

Managing Inflammatory Bowel Disease in 2026

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Disclosures

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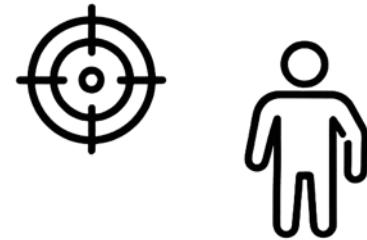


Learning Objectives

- **Discuss how to strategically position emerging therapies for inflammatory bowel disease.**
- **Critically evaluate clinical efficacy, safety, cost-effectiveness, and patient-centered outcomes to optimize individualized patient care.**

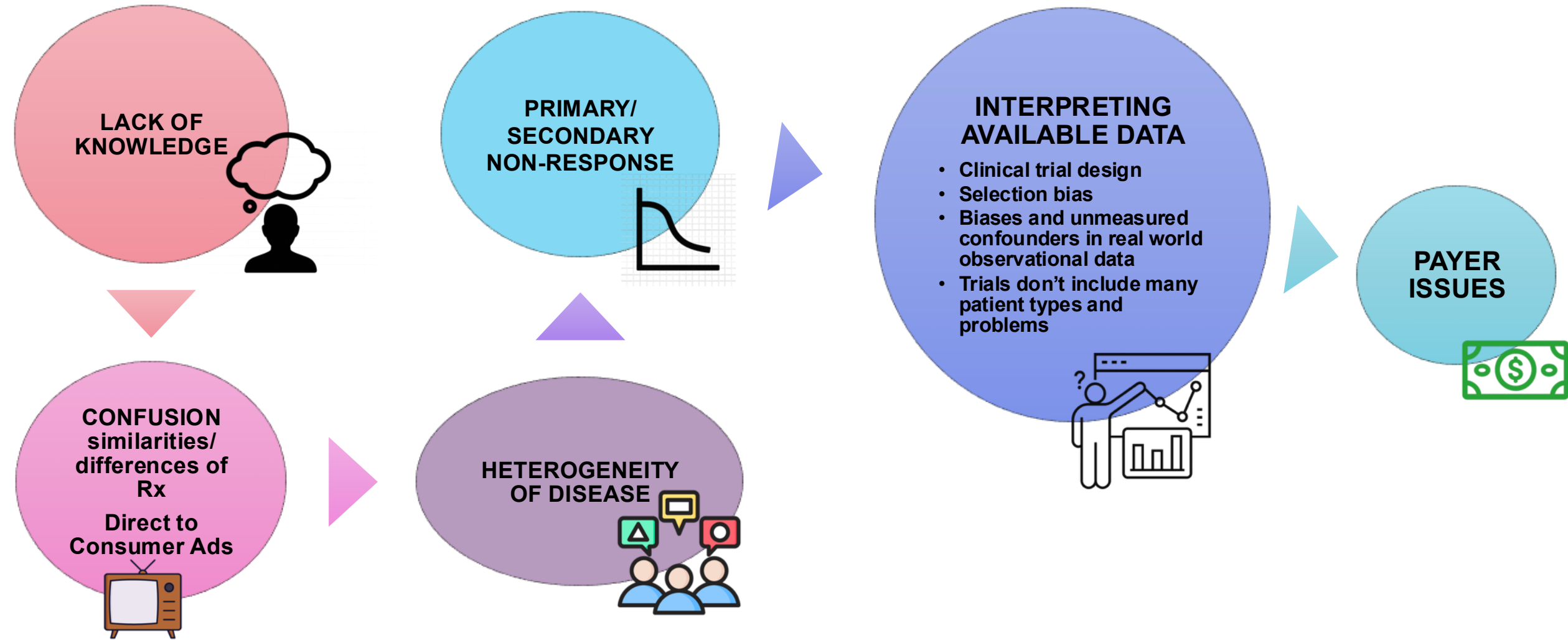
Why This Matters Now

- IBD incidence and prevalence rising globally (including East Asia)
- Therapeutic expansion with persistent ceiling effects
- Disconnect between trial endpoints and patient experience
- Guidelines must evolve to remain clinically relevant





Challenges in Treatments for IBD



Optimal Patient Outcomes in IBD in 2026

- **Unrestricted high quality of life**
- **Sustained control of bowel inflammation**
- **Unencumbered personal and professional functioning**
- **Healthcare that is affordable**



Why Don't We Achieve Preferred Outcomes In Everyone?

