TREATING ULCERATIVE COLITIS IN THE ACUTE CARE SETTING

A Presentation for HealthTrust Members
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LEARNING OBJECTIVES – PHARMACISTS & NURSES

- Recall the current guidelines for acute management of ulcerative colitis and transition to maintenance therapies.
- Recognize treatment plans based on stage of ulcerative colitis and patient-specific factors to optimize safe and effective acute management of ulcerative colitis.
- Identify advantages and challenges of newer pharmacotherapy options for acute management of ulcerative colitis including small molecules, monoclonal antibodies and novel pipeline agents.

LEARNING OBJECTIVES - PHARMACY TECHNICIANS

- Recall medications used in the treatment of ulcerative colitis that are classified as NIOSH hazardous drugs.
- Identify medications that can worsen ulcerative colitis.
- Recognize the appropriate dose for weight-based medication regimens for acute management of ulcerative colitis.

OVERVIEW OF ULCERATIVE COLITIS

EPIDEMIOLOGY

- 6.8 million global cases of IBD
- 20% of patients will require hospitalization
- 20-30% of ASUC
- 25-30% risk of short-term colectomy with ASUC

IBD: inflammatory bowel disease, ASUC: acute severe ulcerative colitis

GBD 2017 Inflammatory Bowel Disease Collaborators. Lancet Gastroenterol Hepatol. 2020 Jan;5(1):17-30. doi: 10.1016/S2468-1253(19)30333-4.

PATHOPHYSIOLOGY

- Chronic immune-mediated condition

Current understanding of mucosal inflammation

- Combination of environmental and host factors
  - Increased reactive oxygen species and cytokines (IL-6)
  - Impaired resolution of inflammation
  - Abnormal shifts in environment of lumen
  - Changes in the gut microbiome
  - Damage to the mucus barriers via emulsifiers or a decrease in goblet cell function

New Findings

- Reduction in mitochondrial genes that code the oxidative phosphorylation chain and mitochondrial biogenesis
- Loss of mitochondrial homeostasis
  - Defective energy production
  - Increased oxidative stress

Porter RJ et al. F1000Res. 2020;9:F1000 Faculty Rev-294. doi: 10.12688/f1000research.20805.1.
Haberman Y et al. *Nat Commun.* 2019;10(1):38. doi: 10.1038/s41467-018-07841-3

RISK FACTORS

Porter RJ et al. F1000Res. 2020;9:F1000 Faculty Rev-294. doi: 10.12688/f1000research.20805.1.
Haberman Y et al. *Nat Commun.* 2019;10(1):38. doi: 10.1038/s41467-018-07841-3

CONTRIBUTING FACTORS TO DISEASE STATE PROCESS

Worsen	Improve
Opioids	Smoking
NSAIDs	Appendicitis
Excipients: lactose, colors, sugar alcohols, preservatives	Dietary supplements: calcium, folic acid, iron

Predictors of aggressive disease and colectomy

- Age <40 years old at diagnosis
- Extensive disease
- Severe endoscopic activity (large or deep ulcers)
- Extra-intestinal manifestations
- Early need for corticosteroids
- Elevated inflammatory markers

NSAID: non-steroidal anti-inflammatory drug

Feuerstein JD et al. Gastroenterology. 2020 Apr;158(5):1450-1461. doi: 10.1053/j.gastro.2020.01.006.

SYMPTOMS

Bloody diarrhea with abdominal pain, abdominal cramping, urgency, and fatigue

Relapsing and remitting mucosal inflammation

Universal involvement of the rectum as first site of inflammation

Acute Severe Ulcerative Colitis (ASUC):

- Hospitalized patients
- Truelove and Witts criteria: ≥6 bloody bowel movements/day with at least one of the following
  - Heart rate >90 beats/minute
  - Temperature >37.8° C
  - Hemoglobin <10.5 g/dl
  - Erythrocyte sedimentation rate >30 mm/h

Feuerstein JD et al. Gastroenterology. 2020 Apr;158(5):1450-1461. doi: 10.1053/j.gastro.2020.01.006.

