission in UC to 52 weeks



Sandborn WJ, et al. *N Engl J Med*. 2017;376:1723-1736.

UC Care Pathway



Therapy for high-risk outpatient not in remission

Options:

- Anti-TNF +/- thiopurine*†
- Vedolizumab +/- immunomodulator‡
- Thiopurine (optimize 6-TGN concentrations)
- Proctocolectomy
- Tofacitinib

Failure to respond to prednisone

Or

- **Anti-TNF with or without thiopurine**
- **Vedolizumab with or without immunomodulator**

Failure to maintain steroid-induced remission on thiopurine

- **Subtherapeutic 6-TGN** (< 230 pmol 6-TGN/8x10^8 RBCs) → **Increase dose and recheck metabolites§**
- **Therapeutic 6-TGN** (> 230 pmol 6-TGN/8x10^8 RBCs) → **Switch to anti-TNF or vedolizumab**

6-TGN = 6-thioguanine nucleotide; RBCs = red blood cells.

*Combination therapy with a thiopurine is more efficacious than anti-TNF monotherapy and should be considered, especially in patients who have failed one or more anti-TNF agents.

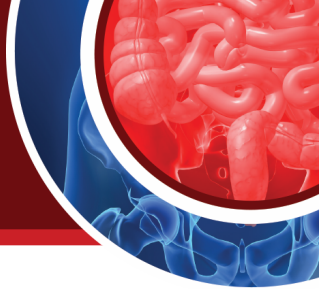
†Extrapolating from data in Chrohn's disease, methotrexate may be used instead of thiopurines to decrease anti-TNF immunogenicity.

‡Extrapolating from data with anti-TNF agents, thiopurines and methotrexate may be used to decrease vedolizumab immunogenicity.

§The addition of allopurinol (while decreasing the thiopurine dose to 1/4 of the previous dose) may be considered at centers with experience with this approach and recognizing the risks of severe myelosuppression and infection.

Dassopoulos T, et al. *Gastroenterology*. 2015;149:238-245.

UC Care Pathway



Therapy for high-risk outpatient not in remission (cont'd)

Loss of response to anti-TNF

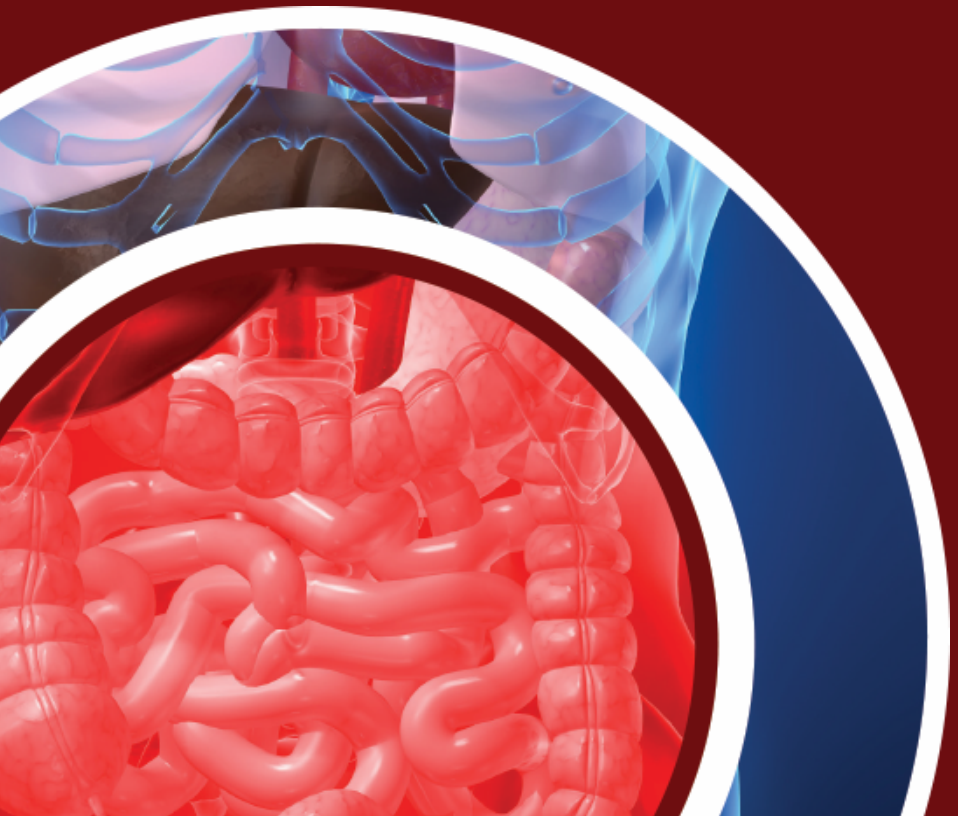
- **Subtherapeutic level (no or low Ab)**
  - Increase dose and/or decrease interval
  - Consider adding immunomodulator
- **Subtherapeutic level (high Ab)**
  - Switch within class
- **Therapeutic level**
  - Switch to vedolizumab with or without immuno-modulator

Loss of response to vedolizumab

- **Increase dose to 300 mg every 4 weeks**
  - Non-response
  - **Switch to anti-TNF with or without thiopurine**

Ab = antibody.

