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Medical Center

Approach to the Hospitalized Patient with Acute Severe Ulcerative Colitis

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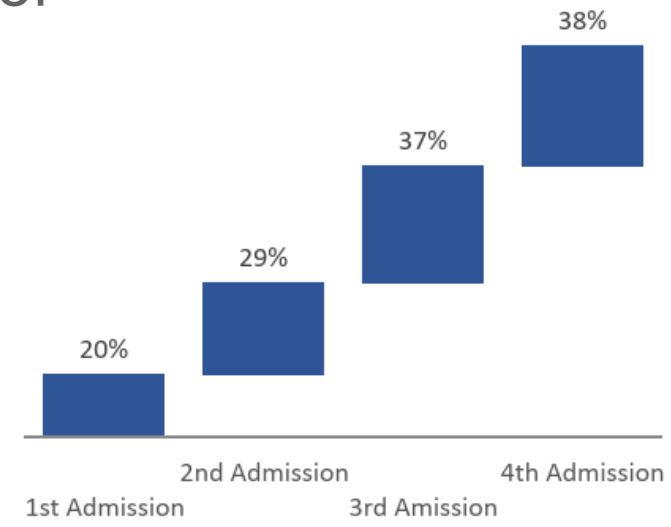
Disclosures

None.

Acute Severe Ulcerative Colitis (ASUC)

- Up to 25% of UC patients develop at least one episode of ASUC requiring hospitalization in their disease courses.
- Mortality:
  - Pre-corticosteroids era: 30-40%
  - Modern era: decreased to 1-3%
- Recent large retrospective cohort study, 2024:
  - 12% undergo colectomy during the same admission
  - 20% undergo colectomy within 1 year of admission



Colectomy rates for ASUC

Dinesen LC. J Crohns Colitis. 2010.
Dong C. Aliment Pharmacol Ther. 2020
Lewis J. Am J Gastroenterol. 2024.

Learning Objectives

- How do we define ASUC? When is hospitalization indicated?
- What initial work-up is needed?
- What is the initial treatment?
- What are the options when patients fail first-line therapy?
- When is surgery indicated?
- Management algorithm from 2025 ACG Clinical Guideline Update on Ulcerative Colitis in Adults

Definition of ASUC

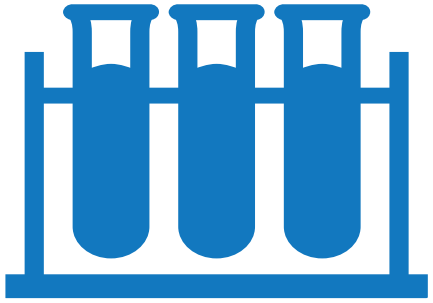
- **Modified Truelove and Witts criteria:**

≥6 stools/day with visible blood, plus ≥ 1 systemic sign of toxicity:

- Tachycardia >90bpm
- Fever
- Anemia <10.5g/dL
- ESR >30mm/hr or CRP >5mg/dL

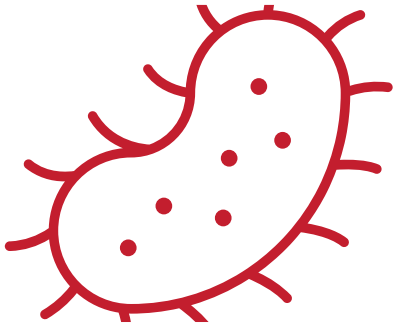
- Severe hemorrhage
- Dehydration
- Concern for acute abdomen on exam
- Resistance to outpatient medical therapies

What evaluations are needed at admission?



- Complete blood count
- Metabolic panel
- Liver function test (albumin)
- Irons study, TB test, viral hepatitis

- C-reactive protein
- Fecal calprotectin



- C. difficile
- CMV colitis

Sigmoidoscopy within first 24hr

- Abdominal X-ray
- CT scan if concern for toxic megacolon or perforation

How are patients treated when first hospitalized?

- IV fluid hydration, electrolyte repletion
- Stop anti-cholinergics, opioids, NSAIDs
- Nutrition: enteral feeding preferred, involve dietician
- DVT prophylaxis with low molecular weight heparin in all patients
- Withhold 5-ASA
- No role of routine use of antibiotics

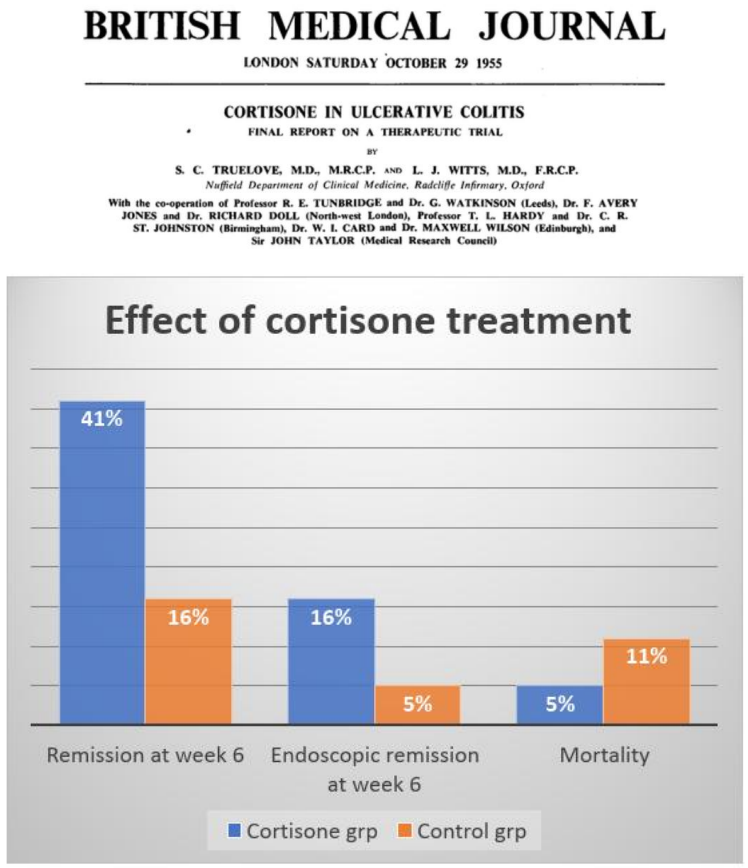
Nguyen GC. Gastroenterology. 2014.
Ra G. J Crohns Colitis. 2013.

How are patients treated when first hospitalized?