SEVERITY SCORING

Truelove and Witts

	Mild	Severe	Fulminant
Stool (#/day)	<4	>6	>10
Blood in stool	Intermittent	Frequent	Continuous
Temperature (°C)	Normal	>37.5	>37.5
Pulse (beats/min)	Normal	>90	>90
Hemoglobin	Normal	<75% normal	Transfusion required
Erythrocyte sedimentation rate (mm/hr)	≤ 30	>30	>30
Colonic features on radiograph	None	Air, edematous wall, thumbprinting	Colonic dilation
Clinical signs	None	Abdominal tenderness	Abdominal distension and tenderness

Feuerstein JD et al. Gastroenterology. 2020 Apr;158(5):1450-1461. doi: 10.1053/j.gastro.2020.01.006.

MANAGEMENT OF ASUC

FIRST LINE - STEROIDS

Corticosteroids are first-line for induction of remission

- Dosing: 40-60 mg methylprednisolone IV or equivalent IV corticosteroid daily for 3-5 days

Mechanism: inhibit gene expression of adhesion molecules during transcription

Adverse effects: infection, metabolic disturbances, and mood disturbances

Effective in 30-40% of cases of ASUC with cumulative risk of relapse of 70-80%

Transition to second line therapy if no response after 5 days

- Oral steroids may be continued if partial response to IV steroids

ASUC: acute severe ulcerative colitis

Turner D et al. Clin Gastroenterol Hepatol. 2007 Jan;5(1):103-10. doi: 10.1016/j.cgh.2006.09.033.
George LA et al. Gastroenterol Clin North Am. 2020 Dec;49(4):705-716. doi: 10.1016/j.gtc.2020.08.001.
Dulai PS et al. Am J Gastroenterol. 2022 Aug;117(8):1288-1295. doi: 10.14309/ajg.0000000000001775.

SECOND LINE - STEROID REFRACTORY

Drug	Infliximab	Cyclosporine
Mechanism	TNFα inhibitor	Calcineurin inhibitor
Dosing	5 mg/kg IV infusion at weeks 0, 2, and 6 then every 8 weeks NYHA III-IV dose ≤5 mg/kg	2-4 mg/kg/day continuous IV infusion then transition to oral 2.3-3 mg/kg every 12 hours when possible
PKPD properties	Onset: 1-2 weeks Half-life: 7-12 days	Absorption: erratic and non-modified formulations can be affected by food, bile acids and GI motility Half-life: biphasic
Monitoring	CBC, LFTs	Trough concentration 100-200 ng/mL
Warnings/ Adverse Events	Infection, hepatotoxicity, autoantibody development, abdominal pain, nausea	NIOSH Group 1 carcinogen, nephrotoxicity, paresthesia, seizures, hepatic injury, infection, hyperkalemia, hypomagnesemia
Drug-Drug Interactions	Other TNFa-blocking agents, tocilizumab, methotrexate	Nephrotoxic agents, CYP-450 3A inhibitors/inducers

NYHA: New York Heart Association NIOSH: National Institute for Occupational safety & Health

Sandimmune (cyclosporine) [prescribing information]. East Hanover, NJ: Novartis; September 2023.
Remicade (infliximab) [prescribing information]. Horsham, PA: Janssen Biotech Inc; October 2021.

CHOICE OF THERAPY

Guideline Recommended ASUC management

First Line

- IV corticosteroids
- Monitor response for 3-5 days
- Can always consider surgery

Second Line

- Anti-TNF naïve: Infliximab or cyclosporine
- Can always consider surgery

Third Line

Colectomy recommended

Third line salvage therapy

- Switch second line agents
- Vedolizumab
- Tofacitinib

Feuerstein JD et al. Gastroenterology. 2020 Apr;158(5):1450-1461. doi: 10.1053/j.gastro.2020.01.006.

SALVAGE THERAPY

- For patients with ASUC refractory to steroids, Anti-TNF agents, and cyclophosphamide
- Colectomy is salvage therapy of choice
- Recent studies investigated off-label use of vedolizumab and tofacitinib for inpatients
  - New data from case study to support further investigation of upadacitinib
- No recommendations provided for inpatient induction with monoclonal antibodies

Feuerstein JD et al. Gastroenterology. 2020 Apr;158(5):1450-1461. doi: 10.1053/j.gastro.2020.01.006.
Dalal RS et al. Inflammatory Bowel Diseases, 2024 Feb; izae038, doi: 10.1093/ibd/izae038.
Feagan BG et al. *N Engl J Med.* 2013;369(8):699–710. doi: 10.1056/NEJMoa1215734.
D'Haens G et al. *Eur J Gastroenterol Hepatol*. 2024 Apr 1;36(4):404-415.