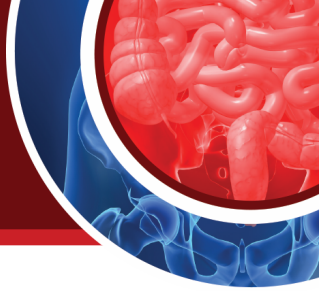
Dassopoulos T, et al. *Gastroenterology*. 2015;149:238-245.



Learning Objective 3

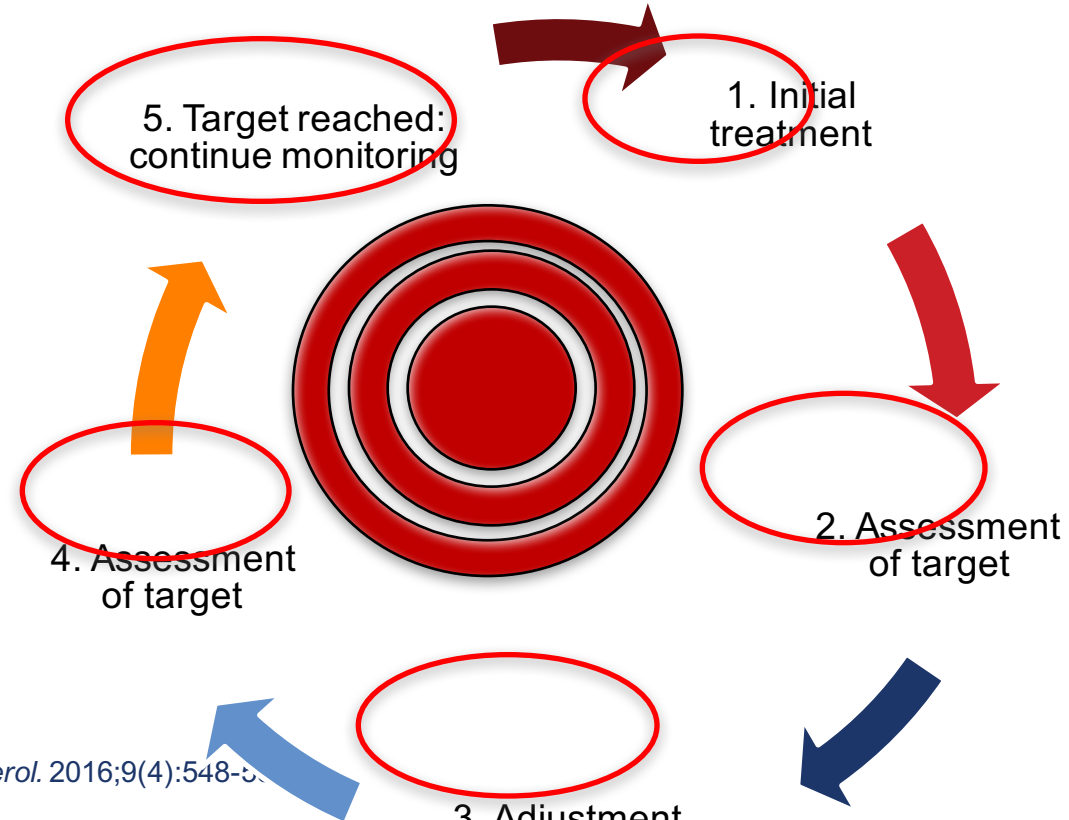
Select appropriate biologic therapy for individual patients with UC, taking into account disease burden, severity, treatment efficacy, safety, personalized risk-benefit profiles, and patient preference.

How to Choose Therapy in UC?



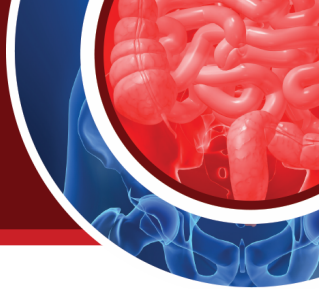
- Severity/prognosis
- Effectiveness
- Safety
- Convenience
- Insurance/coverage

Treating to Achieve a Target Goal



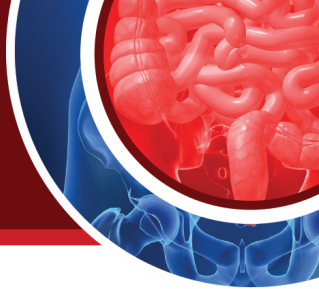
Sofia MA, Rubin DT.
Therap Adv Gastroenterol. 2016;9(4):548-5

Case: MG



- 30-year-old female
- 7 bloody stools per day
- Stool cultures negative
- Endoscopic findings: extensive colitis, deep ulcers

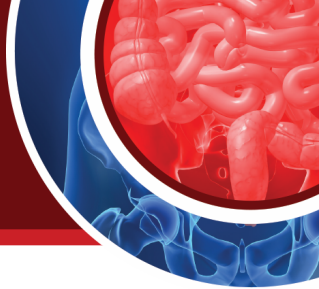
Audience Response



TNF inhibitor monotherapy was introduced for MG, which resulted in remission and treatment was continued for maintenance therapy. After about 4 months, she lost response and has detectable drug and no antibodies. How would you proceed?