- **First line therapy:** parenteral corticosteroids, up to 1mg/kg/d for 3-5 days
  - No benefit beyond 60mg/d of methylprednisolone
  - No significant difference between continuous vs. bolus dosing
  - Continued use for more than 5 days not recommended

Predictors of poor response: high CRP, low albumin, deep ulcers

Landmark study by Truelove and Witts, 1955



BRITISH MEDICAL JOURNAL

LONDON SATURDAY OCTOBER 29 1955

CORTISONE IN ULCERATIVE COLITIS

FINAL REPORT ON A THERAPEUTIC TRIAL

BY

S. C. TRUELOVE, M.D., M.R.C.P. AND L. J. WITTS, M.D., F.R.C.P.

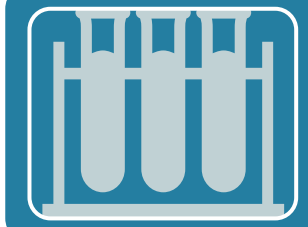
Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford

With the co-operation of Professor R. E. TUNBRIDGE and Dr. G. WATKINSON (Leeds), Dr. F. AVERY JONES and Dr. RICHARD DOLL (North-west London), Professor T. L. HARDY and Dr. C. R. ST. JOHNSTON (Birmingham), Dr. W. I. CARD and Dr. MAXWELL WILSON (Edinburgh), and Sir JOHN TAYLOR (Medical Research Council)

How to assess response to treatment?

Clinical symptoms/abdominal exam:

Rectal bleeding, stool frequency, rectal urgency, abdominal pain



Daily CRP:

Falls at least 10-20% per day, drop by 50-75% by day 3

Intestinal US:

Very useful to detect treatment response as early as day 1

Oxford Index

On day 3:

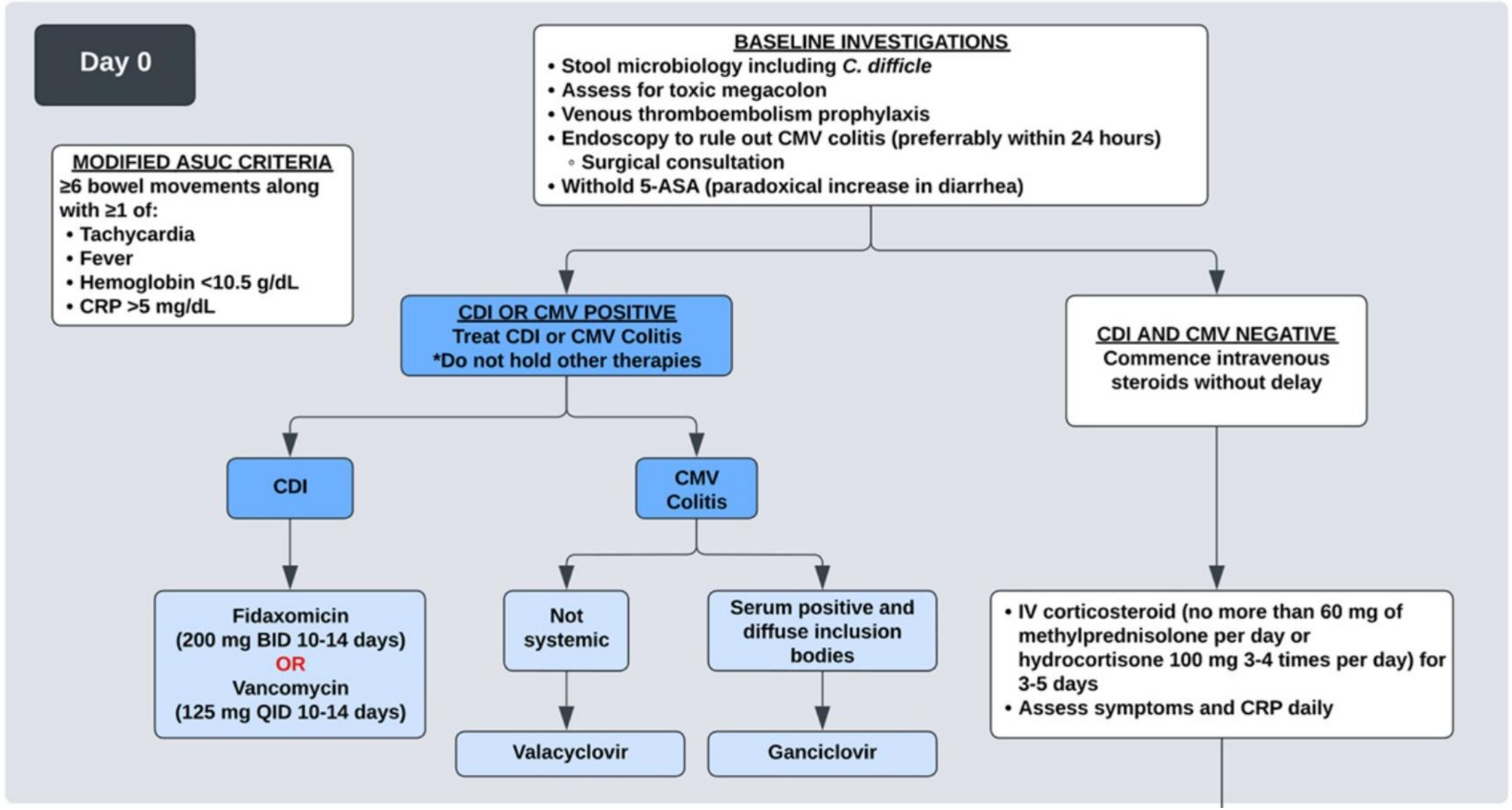
- >8 bowel movements
- Or, 3-8 bowel movements plus CRP >45 mg/L