- We are treating the result of the disease, not the cause
- We are too late
- Therapies don't work
- Therapies are not optimized
- We are treating the wrong problem
- We are treating to the wrong targets/endpoints



Errors of omission
Errors of commission

Undertreatment!
(e.g. mesalamine in Crohn's)

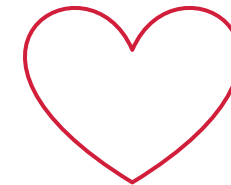
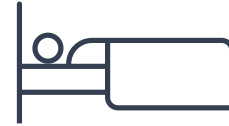
Overtreatment!
(e.g. corticosteroids)

Suboptimal Care Remains Common in IBD

- **Poor adherence to standards^{1,2}**
- **Suboptimal dosing**
- **Prolonged steroid use³**
- **Missed preventive care¹**
- **~80% of patients have suboptimal therapy^{4,5}**
 - Frequent discontinuation, escalation, switching, augmentation^{3,4}
 - Many opportunities for *on-label* treatment optimization!^{5,6}

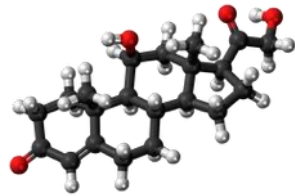
What Matters to Patients with IBD

- **Fatigue and energy**
- **Sleep quality**
- **Mental health (anxiety, depression)**
- **Sexual health and intimacy**
- **Social and occupational function**
- **These define real-world disease burden**

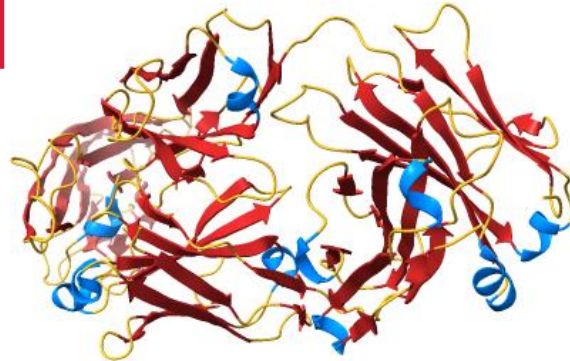


We Have Made Progress in IBD: THREE Treatment Revolutions

Corticosteroids
(1950s)