A. Increase the dose
B. Add an immunomodulator
C. Cycle to another TNF inhibitor
D. Swap to vedolizumab
E. Swap to tofacitinib
F. Not sure

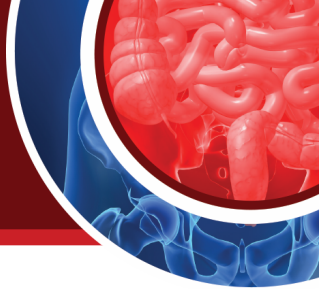
Audience Response



MG was switched to VDZ monotherapy, which resulted in remission and treatment was continued for maintenance therapy. After about 3 months, she discovered she was pregnant. How would you proceed?

A. Stop treatment while she is pregnant and breastfeeding
B. Continue treatment at a reduced dose while she is pregnant and breastfeeding
C. Continue treatment as is
D. Swap to tofacitinib
E. Swap to a different TNF inhibitor than the one she received initially
F. Not sure

So What Should the Targets Be?



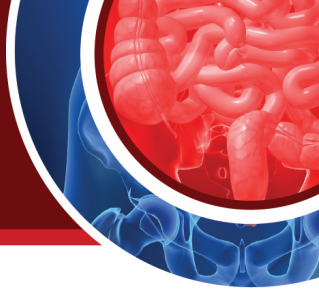
Selecting **T**herapeutic Ta**R**gets in **I**nflammatory Bowel **D**iseas**E**[1]

- Methods: 28 IBD specialists developed recommendations based on a systematic literature review and expert opinion[1]
- Results: 12 recommendations for UC and CD
- UC Target:
  - PRO: Resolution of rectal bleeding and diarrhea/altered bowel habit and
  - Endoscopic remission: Mayo endoscopic subscore of 0-1
  - Histological remission as an adjunctive goal: GS < 2B.0, RHI ≤ 3*, NI ≤ 1[2]
  - Biomarker remission (normal CRP and calprotectin) considered an adjunctive target[1]

*As long as lamina propria neutrophils score = 0 and neutrophil in epithelium score = 0.

1. Peyrin-Biroulet L, et al. *Am J Gastroenterol*. 2015;110:1324-1338. 2. Pai R, et al. *Gastrointest Endosc*. 2018;88:887-898.

PIANO Registry



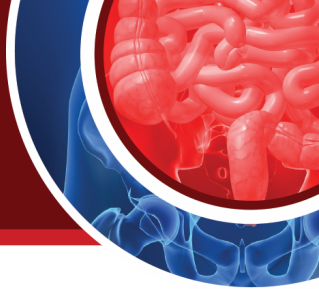
- > 1,400 mothers, > 600 infants exposed to biologic therapy, > 300 infants exposed to azathioprine/6-MP[1]
- No increase in birth defects observed with exposure to medication[1]
- No problems achieving developmental milestones[2,3]
- Minimal to no transfer of most drugs to breast milk[2,3]

These results suggest that these treatments do not need to be stopped during pregnancy or lactation.

6-MP = 6-mercaptopurine.

1. Uma M. *Gastroenterol Hepatol (N Y).* 2015;11(4):273-275.
2. Mahadevan U, et al. *Gastroenterology.* 2019 Jan 16. [Epub ahead of print].
3. Matro R, et al. *Gastroenterology.* 2018;155:696-704.

Pregnancy Care Pathway in IBD



9-month plan

IBD remission

IBD monitoring
- GI visit trimester 1 or 2 and then as needed
- Labs at least every trimester: complete blood count, liver enzymes, albumin (combine with OB labs)

Maternal/fetal monitoring
- Routine antepartum care
- Trimester 3 fetal growth ultrasound
- Examine perineum for evidence of active disease
- Counseling on mode of delivery

Medication
- **Stool softeners as needed**
- **Appropriate antimicrobials as needed**
- **Aminosalicylates and thiopurine monotherapy can continue throughout**
- **Corticosteroids are not maintenance therapy**
  - **Use as indicated for flares**
- **Biologics should continue throughout pregnancy without interruption**
  - **Can time last dose in trimester 3 to deliver infant at presumed drug trough**

Nutrition and weight gain
- **Prenatal vitamin**
  - **Iron may worsen abdominal pain**
- **Trimester 1: check iron/B12 levels**
- **Adequate folate supplementation**
- **Monitor gestational weight gain, which can be low in IBD**
- **Nutrition consult if needed**
  - **Post-surgical changes**
    - **Short bowel**
    - **Ostomy**
  - **Inadequate weight gain**
  - **Active disease**

IBD flare

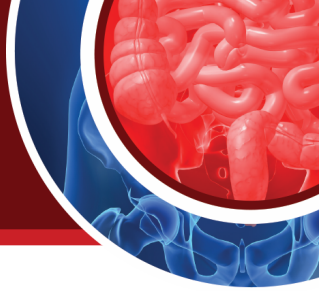
IBD monitoring
- GI follow-up every 2 weeks (patient portal, live, video)
- Adjust medication
- Monitor labs, calprotectin
- Management of flares

Maternal/fetal monitoring
- Consider fetal growth surveillance every 4 weeks after 24 weeks
- Recommend antepartum surveillance for patients with active disease in trimester 3
- Recommend ultrasound cervical length screening at 18-22 weeks gestation with follow-up if indicated by short cervix (< 25 mm) per usual obstetric indications
- Nutrition counseling
- NST/BPP for usual indications
- Patients on steroids should have early glucose screen
- Counseling on mode of delivery

Mahadevan U, et al. *Gastroenterology*. 2019 Jan 16. [Epub ahead of print].