VEDOLIZUMAB

Mechanism	Humanized monoclonal antibody that binds to a4B7 and blocks the migration of memory T-lymphocytes across the endothelium to inflamed tissue
Dosing	300 mg IV infusion over 30 min followed by 30mL 0.9% sodium chloride flush at 0, 2, and 6 weeks then every 8 weeks thereafter May switch to subcutaneous 108 mg once every 2 weeks after 2 IV infusions
PKPD properties	Time to peak (SC): 7 days Half-life: 24 days
Monitoring	Monitor during and immediately after infusion for new onset leukopenia which can present with worsening neurologic function.
Warnings/ Adverse Events	Infusion reactions, hypersensitivity, infection, leukoencephalopathy, liver injury, malignancy, nasopharyngitis, headache
Drug-Drug Interactions	Live vaccines, TNF blockers, natalizumab

Entyvio (vedolizumab) [prescribing information]. Lexington, MA: Takeda Pharmaceuticals USA Inc; September 2023.

CLINICAL TRIALS VEDOLIZUMAB

Title	Vedolizumab as induction and maintenance therapy for ulcerative colitis.	Post hoc analysis of patient-reported outcomes from the VISIBLE 1 and 2 studies.
Population	• Adult patients with Mayo clinic score 6-12, sigmoidoscopy score ≥2, disease extension ≥15 cm • Treatment failure of guideline recommended therapy	• Adult patients with Mayo clinic score 6-12, diagnosed >3-6 months prior to randomization, disease extension ≥15 cm
Methods	Two integrated randomized 3:2, double-blind, placebo-controlled	Phase 3 open-label, randomized, placebo-controlled
Comparators	• Vedolizumab 300 mg IV vs placebo at 0 and 2 weeks N=374 • Open-label vedolizumab 300 mg IV at 0 and 2 weeks • Response at 6 weeks → SUBQ q8 week vs q4 week vs placebo	• Vedolizumab 300 mg IV vs placebo at 0 and 2 weeks N=994 • Protocol allowed prednisone ≤30 mg/day po or budesonide ≤9 mg/day po, immunosuppressive agents, and 5-aminosalicyclic acids
Primary outcome	Response- reduction in Mayo Clinic score by minimum 3 points, 30% decrease from baseline, reduction in rectal bleeding score by 1 point	Patient reported outcomes in stool frequency (SF) and rectal bleeding (RB) at week 6
Results	106 (47.1%) vedolizumab vs 38 (25.5%) placebo (difference 21.7 points; 95% CI, 11.6 to 31.7; P<0.001)	Patient reported clinical remission (combined SF and RB outcomes) • Anti-TNFα-naive (18.7%) patients vs. anti-TNFα experienced (12.3%) • Moderate (24.5%) vs. severe (10.5%) disease SF 14.8% with CS vs 19.5% w/o CS RB 42.6% with CS vs 46.7% w/o CS

CS: corticosteroid SF: stool frequency RB: rectal bleeding

Feagan BG et al. *N Engl J Med.* 2013;369(8):699–710. doi: 10.1056/NEJMoa1215734.
D'Haens G et al. *Eur J Gastroenterol Hepatol*. 2024 Apr 1;36(4):404-415.

TOFACITINIB

Mechanism	Janus kinas inhibitor (JAK)- prevents phosphorylation and activation of Signal Transducers and Activators of Transcription (STATS)
Dosing	Immediate release: Induction 10 mg by mouth BID for 8 weeks Extended-release: 22 mg by mouth daily for 8 weeks Dose adjustments for concomitant use with CYP3A4 or CYP2C19 inhibitors, renal impairment, hepatic impairment, and ANC 500-1000 cells/mm3
PKPD properties	Half-life: IR 3 hours, XR 6-8 hours
Monitoring	Recommended to monitor for changes in lymphocytes, neutrophils, hemoglobin, liver enzymes, and lipids
Warnings/ Adverse Events	NIOSH hazardous agent with black box warning for lymphoma and other malignancies, serious infection like tuberculosis, and thrombosis.
Drug-Drug Interactions	Strong CYP3A4 inhibitors, moderate CYP3A4 inhibitors with strong CYP2C19 inhibitors, strong CYP3A4 inducers, and immunosuppressive agents.