➢ predicts a colectomy with 85% success

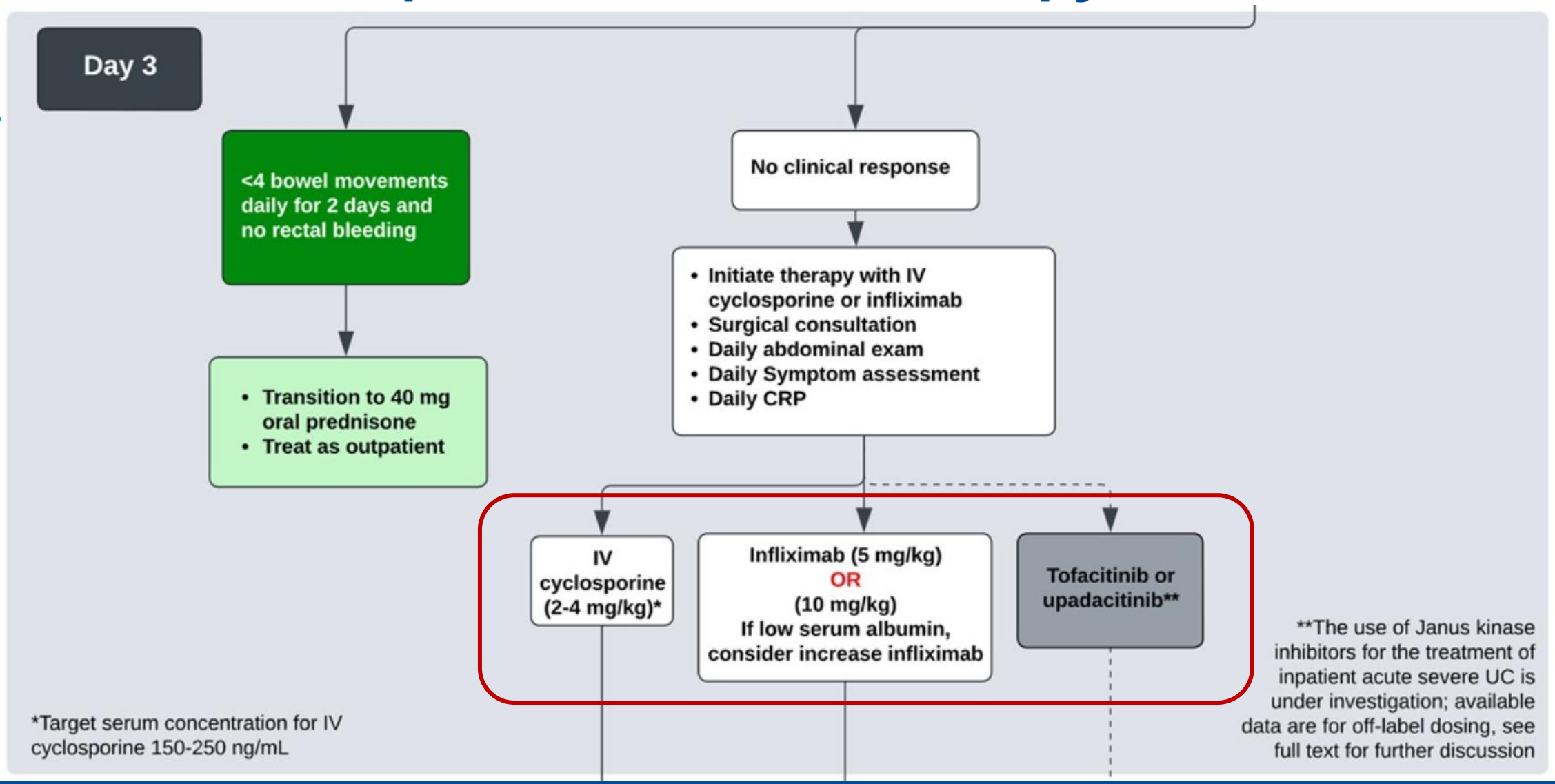
Day 3 – Decision point ➢ **Transition to oral prednisone vs. rescue therapy**

Travis SP. Gut. 1996.

2025 ACG Clinical Guideline Update: Ulcerative Colitis in Adults

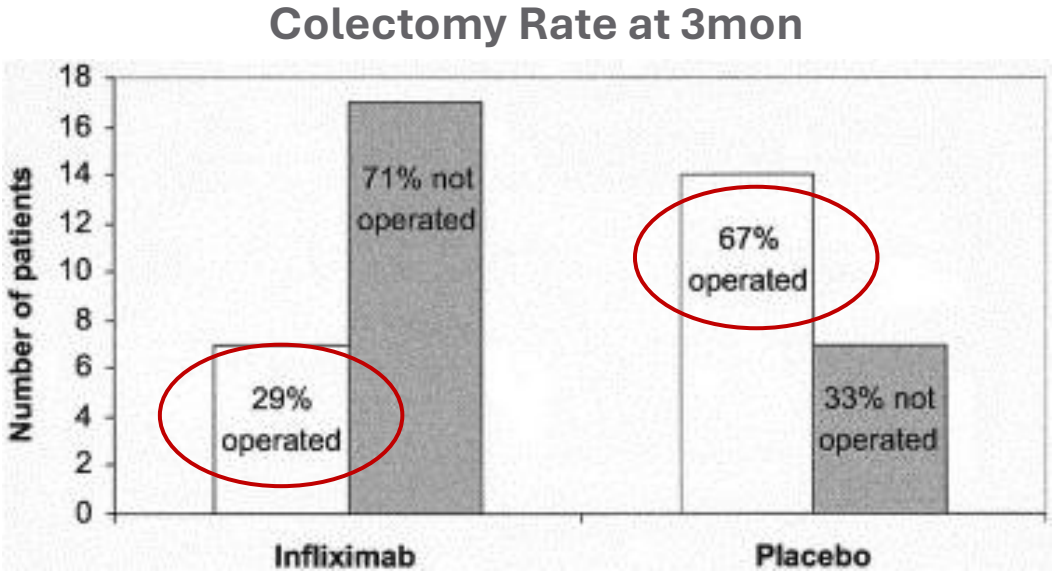


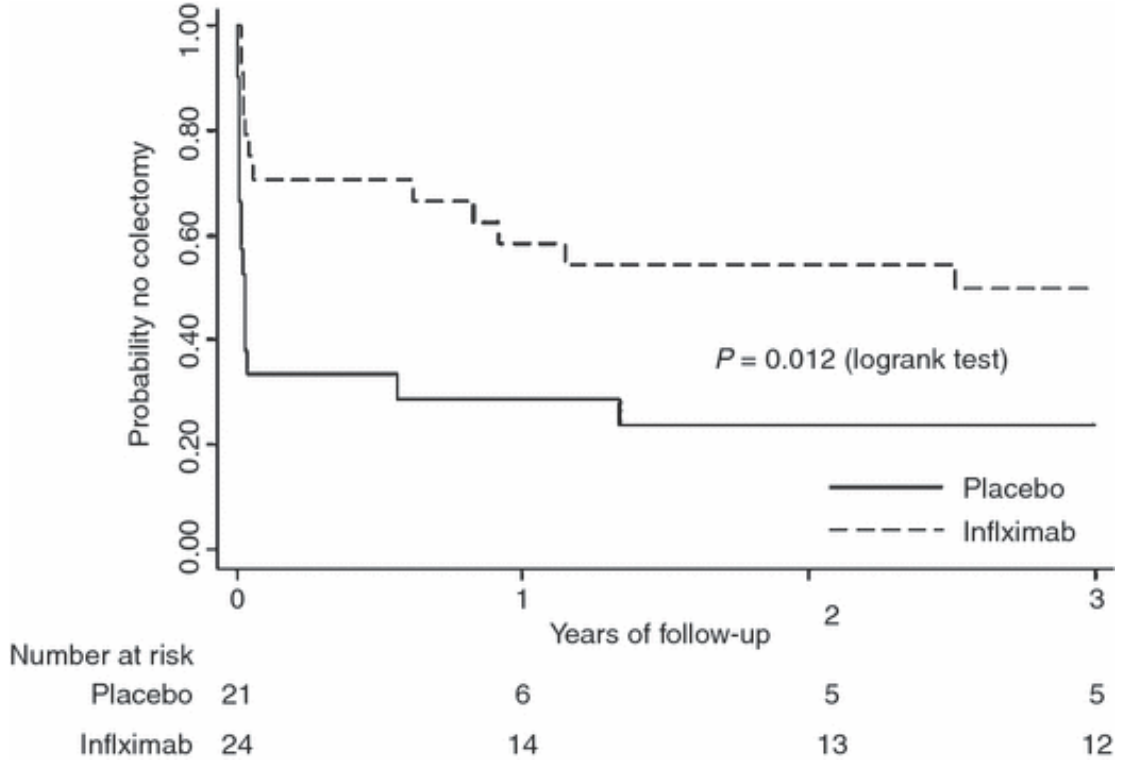
What are the options for rescue therapy?