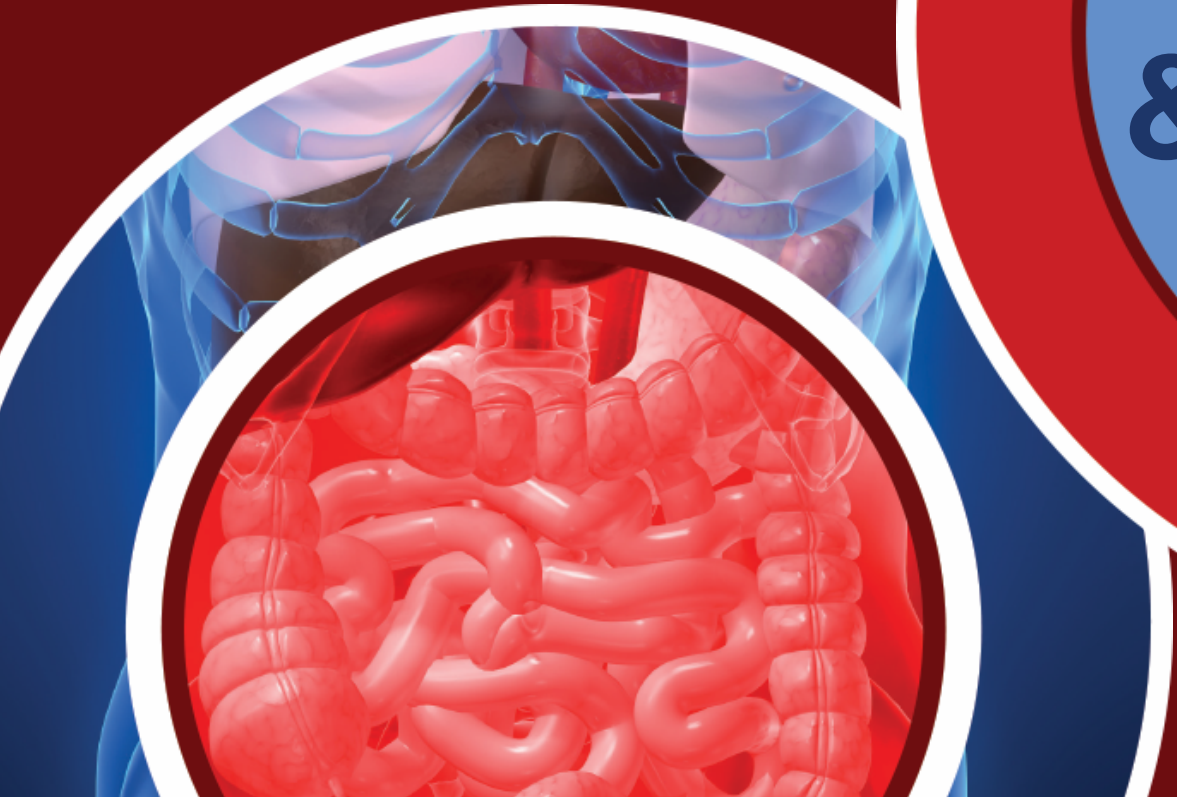
SMART Goals

Specific, **M**easurable, **A**ttainable, **R**elevant, **T**imely

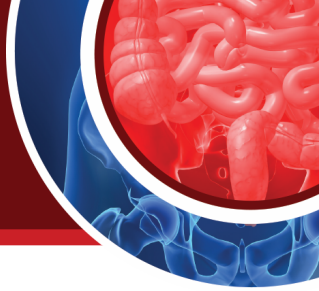


- Stratify risk in your patients with UC
- Measure mucosal inflammation objectively
- Initiate therapy to achieve targets in moderate-to-severe patients with UC
- Optimize therapies based on safety, efficacy, and pharmacokinetics

Questions & Answers



Downloadable Resources



Downloadable resources will be available at

www.CMEOutfitters.com/UCmgmtResources

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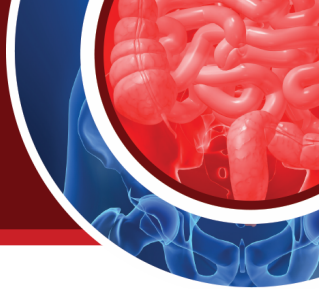