NIOSH: National Institute for Occupational Safety & Health
ANC: absolute neutrophil count

Xeljanz/Xeljanz XR (tofacitinib) [prescribing information]. New York, NY: Pfizer Inc; January 2022.

CLINICAL TRIAL TOFACITINIB

Authors/Title	Tofacitinib for Biologic-Experienced Hospitalized Patients With Acute Severe Ulcerative Colitis: A Retrospective Case-Control Study.
Population	• Adult patients with clinical ASUC naive to tofacitinib • Naïve to tofacitinib • Did not receive infliximab during index admission • No previous colectomy
Methods	Retrospective chart review from January 2014 to February 2021 Tofacitinib group randomly matched 1:3 by gender, date of admission, and inpatient provider

Comparators	• Tofacitinib 10mg po BID until discharge or 10mg po TID for 9 doses then 10mg po BID N=40
	  • 16 (40%) standard dosing
	  • 24 (60%) accelerated dosing
	• N=113

Primary outcome	Colectomy risk within 90 days of index hospitalization date
Results	6 (15%) total tofacitinib vs 23 (20.4%) control group HR 0.28 (95% CI 0.10 to 0.81, P=0.018) Covariate predictors: • Albumin nadir (HR 0.27, 95% CI 0.12, 0.59, P= 0.001) • Number of failed targeted therapies (HR 1.61, 95% CI 1.13, 2.29, P= 0.009) • Colonic dilation (HR 4.13, 95% CI 1.39, 12.3, P= 0.011) • Endoscopic Mayo score (HR 6.28, 95% CI 1.85, 21.4, P= 0.003)

Berinstein JA et al. Clin Gastroenterol Hepatol. 2021 Oct;19(10):2112-2120.e1. doi: 10.1016/j.cgh.2021.05.038.

BIOLOGICS FOR THE INDUCTION OF MAINTENANCE THERAPY

Drug	Ustekinumab	Adalimumab	Golimumab
Mechanism	Human IgG1Ķ monoclonal antibody IL-12 and IL-23.	Blocks TNFα interaction with cell surface receptors	Blocks TNFα interaction with cell surface receptors
Standard Dosing	Induction: one-time dose ≤55 kg 260 mg IV 55-85 kg 390 mg IV >85 kg 520 mg IV Maintenance: 90 mg SC injection every 8 weeks	Induction: 160 mg SC (four 40 mg SC injections in one day or two 40 mg SC injections for two days) then 80 SC mg two weeks later Maintenance: two weeks later start 40 mg SC every other week	Induction: 200 mg SC at week 0 then 100 mg SC at week 2 Maintenance: 100 mg SC every 4 weeks thereafter
PKPD properties	CYP3A4 metabolism Half-life: 8-14 hours	Onset: response determined after 3-4 months	Metabolism pathway is unknown Half-life: 2 weeks
Monitoring / Warnings	Monitor for signs of infection (TB and invasive fungal) and malignancy		
Drug-Drug Interactions	Live vaccines, CYP3A4 inducers/inhibitors	Live vaccines, CYP450 substrates	Live vaccines, other biologic agents, methotrexate, CYP450 inducers/inhibitors

Stelara (ustekinumab) [prescribing information]. Horsham, PA: Janssen Biotech Inc; March 2023.
Humira (adalimumab) [prescribing information]. North Chicago, IL: AbbVie Inc; November 2023.
Simponi Aria (golimumab) [prescribing information]. Horsham, PA: Janssen Biotech Inc; July 2023.

SMALL MOLECULE FOR THE INDUCTION OF MAINTENANCE THERAPY

Drug	Updacitinib
Mechanism	Janus kinas inhibitor (JAK)- prevents phosphorylation and activation of Signal Transducers and Activators of Transcription (STATS)
Standard Dosing	Induction: 45 mg once daily for 8 weeks; maintenance: 15 mg once daily; may increase to 30 mg once daily
PKPD properties	CYP3A4 metabolism Half-life: 8-14 hours
Monitoring/ Warnings	Not a NIOSH drug but does meet requirements for NIOSH. Monitor for signs of infection (TB and invasive fungal), thrombosis, and malignancy.
Drug-Drug Interactions	Live vaccines, CYP3A4 inducers/inhibitors