Infliximab reduced colectomy in steroid refractory patients

- Swedish-Danish RCT, 2005: 45 patients not responding to 4 days of corticosteroid therapy were randomized to a single infusion of infliximab 5 mg/kg or placebo.





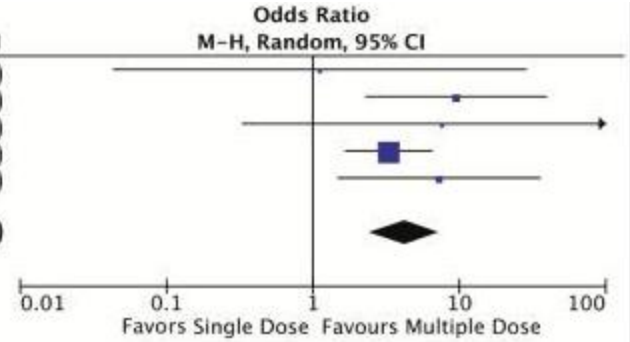
Järnerot G. Gastroenterology. 2005.
Gustavsson A. Aliment Pharmacol Ther. 2010.

Dose high-dose or accelerated Infliximab induction improve outcome?

- Meta-analysis, 2019
- Forty-one cohorts (n = 2158 cases) included
- Colectomy-free survival at 3 months
- 5-mg/kg multiple (≥2) doses superior to single-dose induction (OR 4.24)
- Dose intensification with either high-dose or accelerated strategies was not significantly different to 5-mg/kg standard induction

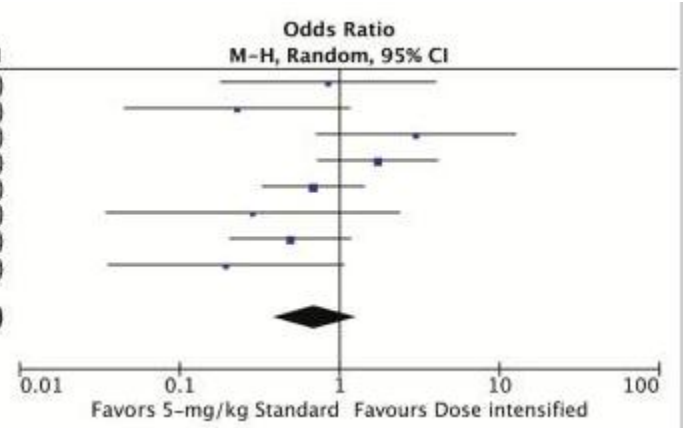
Study or Subgroup	5-mg/kg Multiple Dose Events	Total	5-mg/kg Single Dose Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Beswick 2016	19	21	3	3	2.9%	1.11 (0.04 to 28.52)
Kohn 2007	54	57	17	26	15.2%	9.53 (2.31 to 39.26)
Shepherd 2014	4	4	6	11	3.1%	7.62 (0.33 to 175.01)
Sjoberg 2013	73	87	76	124	66.6%	3.29 (1.67 to 6.48)
Van Langenberg 2015	45	47	31	41	12.1%	7.26 (1.49 to 35.44)
Total (95% CI)		**216**		**205**	**100.0%**	**4.24 (2.44 to 7.36)**
Total events	195		133			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.02$, df = 4 ($P = 0.55$); $I^2 = 0\%$
Test for overall effect: Z = 5.12 ($P < 0.00001$)



Study or Subgroup	Dose intensified Events	Total	5-mg/kg Standard induction Events	Total	Weight	Odds Ratio M-H, Random, 95% CI
Al Khoury 2017	22	28	13	16	9.8%	0.85 (0.18 to 3.97)
An 2017	32	40	35	37	9.2%	0.23 (0.05 to 1.16)
Gibson 2015	12	15	20	35	10.8%	3.00 (0.72 to 12.55)
Gibson 2018	49	58	66	87	17.8%	1.73 (0.73 to 4.11)
Nalagatla 2018	65	81	113	132	19.9%	0.68 (0.33 to 1.42)
Seah 2017	8	10	28	30	6.2%	0.29 (0.03 to 2.36)
Shah 2018	25	37	72	89	17.7%	0.49 (0.21 to 1.17)
Sly 2017	14	23	16	18	8.7%	0.19 (0.04 1.06)
Total (95% CI)		**292**		**444**	**100.0%**	**0.70 (0.39 to 1.27)**
Total events	227		363			

Heterogeneity: $Tau^2 = 0.33$; $Chi^2 = 13.51$, df = 7 ($P = 0.06$); $I^2 = 48\%$
Test for overall effect: Z = 1.17 ($P = 0.24$)



Choy MC. Inflamm Bowel Dis. 2019.

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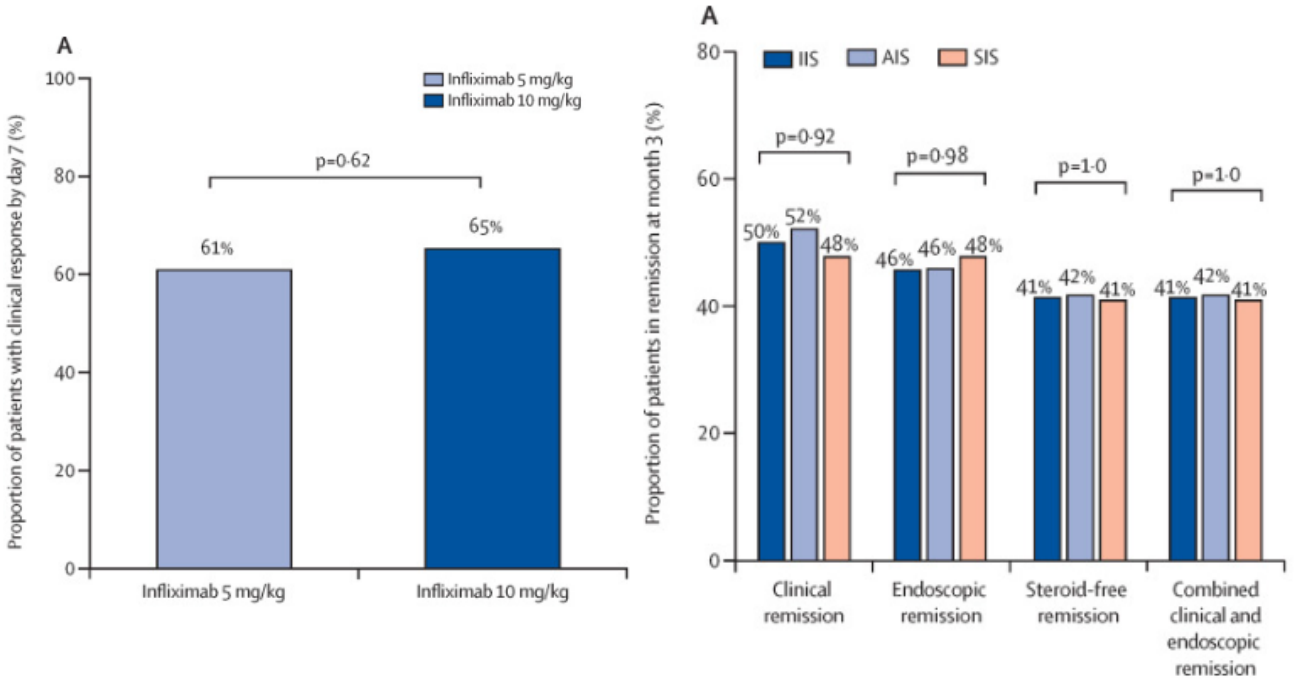
PREDICT-UC study – higher dose helpful for patients with low albumin