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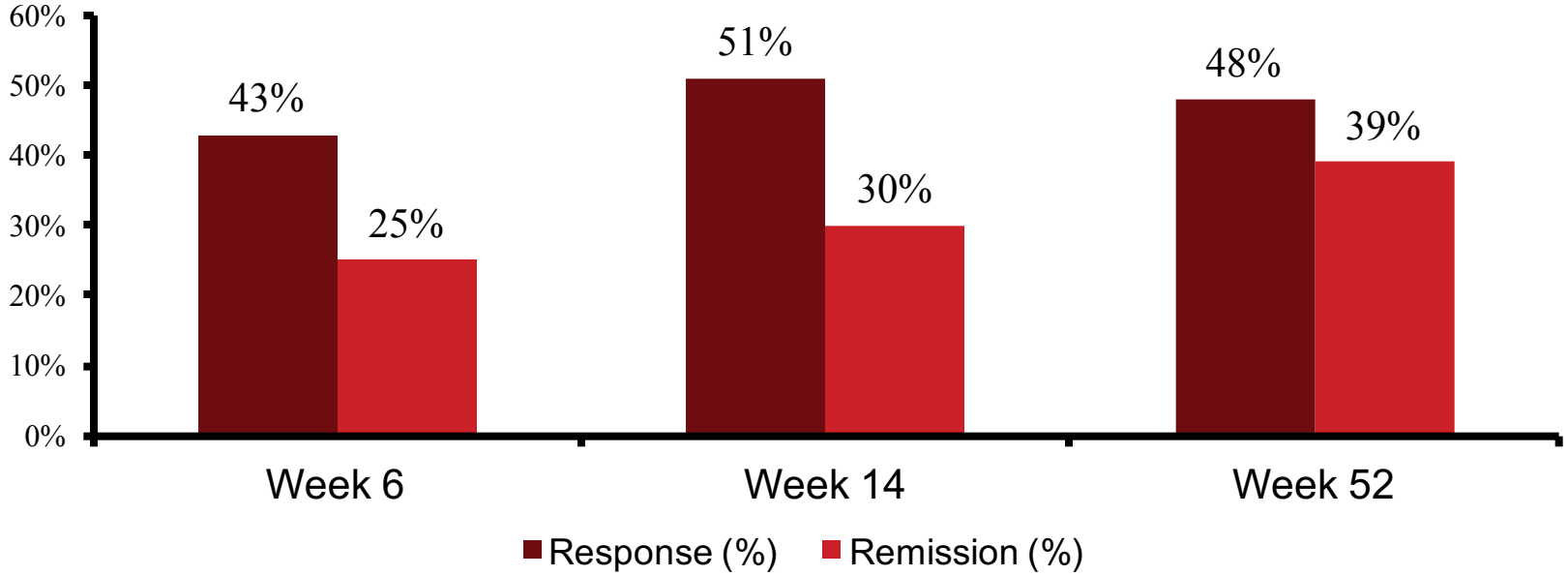
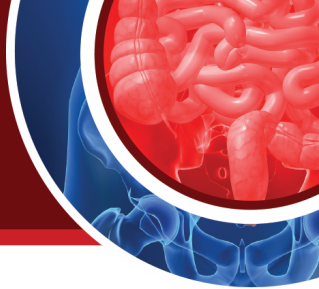
Real-World Effectiveness of VDZ in UC

- Pooled analysis, 9 studies, 571 patients with UC
- Adverse effects were minor and occurred in 30.6% of the patients

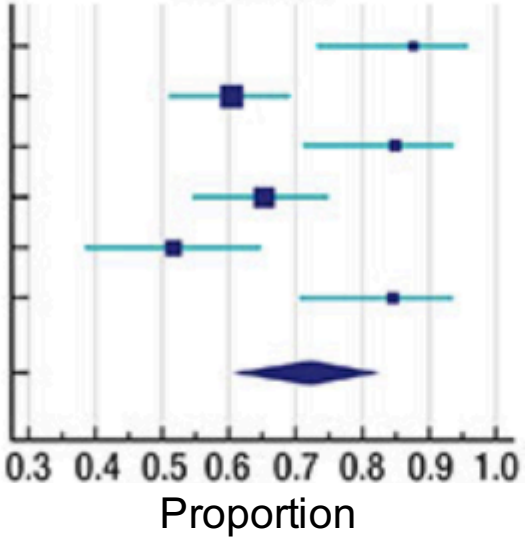


Engel T, et al. *J Crohns Colitis.* 2018;24:245-257.