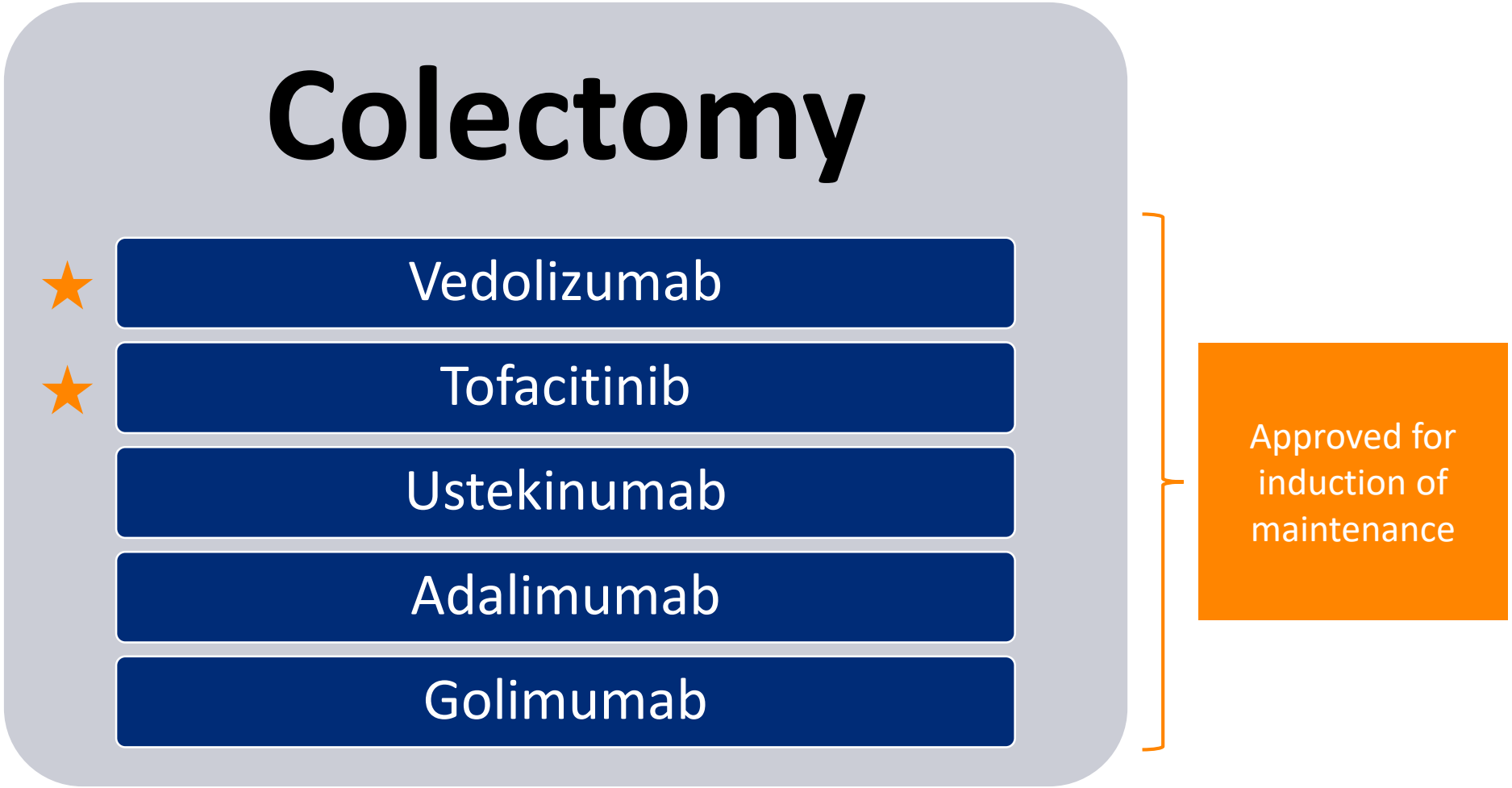
Rinvoq (upadacitinib) [prescribing information]. North Chicago, IL: AbbVie Inc; November 2023.
Dalal RS et al. Inflammatory Bowel Diseases, 2024 Feb; izae038, doi: 10.1093/ibd/izae038.