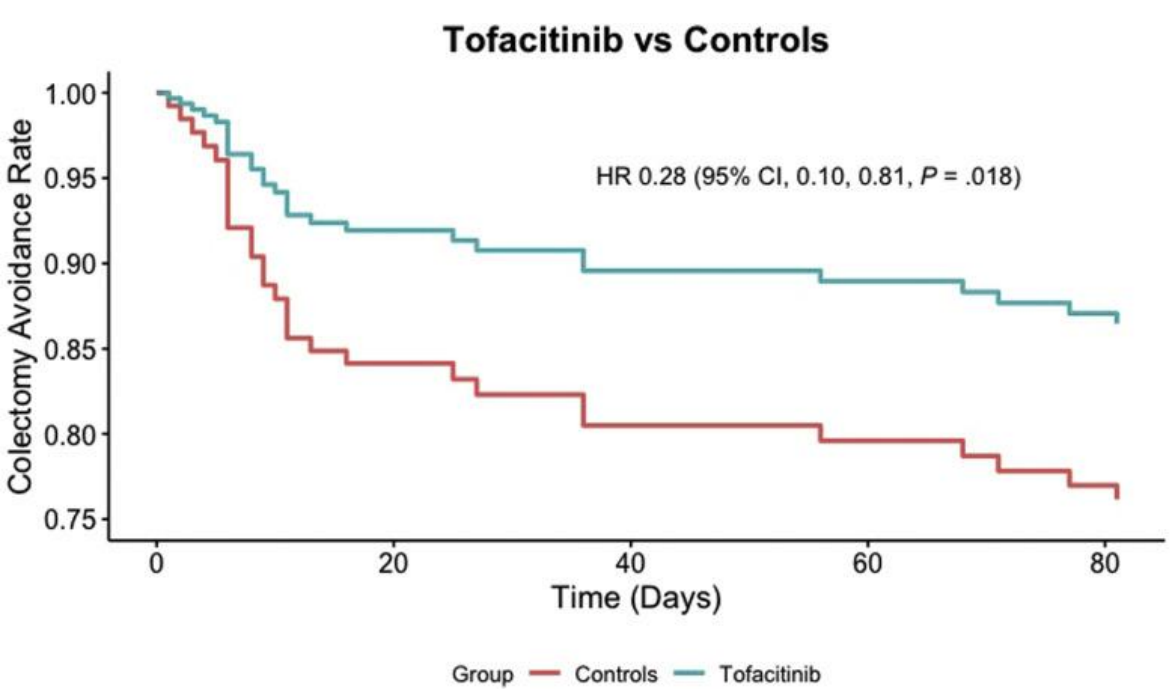
- Open label, multicenter RCT, Australia, 2024
- 138 steroid-refractory ASUC patients
- First dose of 10 mg/kg infliximab not superior to 5mg/kg in achieving day 7 clinical response
- Intensified, accelerated, and standard induction showed no difference in clinical response by day 14, or remission or colectomy rates by month 3
- However, in patients with **low albumin (< 2.5mg/dL) and high CRP (> 50mg/L)**, higher dose of IFX led to higher rate of day 7 clinical response (numerically better but not statistically significant)

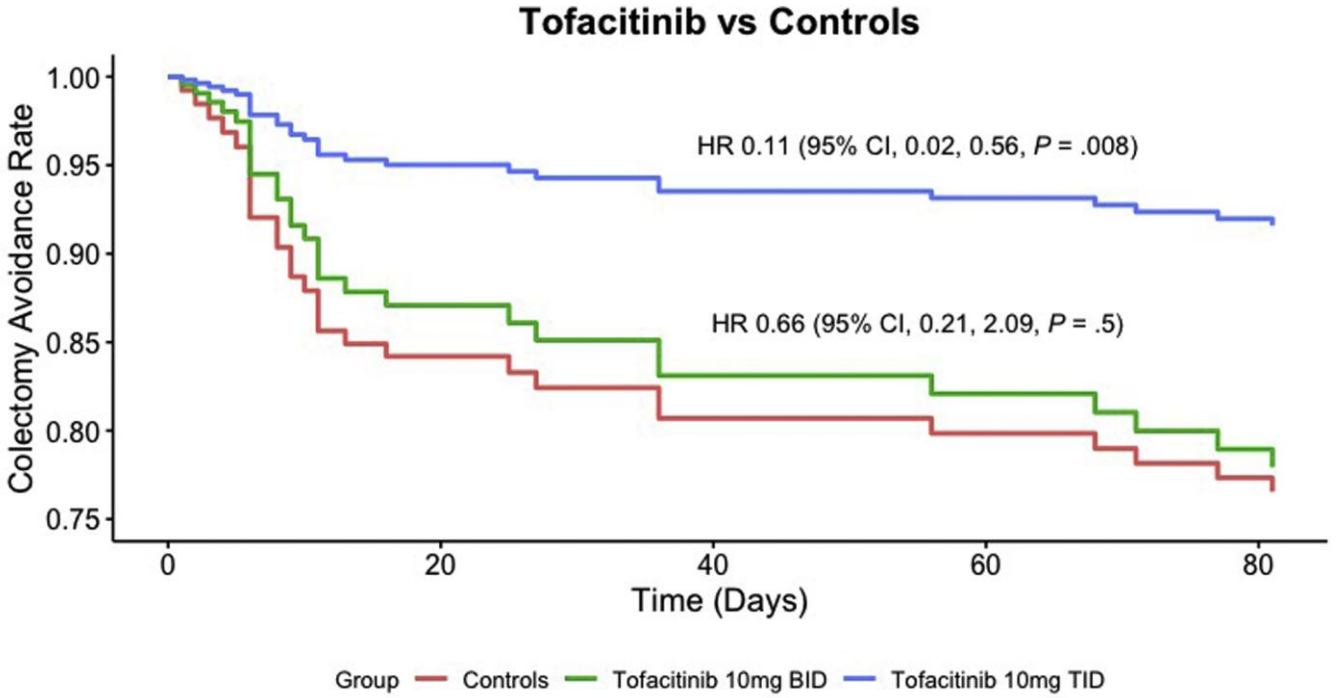


Choy MC. Lancet Gastroenterol Hepatol. 2024.