VDZ Persistence in Patients with UC at 12 Months



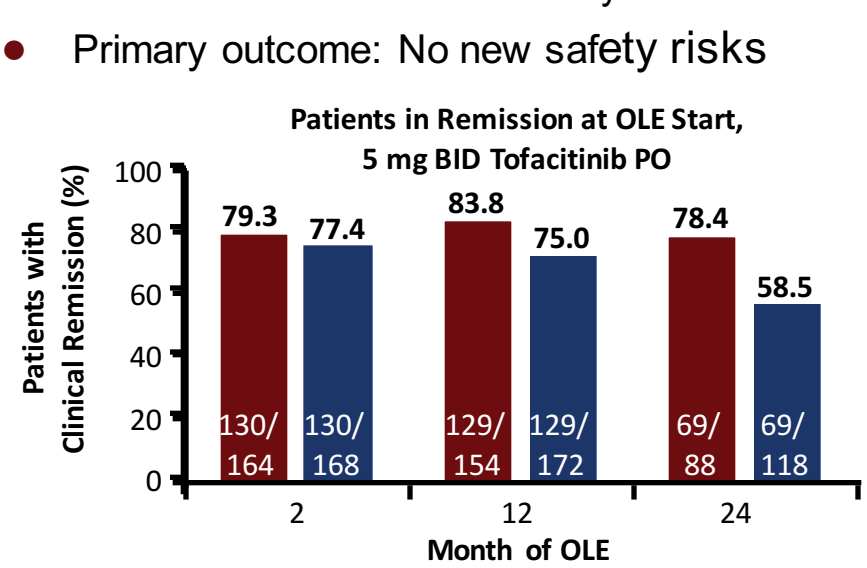
	12 Months	n/N	Rate (95% CI)
Allegretti et al. 2017		35/40	87.5 (73.1-95.8)
Amiot et al. 2017		73/121	60.3 (51.0-69.1)
Cummings et al. 2016		39/46	84.7 (71.1-93.6)
Eriksson et al. 2017		60/92	65.2 (54.5-74.8)
Stallmach et al. 2016		31/60	51.6 (38.3-64.7)
Vivio et al. 2016		38/45	84.4 (70.5-93.5)
Total (random effects)		276/404	72.2 (60.4-82.6)

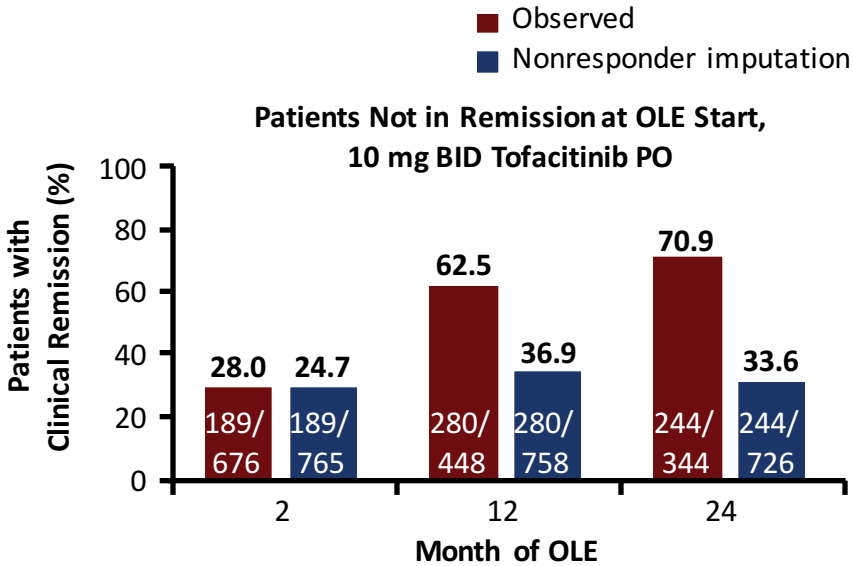


Demuth D, et al. ACG 2018. Abstract P1347.

Tofacitinib Maintenance in UC

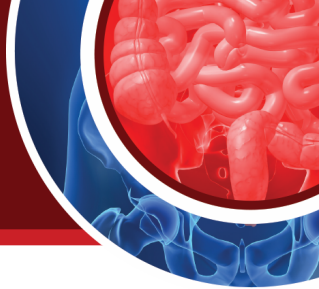
- Open-label, multicenter, long-term extension phase III study of adults with moderate-to-severe UC (N = 944)
  - Included nonresponders from 12-week OCTAVE induction study and participants of 52-week OCTAVE maintenance study
- Primary outcome: No new safety risks





Lichtenstein GR. ACG 2018. Abstract 13.

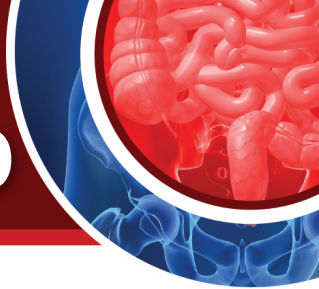
Audience Response



How would you stratify MG's risk for colectomy?

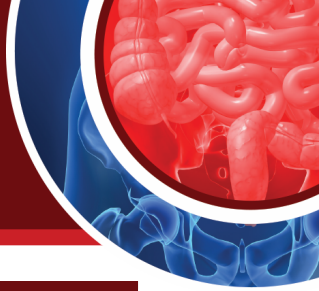
A. Low
B. Moderate-high
C. Not sure

The Roadmap to Incorporation of Mucosal Healing as an Endpoint in IBD



- Define mucosal healing (MH)
- Demonstrate that MH is associated with better short-term and longer-term outcomes
- Understand which therapies can achieve MH
- Develop strategies to achieve MH after initiation of therapy
- Perform prospective studies to show that MH is a viable, safe, and cost-effective target of treatment

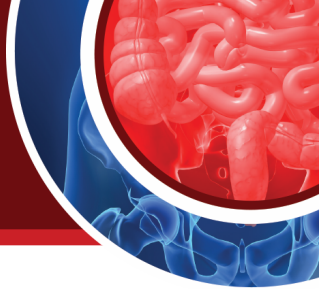
Endoscopic Indices of Severity in UC



Descriptor (Score most severe lesions)	Likert Scale Anchor Points
Vascular pattern	Normal (0)
Bleeding	Patchy obliteration (1)
	Obliterated (2)
	None (0)
	Mucosal (1)
Erosions and ulcers	None (0)
	Erosions (1)
	Superficial ulcer (2)
	Deep ulcer (3)

Travis SPL, et al. *Gastroenterology*. 2013;145:987-995.