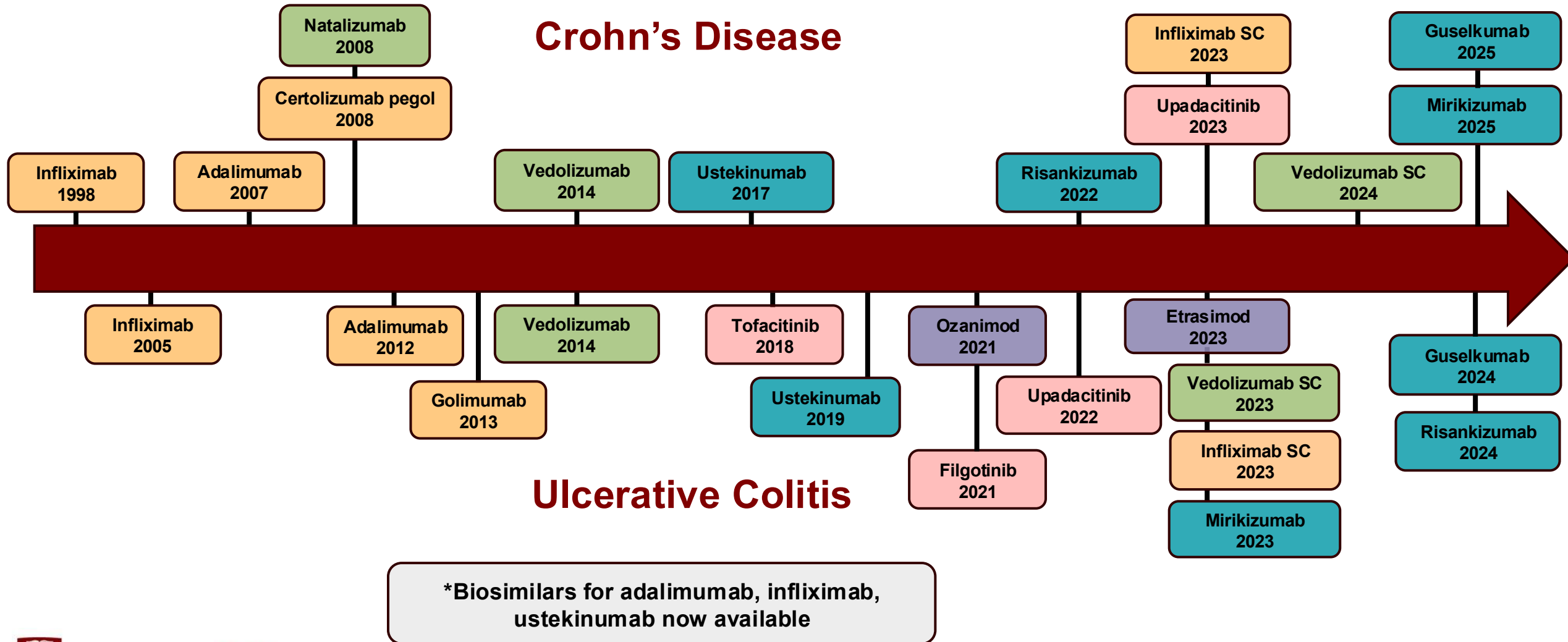
Infliximab (1997)
and subsequent
mAbs



Targeted synthetic
small molecules
(Tofacitinib, 2018)



Proliferation of Advanced Therapies in IBD



Medical Treatment Options for IBD

Class of Therapy Treatment	Treatment	Comment	
Diet	EEN or PEN	CD only	Conventional Therapies (Traditional)
5-ASA	Mesalamine Sulfasalazine	Oral and rectal	
Corticosteroids	Budesonide Prednisone/Methylpred	Oral and rectal	
Immunomodulators	6-mercaptopurine Azathioprine	Pharmacogenomics TPMT, NUDT15	Conventional Synthetic Therapies (Immunomodulators)
	Methotrexate	CD only	
Calcineurin inhibitors	Cyclosporine Tacrolimus	IV and oral	
Anti-integrin	Natalizumab Vedolizumab	IV and SC maintenance	Biological Therapies
Anti-IL-23 (p40: IL-12/23 p19: IL-23)	Guselkumab (p19/CD64) Mirikizumab (p19) Risankizumab (p19) Ustekinumab (p40)	IV and SC maintenance Biosimilars to ustekinumab	
Anti-TNF	Adalimumab Certolizumab pegol Golimumab Infliximab	Infliximab IV and SC maintenance Biosimilars to IFX and ADA	
Janus kinase inhibitors	Filgotinib (JAK1) Tofacitinib (JAK1,2,3) Upadacitinib (JAK1)	Oral Fligotinib EU only	Targeted Synthetic Small Molecules
S1P receptor modulators	Etrasimod (S1P _{1,4,5}) Ozanimod (S1P _{1,5})	Oral	

Medical Treatment Options for IBD

Class of Therapy Treatment	
5-ASA	Conventional therapies
Corticosteroids	
Immunomodulators	
Calcineurin inhibitors	
Anti-integrin	Advanced therapies
Anti-IL-23 (p40: IL-12/23 p19: IL-23)	
Anti-TNF	
Janus kinase inhibitors	
S1P receptor modulators	

Primary Goal: Remission

1. SYMPTOMATIC REMISSION

- No pain
- No bleeding
- Normal stool frequency
- No urgency

2. DEEP REMISSION

- Endoscopic improvement
- Normalized labs, growth, and development
- Disease Modification
- Movement towards transmural healing

3. FUNCTIONAL REMISSION

- Unencumbered functioning
- Extra-intestinal manifestations addressed
- Mental health addressed

Explain it to your patient: “We want you to feel perfect, and we want it to last forever.”