CLINICAL TRIAL SMALL MOLECULE INDUCTION OF MAINTENANCE THERAPY

Title	Clinical Outcomes at 8-16 Weeks After Upadacitinib Initiation for Acute Severe Ulcerative Colitis: A Case Series in the United States
Population	• Case series studies with 9 patients started on upadacitinib 45 mg daily while inpatient for ASUC • 7 had prior TNF exposure and 3 had infliximab during the index hospital admission • 7 were determined clinically refractory to corticosteroids
Methods	Case series Upadacitinib started at 30 mg po
Comparators	• Clinical response: reduction in simple clinical colitis activity index [SCCAI] by ≥3 points • Corticosteroid free clinical remission: SCCAI ≤2 with no use of oral corticosteroids
Results	• 6 patients remained on upadacitinib with clinical response and corticosteroid-free clinical remission • 5 on upadacitinib 30 mg po daily and 1 on upadacitinib 45 mg po daily • 1 patient achieved endoscopic response • None achieved endoscopic remission

Rinvoq (upadacitinib) [prescribing information]. North Chicago, IL: AbbVie Inc; November 2023.
Dalal RS et al. Inflammatory Bowel Diseases, 2024 Feb; izae038, doi: 10.1093/ibd/izae038.

OVERVIEW OF SALVAGE THERAPY



★ Trialed inpatient

NEWLY APPROVED

MIRIKIZUMAB

Mechanism	Humanized IgG4 monoclonal antibody that binds to p19 subunit of IL-23 and prevents differentiation, expansion, and survival of T-cells
Dosing	300 mg IV infusion over 30 min at 0, 4, and 8 weeks then 200 mg SC at 12 weeks and every 4 weeks thereafter
Indication	Induction of maintenance therapy
PKPD properties	Half-life: 9.3 days
Monitoring	Monitor for signs and symptoms of infection
Warnings/ Adverse Events	Hypersensitivity reactions, infection, tuberculosis, hepatotoxicity
Drug-Drug Interactions	Live vaccines, immunosuppressants

Omvoh (mirikizumab) [prescribing information]. Indianapolis, IN: Eli Lilly and Company; October 2023.

CLINICAL TRIAL MIRIKIZUMAB

Title	Mirikizumab as Induction and Maintenance Therapy for Ulcerative Colitis
Population	• Adult patients with Mayo score 4-9, endoscopic score 2-3
Methods	Two phase 3, randomized, double-blind, placebo-controlled 3:1 randomization in induction phase, 2:1 randomization in maintenance phase
Comparators	• Induction: 300 mg mirikizumab IV vs placebo every 4 weeks for 12 weeks N=1281 • Maintenance: 200 mg mirikizumab SC vs placebo every 4 weeks for 40 weeks N=544 • Concomitant 5-aminosalicyclic acid, oral steroids, and immunomodulators were allowed
Primary outcome	Clinical remission at week 12 and 52 Mayo stool-frequency score of 0 or reduction by 1 point from baseline, rectal bleeding score 0, and endoscopic score 0-1
Results	• Induction: mirikizumab 24.2% vs placebo 13.3% P<0.001 (11.1-point difference; 99.875% CI 3.2-19.1) • Maintenance: mirikizumab 49.9% vs placebo 25.1 P<0.001 (23.2-point difference; 95% CI 15.2-31.2)

D'Haens G et al.N Engl J Med. 2023 Jun 29;388(26):2444-2455. doi: 10.1056/NEJMoa2207940.

S1P RECEPTOR MODULATORS

Medication	Ozanimod	Etrasimod
Mechanism	Sphingosine 1-phosphate receptors 1 and 5. Decreases lymphocyte mobility from lymph nodes. Etrasimod also has activity at S1P 3 and 4.	
Dosing	Initial: Day 1-4: 0.23 mg po once daily, Day 5-7: 0.46 mg po once daily Maintenance dose: 0.92 mg po once daily day 8	2 mg po once daily
PKPD properties	Two active metabolites formed from CYP3A4 metabolism	No active metabolites but is metabolized by CYP2C8, CYP2C9, and CYP3A4
Monitoring	Monitor for signs and symptoms of infection and liver injury	Monitor for signs and symptoms of infection
Warnings/ Adverse Events	Infection, hepatotoxicity, bradycardia, and hypotension	Infection, bradycardia, and hypertension
Drug-Drug Interactions	CYP2C8 and CYP3A4 inducers/inhibitors	CYP2C8, CYP2C19, and CYP3A4 inducers/inhibitors

- Case series published using ozanimod as maintenance therapy after induction with cyclosporine in ASUC.