Tofacitinib reduced colectomy rate at high-intensity dose

- Retrospective case-control study in biologic-experienced ASUC patients on concomitant IVCS

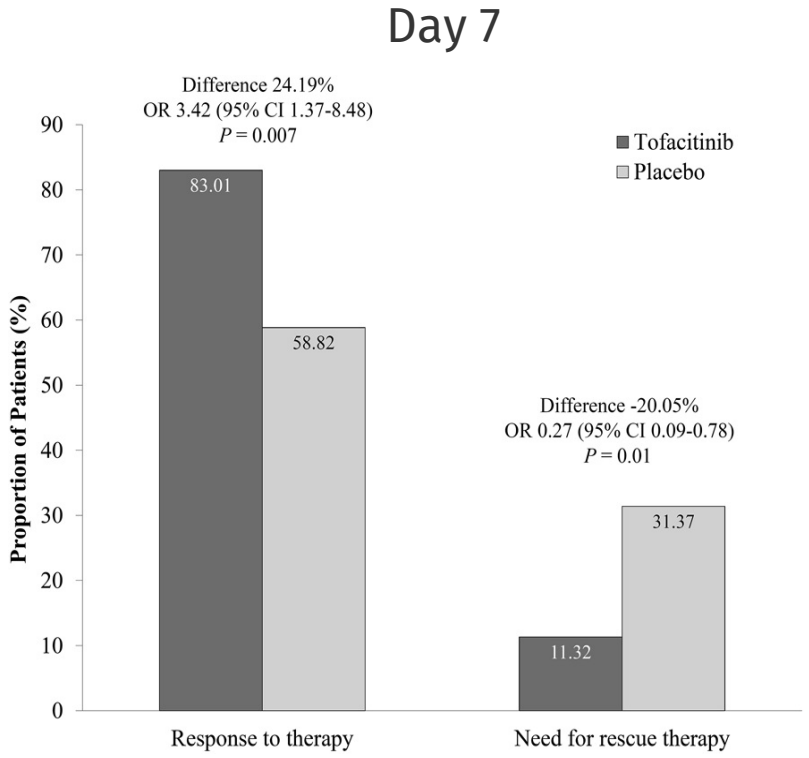


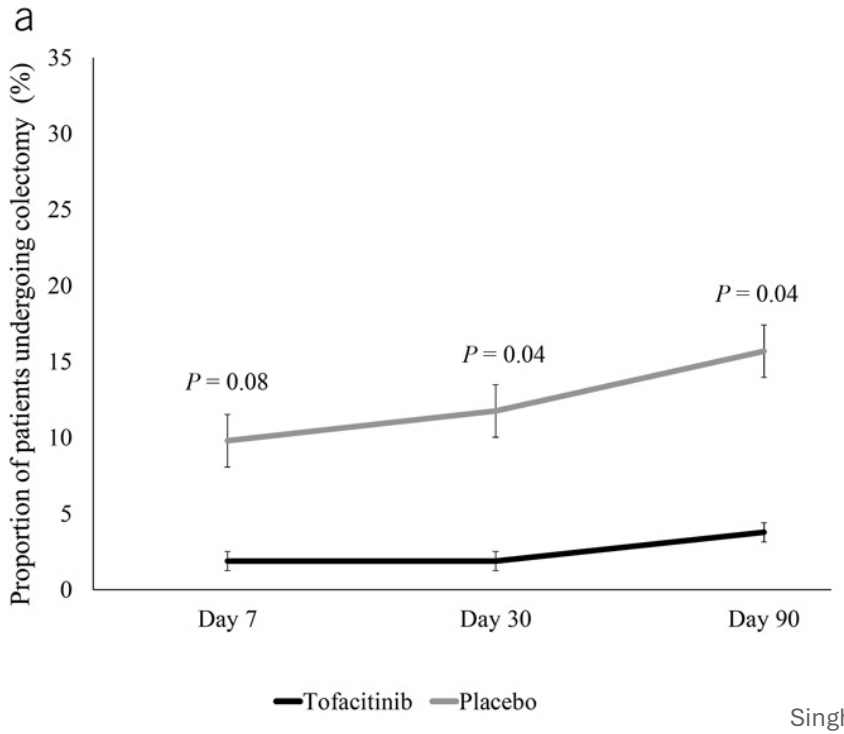


Berinstein JA. Clin Gastroenterol Hepatol. 2021.

TACOS study – fast response, less need for rescue therapy and colectomy

- Large single-center double-blinded RCT in India: Tofa 10mg TID (n = 53) vs. placebo (n = 51) x7 days while on IVCS





Singh A. Am J Gastroenterol. 2024.

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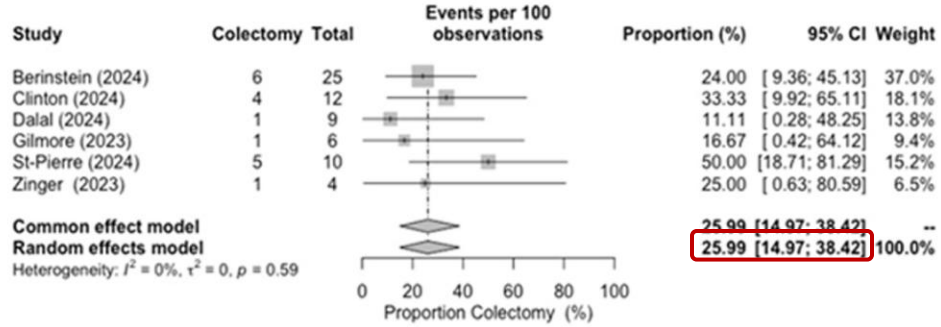
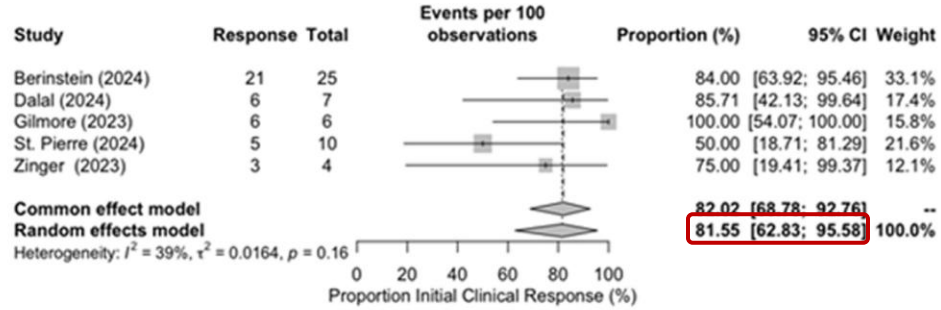
Upadacitinib Meta-Analysis

- Six studies (small case series, uncontrolled retrospective cohort), 66 patients
- Pooled data demonstrated low rates of colectomy, high rates of initial clinical response and corticosteroid-free remission.
- Serious adverse event rate ~1%: two patients with postoperative VTE.