Considerations in Positioning Therapies in IBD

1

Patient Factors

- Phenotype
- Comorbidities
 - EIMS
- Pregnancy

2

Efficacy

- Available evidence
- Clinical trial vs. real-world
- Advanced therapy naïve/exposed

3

Safety

- Severity of disease!
- Drug-related AEs
- Disease-related AEs

Convenience

- Mode of delivery
- Frequency of dose

Access

- Insurance coverage
- Cost and time to patient

5

4

Comparing Therapies Based on Efficacy and Safety

Efficacy

- Pivotal randomized controlled trials with active comparators
- Prospective randomized head-to-head trials
- Post-marketing data (phase 4)
- Clinical decision tools
- Network meta-analysis
- Real world evidence (retrospective or prospective)
- Case reports
- Expert opinion

Strength of Data

Stronger



Weaker

Safety

- Pivotal randomized controlled trials with active comparators
- Pooled analyses from all disease states
- Post-marketing data (phase 4)
- Safety registries (FDA AERS)
- Administrative datasets
- Real world evidence (retrospective or prospective)
- Case reports
- Expert opinion

The 9 Pearls of IBD Treatment Optimization

- 1. Treat EARLY**
- 2. Choose Wisely: First Line Therapy**
- 3. Avoid Corticosteroids!**
- 4. Treat to a Target**
- 5. Develop an Approach to Non-Response**
- 6. Combine Therapies When Rational and Safe**
- 7. Change the Patient!**
- 8. Eat to Target?**
- 9. Personalize Your Approach (N=1)**

1. Treat Early

- **Choose therapy that matches the activity of the disease**
 - *Moderately to severely active IBD should be managed with treatments for moderately to severely active IBD!*
- **Choose therapy that matches the prognosis of the disease**
 - Understand risk factors for poor outcomes
 - Stratify therapy, monitoring, and follow-up to address these
- **Don't wait!**



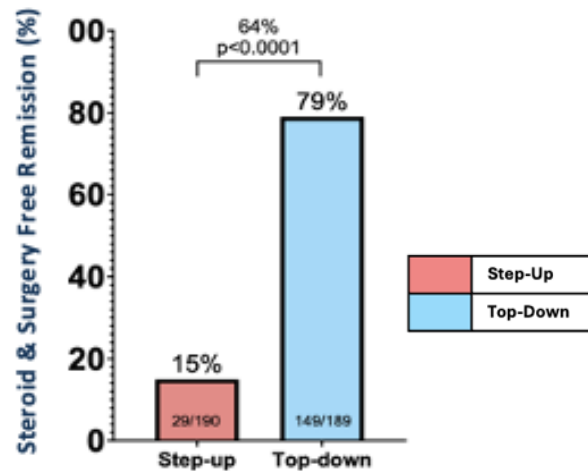
“WHEN” may matter more than “WHAT”

Treating Early in Crohn's Disease: A Consistent Message

PROFILE: Infliximab Step-Up vs. Top-Down

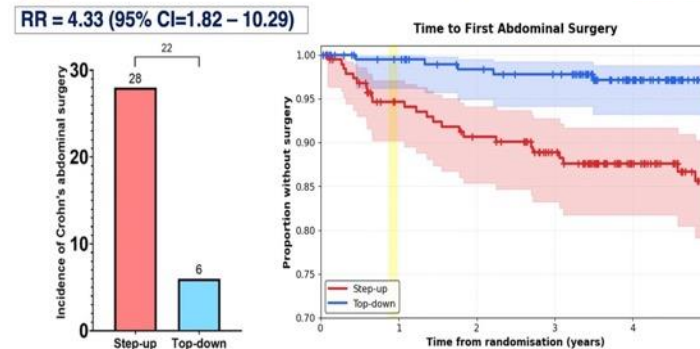
Median Crohn's Disease duration: 12 days