Velsipity (etrasimod) [prescribing information]. New York, NY: Pfizer Labs; October 2023.
Zeposia (ozanimod) [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; August 2023.
Suilik HA et al. Inflamm Res. 2024 Feb;73(2):183-198. doi: 10.1007/s00011-023-01829-6.
Cohen NA et al. ACG Case Rep J. 2022 Jul 21;9(7):e00832. doi: 10.14309/crj.0000000000000832.

CLINICAL TRIALS S1P RECEPTOR MODULATORS

Title	Ozanimod as Induction and Maintenance Therapy for Ulcerative Colitis.	Achievement of clinical, endoscopic, and histologic outcomes in patients with ulcerative colitis treated with etrasimod, and association with fecal calprotectin and C-reactive protein: results from the Phase 2 OASIS trial.
Population	Adult patients 18-75 years old with Mayo score of 6-12, endoscopic score ≥2, RB ≥1, SF ≥1	Adult patients 18-80 years old with Mayo score 4-9, endoscopic score ≥2, RB ≥1, failure of conventional or biologic therapy
Methods	• Phase 3, multicenter, randomized double-blind, placebo-controlled trial • Conventional oral therapy started ≥2 weeks before screening and continued for 10-week induction • 52-week maintenance with steroid taper • N=1012 (induction) and N=457 (maintenance)	• Phase 2, double-blind, placebo-controlled • 1:1:1 randomization etrasimod 1 mg, etrasimod 2 mg and placebo once daily for 12 weeks • N= 156
Primary outcome	Clinical remission	Endoscopic improvement and histologic remission
Results	Induction period: ozanimod 18.4% vs. placebo 6.0%, P<0.001 Maintenance period: ozanimod 37.0% vs. placebo 18.5%, P<0.001	Etrasimod 1 mg versus placebo [8.2% vs 4.1%; 90% CI, -4.3-11.5; p = 0.231] Etrasimod 2 mg versus placebo [19.5% vs 4.1%; 90% CI, 4.3-26.4; p = 0.010]

Sandborn WJ et al. N Engl J Med. 2021 Sep 30;385(14):1280-1291. doi: 10.1056/NEJMoa2033617.
Yarur AJ et al. J Crohns Colitis. 2024 Jan 20:jjae007. doi: 10.1093/ecco-jcc/jjae007.

ADVANTAGES AND DISADVANTAGES OF NEW THERAPY

Small Molecule Agents Tofacitinib, Upadacitinib, Ozanimod, Etrasimod	
Advantages	**Disadvantages**
• Ease of administration (oral tablets)	• Cost
• Delay or resolve need for surgical intervention	• Drug-drug interactions
• Therapy options after failure of guideline recommended management	• Organ dysfunction requires dose adjustment

Biologic Agents Vedolizumab, Ustekinumab, Adalimumab, Golimumab, Mirikizumab	
Advantages	**Disadvantages**
• Resolution of symptoms	• Cost
• Delay or resolve need for surgical intervention	• Immunosuppression
• Therapy options after failure of guideline recommended management	• Injectable/Infusion delivery method

Feuerstein JD et al. Gastroenterology. 2020 Apr;158(5):1450-1461. doi: 10.1053/j.gastro.2020.01.006.
Sandborn WJ et al. Gastroenterol Hepatol. 2021 Apr;17(4 Suppl 4):3-13.

DISCHARGE PLANNING

TRANSITIONING TO OUTPATIENT

Steroids

- Observe for 24 hours prior the discharge
- May discharge if blood is visible in stool or stool frequency is above baseline
- 40 mg of oral prednisone once daily

Second line therapy

- Infliximab: after initial dose, two infusions every 4 weeks must be completed before starting every 8-week infusion schedule
- Cyclosporine: patient may transition to oral dosing after resolution of symptoms and hemodynamically stable

Biologic agents

- Make sure patients are up to date on vaccinations
- Monitor patients during infusions and immediately after

Small molecule agents

- Check for drug-drug interactions
- Appropriately dose adjust based on discharge labs and organ function

Turner D et al. Clin Gastroenterol Hepatol. 2007 Jan;5(1):103-10. doi: 10.1016/j.cgh.2006.09.033.
George LA et al. Gastroenterol Clin North Am. 2020 Dec;49(4):705-716. doi: 10.1016/j.gtc.2020.08.001.
Dulai PS et al. Am J Gastroenterol. 2022 Aug 1;117(8):1288-1295. doi: 10.14309/ajg.0000000000001775.