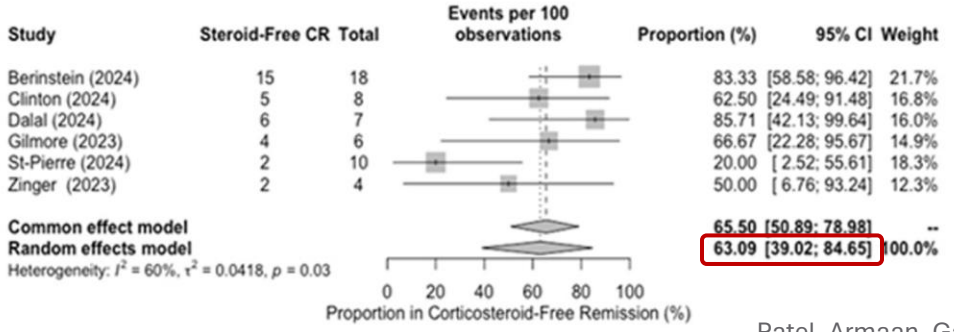
Colectomy Rate



Initial Clinical Response Rate



Corticosteroid-Free Remission Rate



Patel, Armaan. Gastroenterology. 2025.

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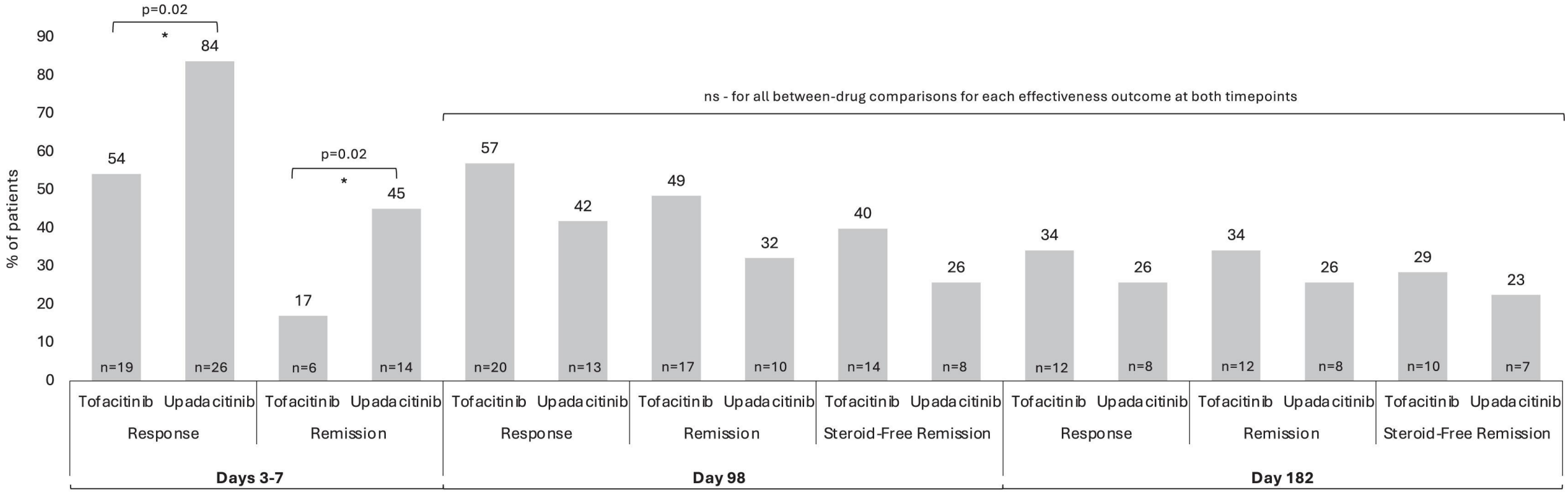
Upadacitinib vs. Tofacitinib as rescue therapy - similar effectiveness and safety profiles

- Multicenter retrospective study, 2019 – 2024. 111 patients (60 tofacitinib, 51 upadacitinib)



Honap S. Clin Gastroenterol Hepatol. 2025.

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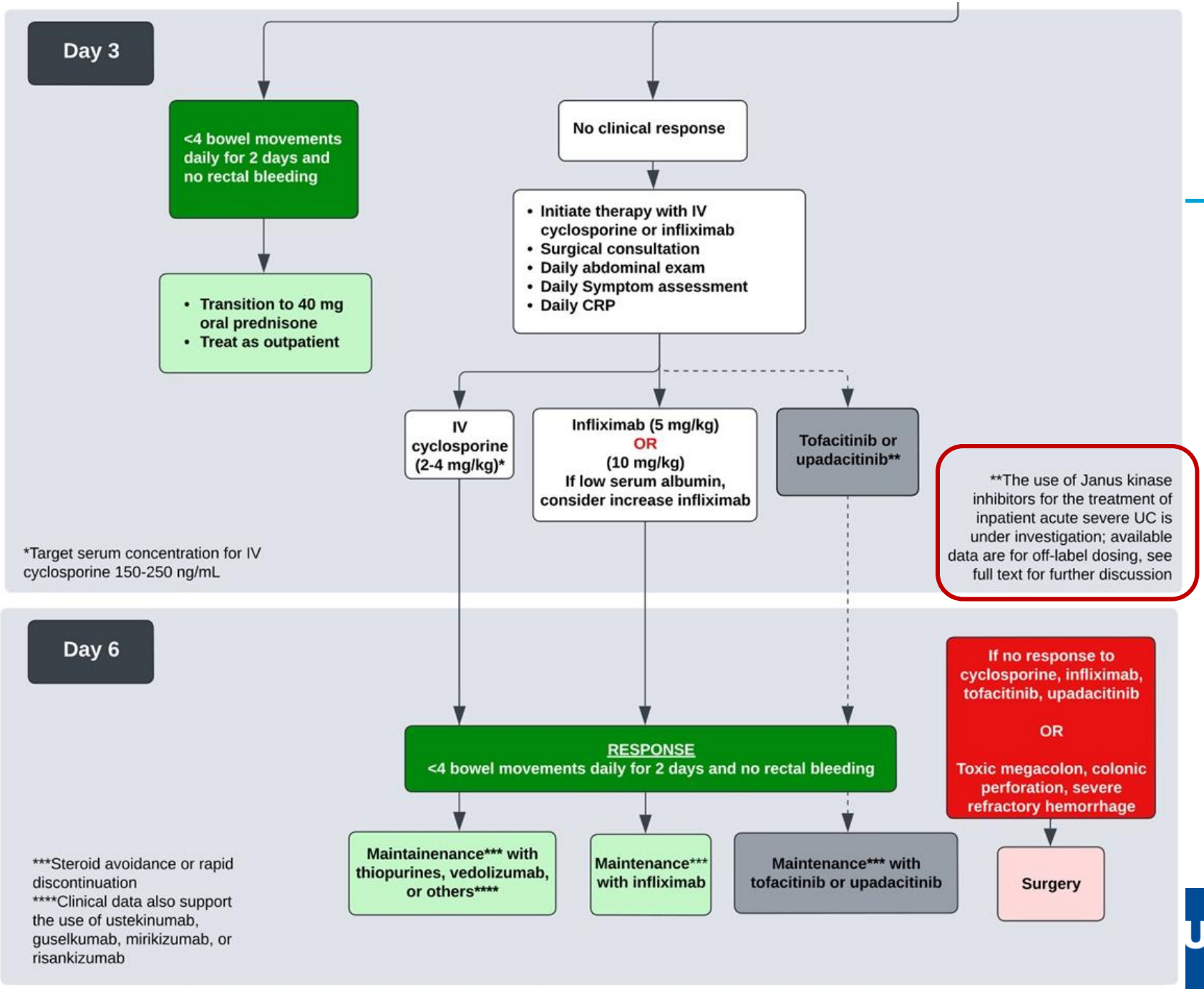