Wk 48 Sustained Steroid-free and
Surgery-free Remission



5 Year Follow-up

Abdominal surgeries over 5-years

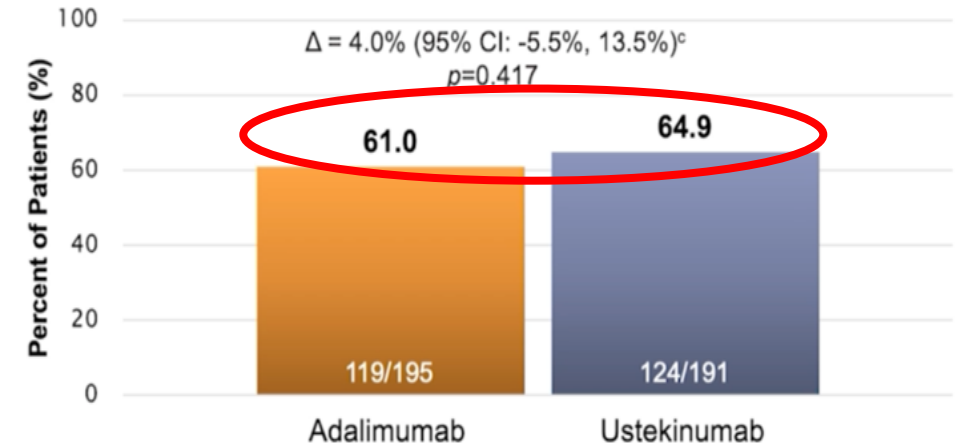


SEAVUE:

Adalimumab v Ustekinumab

Median Crohn's Disease duration: 3.6 years

Clinical Remission (CDAI < 150) at week 52



Noor N, et al. *Lancet Gastroenterol Hepatol*. 2024;9(5):415-427.

Noor N, et al. ECCO 2026 OP05.

Sands BE et al. *Lancet*. 2022;399(10342):2200-2211.

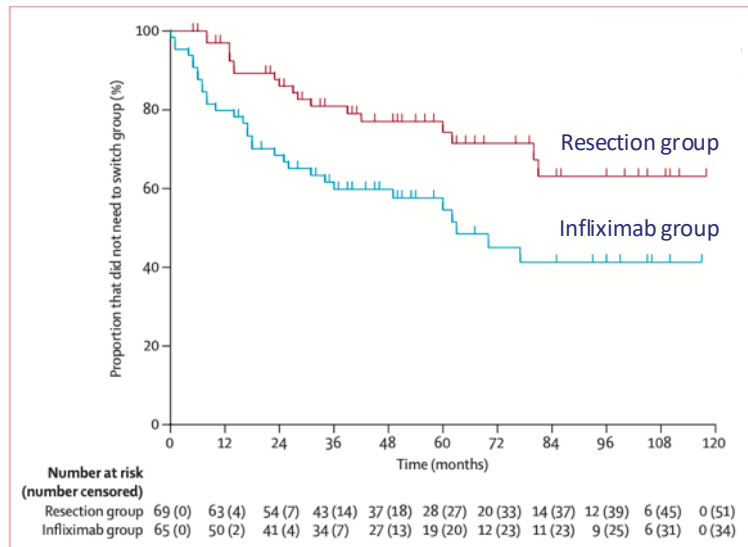
Surgery First is Also “Top-Down”

Lancet Gastroenterol Hepatol. 2017;2:785–92.

Laparoscopic ileocaecal resection versus infliximab for terminal ileitis in Crohn’s disease: a randomised controlled, open-label, multicentre trial

Cyriel Y Ponsioen, E Joline de Groof, Emma J Eshuis, Tjibbe J Gardenbroek, Patrick M M Bossuyt, Ailsa Hart, Janindra Warusavitarne, Christianne J Buskens, Ad A van Bodegraven, Menno A Brink, Esther C J Consten, Bart A van Wagensveld, Marno C M Rijk, Rogier M P H Crolla, Casper G Noomen, Alexander P J Houdijk, Rosalie C Mallant, Maarten Boom, Willem A Marsman, Hein B Stockmann, Bregje Mol, A Jeroen de Groof, Pieter C Stokkers, Geert R D’Haens, Willem A Bemelman, on behalf of the LIR!C study group*