THERAPIES IN THE PIPELINE

MECHANISMS IN THE PIPELINE

- Novel mechanisms of action currently in investigation for use in severe refractory ulcerative colitis with possible inpatient management application

Anti-IL 23	JAK/STAT	Anti-integrin
• Risankizumab-QUASAR	• Filgotinib-FINCH 4 • Brepocitinib-VALOR	• Etrolizumab-HIBISCUS

Assessment Question 1

What is a potential advantage of tofacitinib over infliximab for the treatment of acute refractory UC?

A. Tofacitinib does not have a risk for thrombotic events.

B. No renal dose adjustment is necessary.

C. Tofacitinib may be an option for acute UC flares in patients with biologic refractory UC.

D. Tofacitinib is dosed less frequently than infliximab.

Assessment Question 1

What is a potential advantage of tofacitinib over infliximab for the treatment of acute refractory UC?

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C. Tofacitinib may be an option for acute UC flares in patients with biologic refractory UC.

D. Tofacitinib is dosed less frequently than infliximab.

Correct Answer- C

Assessment Question 2

Which of the following medications are known to cause UC flares?

A. Naproxen

B. Rifaximin

C. Prednisone

D. Amlodipine

Assessment Question 2

Which of the following medications are known to cause UC flares?

A. Naproxen
B. Rifaximin
C. Prednisone
D. Amlodipine

Correct Answer- A

Assessment Question 3

AC is a 36-year-old male that presents to the hospital with abdominal tenderness and more than 5 bloody stools a day. He has a past medical history of ulcerative colitis in remission after starting infliximab as an outpatient with no hospitalizations for UC flares in the past. He recently started taking cetirizine for seasonal allergies. What is the first line option for inpatient management of ulcerative colitis?

A. Cyclosporine 2-4 mg/kg/day IV

B. Methylprednisolone 40-60 mg IV in 1-3 divided doses for 5 days

C. Tofacitinib 10 mg twice daily by mouth for 8 weeks

D. Infliximab 5mg/kg IV at 0, 2, and 6 weeks then every 8 weeks

Assessment Question 3

AC is a 36-year-old male that presents to the hospital with abdominal tenderness and more than 5 bloody stools a day. He has a past medical history of ulcerative colitis in remission after starting infliximab as an outpatient with no hospitalizations for UC flares in the past. He recently started taking cetirizine for seasonal allergies. What is the first line option for inpatient management of ulcerative colitis?

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B. Methylprednisolone 40-60 mg IV in 1-3 divided doses for 5 days

C. Tofacitinib 10 mg twice daily by mouth for 8 weeks

D. Infliximab 5mg/kg IV at 0, 2, and 6 weeks then every 8 weeks

Correct Answer- B

Assessment Question 4

Which medication is not a hazardous drug?

A. Tofacitinib
B. Cyclosporine
C. Infliximab
D. Methotrexate

Assessment Question 4

Which medication is not a hazardous drug?

A. Tofacitinib
B. Cyclosporine
C. Infliximab
D. Methotrexate

Correct Answer- C

Assessment Question 5

RG is a 64-year-old female with acute severe ulcerative colitis refractory to steroid therapy. She is 72 kg and is starting cyclosporine for rescue therapy. What is the appropriate dose for RG?

A. 250 mg IV every 12 hours

B. 100 mg IV every 8 hours

C. 250 mg IV as a continuous infusion

D. 100 mg IV as a continuous infusion

Assessment Question 5

RG is a 64-year-old female with acute severe ulcerative colitis refractory to steroid therapy. She is 72 kg and is starting cyclosporine for rescue therapy. What is the appropriate dose for RG?

A. 250 mg IV every 12 hours

B. 100 mg IV every 8 hours

C. 250 mg IV as a continuous infusion

D. 100 mg IV as a continuous infusion

Correct Answer- C

Assessment Question 6

ST is a 47-year-old male that is ready for discharge after a complicated hospital admission for an ulcerative colitis flare. During the admission he was initiated on infliximab but was found to be nonresponsive. What agent would be the best choice to start after discharge for induction of remission? Select all that apply.

A. Vedolizumab
B. Ustekinumab
C. Tofacitinib
D. Adalimumab
E. Surgical management

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Correct Answer- All of the above

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Thank you!

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