Day 3
<4 bowel movements daily for 2 days and no rectal bleeding
• Transition to 40 mg oral prednisone
• Treat as outpatient
No clinical response
• Initiate therapy with IV cyclosporine or infliximab
• Surgical consultation
• Daily abdominal exam
• Daily Symptom assessment
• Daily CRP
IV cyclosporine (2-4 mg/kg)*
Infliximab (5 mg/kg) OR (10 mg/kg) If low serum albumin, consider increase infliximab
Tofacitinib or upadacitinib**
**The use of Janus kinase inhibitors for the treatment of inpatient acute severe UC is under investigation; available data are for off-label dosing, see full text for further discussion
*Target serum concentration for IV cyclosporine 150-250 ng/mL
Day 6
RESPONSE
<4 bowel movements daily for 2 days and no rectal bleeding
If no response to cyclosporine, infliximab, tofacitinib, upadacitinib
OR
Toxic megacolon, colonic perforation, severe refractory hemorrhage
Maintainenance*** with thiopurines, vedolizumab, or others****
Maintenance*** with infliximab
Maintenance*** with tofacitinib or upadacitinib
Surgery
***Steroid avoidance or rapid discontinuation
****Clinical data also support the use of ustekinumab, guselkumab, mirikizumab, or risankizumab

When is colectomy indicated?

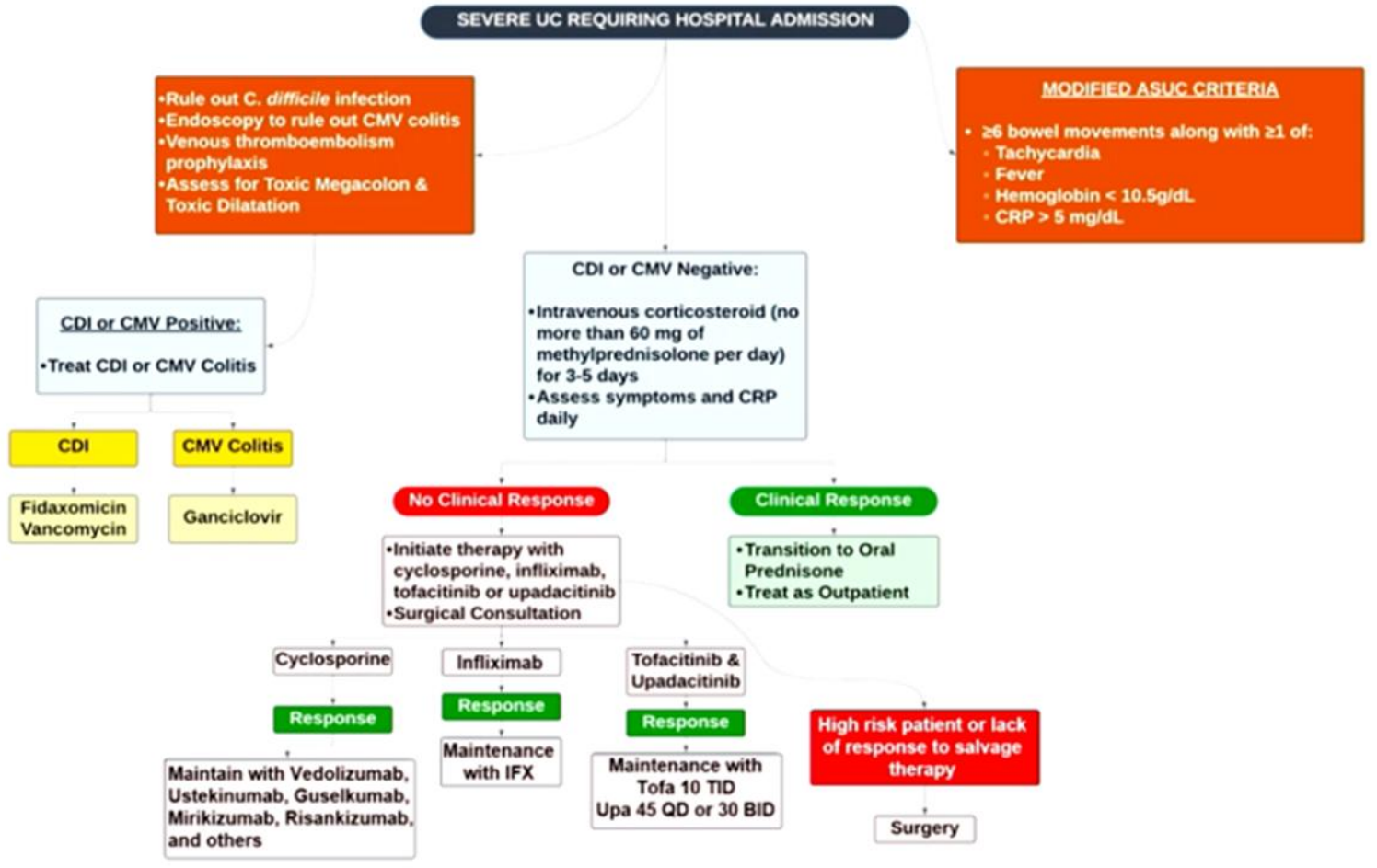
- **Absolute indications for surgery:** toxic megacolon, colonic perforation, refractory hemorrhage
- **Colectomy indicated in patients with failure to respond to medical therapy**
- **Proctocolectomy with ileal pouch anal anastomosis** with 3-stage approach is the surgical procedure of choice

- Start talking to patient about surgery on day 1
- Consult colorectal surgery team when starting rescue therapy
  (~20% chance need surgery in the next 90 days if requiring rescue therapy)
- Stop steroids if surgery is inevitable

When can patients be discharged, and what afterward?

- <4 BM/d with minimal blood, urgency manageable, eating, walking, CRP downtrending, on home meds for 24h.
- Prednisone taper
- **Requiring hospitalization is an indication for advanced therapy**
- Plan in place for maintenance therapy with steroid-sparing drugs (insurance authorization)
- Continue to trend calprotectin and CRP after discharge at outpatient follow-up

2025 ACG Clinical Guideline Update: Ulcerative Colitis in Adults



Thank you!

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