Time to Switch Treatment



Crohn’s Disease

- Not just for obstruction!
- Gain control of the disease
- “Reset” in proper patients
- Proactive monitoring and prevention
- Treatments work better in prevention phase
- Expectant management of post-operative symptoms

2. Choose Wisely: First Line Therapy

- Avoid ineffective cycling (steroids and “repeating the same mistake twice”)
- No longer have to go “through” conventional therapy (multiple guidelines)
- **Prognosis should guide therapy as much as activity**

Poor Prognostic Factors in IBD

- Young diagnosis
- More bowel involvement
- Perianal disease
- Deep ulcers
- Stricturing and/or penetrating behavior
- High CRP and ESR
- Steroid-requiring disease
- History of hospitalization
- Infection: *C. difficile* & CMV

Lichtenstein GR, et al. *Am J Gastroenterol*. 2018;113(4):481-517.
Sandborn WJ. *Gastroenterology*. 2014;147(3):702-703.
Rubin DT, et al. *Am J Gastroenterol*. 2025;120(6):1187-1224.
Dassopoulos T, et al. *Gastroenterology*. 2015;149(1):238-45.

Other Considerations

- Extra-intestinal manifestations (joints, skin, PSC)
- Steroid-dependence
- Delayed growth
- Mental health disorders
- Under/Un-insured

Jose FA, et al. *J Pediatr Gastroenterol Nutr*. 2008;46(2):124-33.
Waljee AK, et al. *PLoS One*. 2016;11(6):e0158017.
Amaro F, et al. *Biomedicines*. 2020;8(11):458.
Szigethy E, et al. *Clin Gastroenterol Hepatol*. 2017;15(7):986-997.
Nguyen GC, et al. *Inflamm Bowel Dis*. 2009;15(5):726-33.

Clinical Considerations for Choice of Treatment in IBD

IBD SCENARIOS

Clinical Scenario	Therapy Consideration
Perianal Crohn's disease	Anti-TNF (IV/SC) Upadacitinib (ORAL) ¹ Guselkumab (SC) ⁴
Moderately active ulcerative colitis after 5-ASA	S1P receptor modulators (ORAL) Anti-TNF, Vedolizumab, anti-IL23
Post-operative Crohn's ileocecal resection and anastomosis	Anti-TNF Vedolizumab ² (probably anti-IL23)
Acute severe UC (hospitalized)	Infliximab (IV) Cyclosporine (IV) JAK inhibitors (PO) ³

¹Colombel JF, et al. *Clin Gastroenterol Hepatol*. 2025;23(6):1019-1029.

²D'Haens G, et al. *Lancet Gastroenterol Hepatol*. 2025;10(1):26-33.

³Berinstein JA, et al. *Am J Gastroenterol*. 2024;10.14309/ajg.0000000000002674.

⁴Peyrin-Biroulet L, et al. Guselkumab for Perianal Fistulizing Crohn's Disease: Week 24 Results from the Phase 3, Randomized, Double-blind, Placebo-Controlled, Multicenter FUZION Study. Abstract 1058b. Presented at DDW, 2026, Chicago, IL.