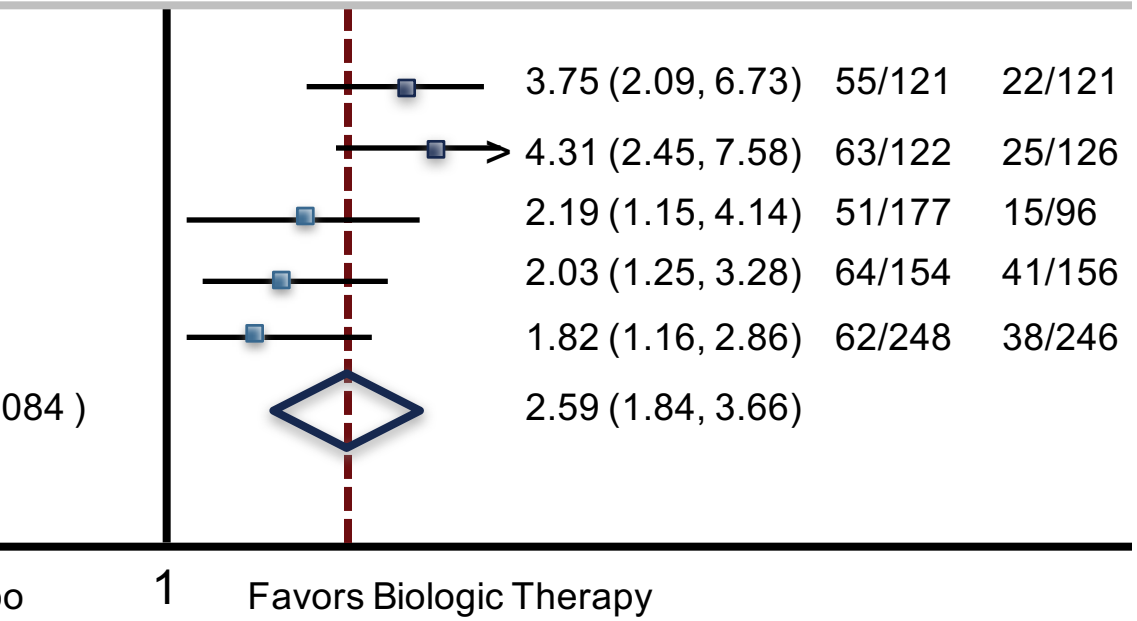
Movement to Objective Measures of Control and Chronic Care Model of IBD



Goal	Clinical Parameters	Outcomes
Response	Improved symptoms	Improved QoL
Remission	No symptoms Normal labs	Decreased hospitalization
Deep remission	Normal endoscopy Mucosal healing	Appropriate timing of surgery Minimal or no disability

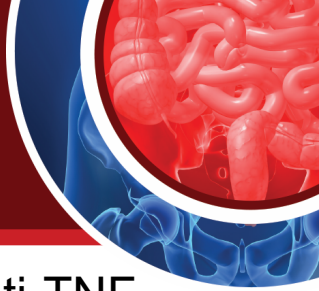
SUSTAINED DISEASE CONTROL

Effectiveness of Biologics in Attaining Mucosal Healing in UC: Maintenance Trials



Cholapranee A, et al. *Aliment Pharmacol Ther*. 2017.45(10):1291-1302.

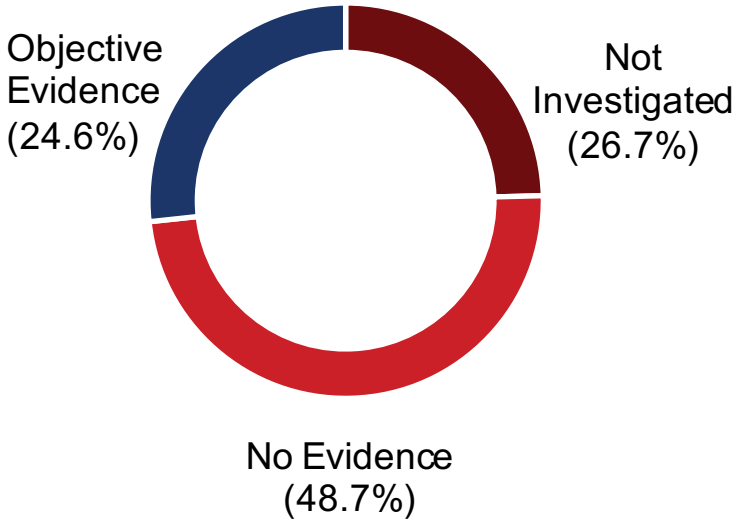
Dose Augmentation of Anti-TNFs



- Retrospective, single-center review of N = 529 patients receiving anti-TNF for IBD
  - 195 instances of dose augmentation identified
  - Instances examined for biochemical, imaging, or endoscopic evidence of inflammation

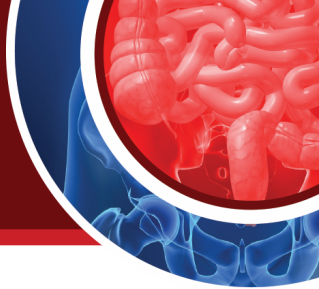
Patient Characteristics	
Patients with dose augmentations, n • CD • UC	151 117 34
Mean age at diagnosis, years	25.5
Female, %	50.3

Evidence of Inflammation Among 195 Instances of Dose Augmentation



Elias E, et al. ACG 2018. Abstract 54.

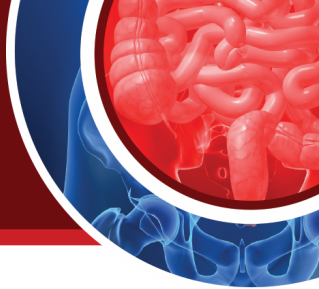
Shifts in Vedolizumab Utilization Across the United States Are Associated with Improved Outcomes



VICTORY Cohort	Crohn's Disease		*P* Value	Ulcerative Colitis		*P* Value
	Era 1* (n = 325)	Era 2‡ (n = 325)		Era 1* (n = 182)	Era 2‡ (n = 255)	
Disease duration, median (IQR), years	12 (6 - 21)	11 (6 - 17)	.23	6 (3 - 12)	6 (2 - 13)	.31
Hospitalized in prior 1 year, n (%)	122 (38)	113 (35)	.51	42 (23)	68 (27)	.44
Severe endoscopic disease, n (%)	81 (39)	87 (36)	.50	50 (39)	84 (41)	.73
Steroid-refractory or -dependent, n (%)	134 (41)	111 (34)	.08	103 (57)	105 (41)	< .01
No prior IS or TNF antagonist exposure, n (%)	7 (2)	23 (7)	< .01	22 (12)	59 (23)	< .01
TNF antagonist naïve, n (%)	20 (6)	40 (12)	< .01	52 (29)	91 (36)	.37
1 prior TNF antagonist n (%)	64 (20)	91 (28)		87 (48)	108 (42)	
≥2 prior TNF antagonists, n (%)	241 (74)	194 (60)		43 (24)	56 (22)	

*First 12 months of VDZ launch. ‡Subsequent 24 months. Koliani-Pace J, et al. ACG 2018. Abstract P0444.

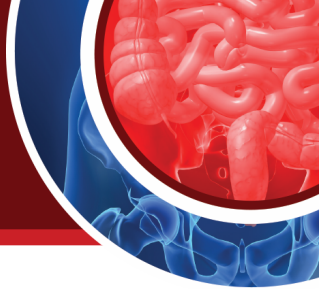
Shifts in Vedolizumab Utilization Across the United States Are Associated with Improved Outcomes



Truven Cohort**	Crohn's Disease		*P* value	Ulcerative Colitis		*P* Value
	Era 1* (n = 213)	Era 2‡ (n = 1,232)		Era 1* (n = 116)	Era 2‡ (n = 1,013)	
Disease duration, median (interquartile range), years	2.4 (1.2 - 5.6)	2.9 (1.3 - 5.1)	.38	2 (1.3 - 3.5)	2.4 (1 - 4)	.42
Hospitalized in prior 1 year, n (%)	48 (23)	228 (19)	.17	19 (16)	122 (11)	.19
No prior IS or TNF antagonist exposure, n (%)	43 (20)	223 (18)	.47	20 (17)	257 (25)	.05
TNF antagonist naïve, n (%)	61 (29)	339 (28)	.04	28 (24)	382 (38)	< .01
1 prior TNF antagonist n (%)	89 (42)	617 (50)		50 (43)	471 (47)	
≥2 prior TNF antagonists, n (%)	63 (30)	276 (22)		38 (33)	160 (16)	

*First 12 months of VDZ launch. ‡Subsequent 24 months.
**For Truven cohort, patients were TNF antagonist naïve during run-in period (≥ 6 months and at most 16.5 years).
Koliani-Pace J, et al. ACG 2018. Abstract P0444.

Therapeutic Drug Monitoring: Real-World Experience



Methods

- Therapeutic drug monitoring performed in patients with symptoms or endoscopic, biologic markers of active IBD (N = 341) despite treatment with biologics
  - Biologics: TNF inhibitors, ustekinumab, or vedolizumab
  - 70% of patients had CD

Results

- 2.9% (10/341) had antidrug antibodies, all 10 were anti-TNF antibodies
  - No anti-vedolizumab (0/67) or anti-ustekinumab (0/57) antibodies

↓

- Of those with antidrug antibodies, **90%** were switched to another biologic

↓

- Of those switched, **75%** achieved clinical remission

Glassner KL, et al. ACG 2018. Abstract P0461.