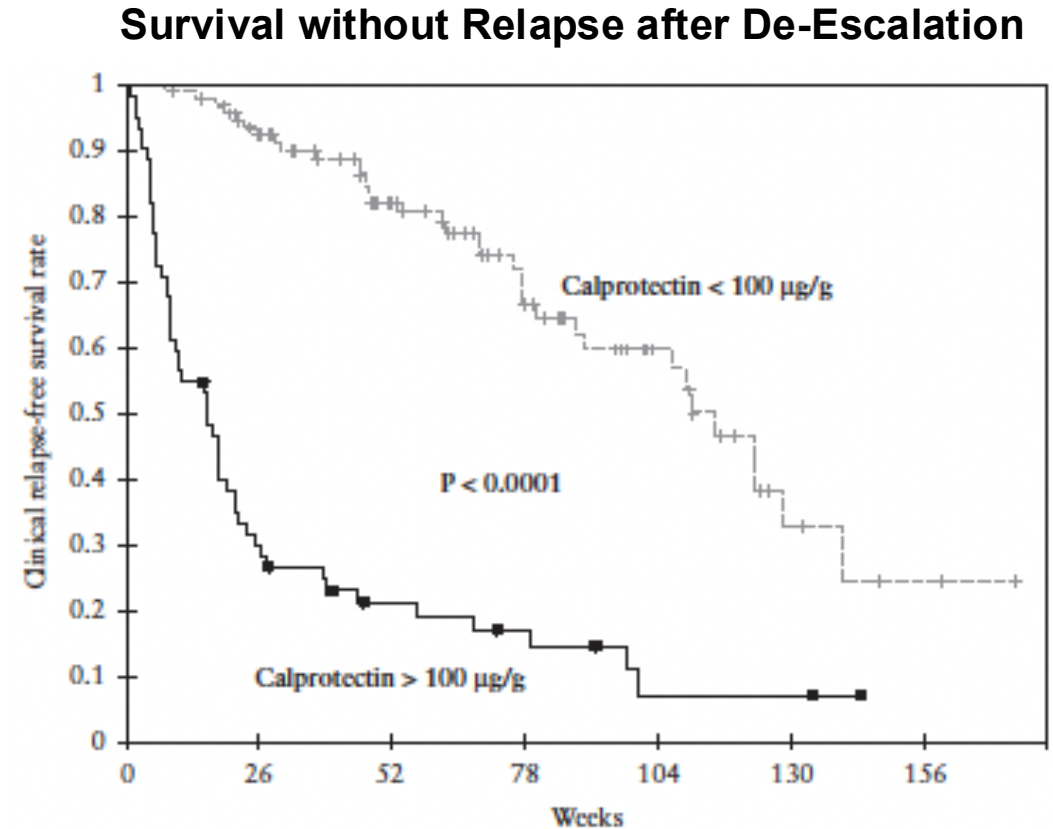
Clinical Scenario/ Co-existing Condition	Therapy Consideration
Enteropathic Arthropathy	Sulfasalazine, Methotrexate, Anti-TNF, JAKinib
Psoriatic Arthritis	Anti-TNF, JAKinib, IL-23 Therapies, MTX
Rheumatoid Arthritis	Anti-TNF, JAKinib, MTX
Spondyloarthritis (AnkSpon and Sacroileitis)	Anti-TNF, JAKinib
Plaque Psoriasis	Anti-TNF, IL-23 Therapies, MTX
TNF-induced palmar plantar pustulosis	Non-anti-TNF, Favor IL-23 (?)
Alopecia	JAKinib
Multiple Sclerosis	Natalizumab (CD), Ozanimod (UC) (maybe Etrasimod (UC))
Perianal disease	Anti-TNF (IV/SC), Upadacitinib (ORAL)

JOINTS

SKIN

3. Avoid Corticosteroids!

- Do you really need them?
- Start effective therapy early
- “ONE AND DONE” approach
- **“Have courage in your convictions”**
- Steroids are often tapered too long
 - If your new therapy is working, stop the steroids! (FCP<100)



Buisson A, et al. *J Crohns Colitis*. 2019;13(8):1012-1024.

Percentage of Patients Not Receiving Corticosteroids at Baseline (Start of Induction) in Phase 3 Trials for IBD

Ulcerative Colitis Trials

THERAPY	NOT ON STEROIDS AT BASELINE/START OF INDUCTION	
Infliximab	ACT-1 / ACT-2	46% / 43%
Adalimumab	ULTRA-1	49%
Golimumab	PURSUIT	47%
Vedolizumab	GEMINI-1	52%
Ustekinumab	UNIFI	46%
Guselkumab	QUASAR	53%
Mirikizumab	LUCENT-1	57%
Risankizumab	INSPIRE	52%
Tofacitinib	OCTAVE-1 / OCTAVE-2	55% / 53%
Upadacitinib	U-ACHIEVE / U-ACCOMPLISH	60% / 62%
Filgotinib	SELECTION	54%
Ozanimod	TRUE NORTH	62%
Etrasimod	ELEVATE UC 12 / 52	73% / 68%

~Time



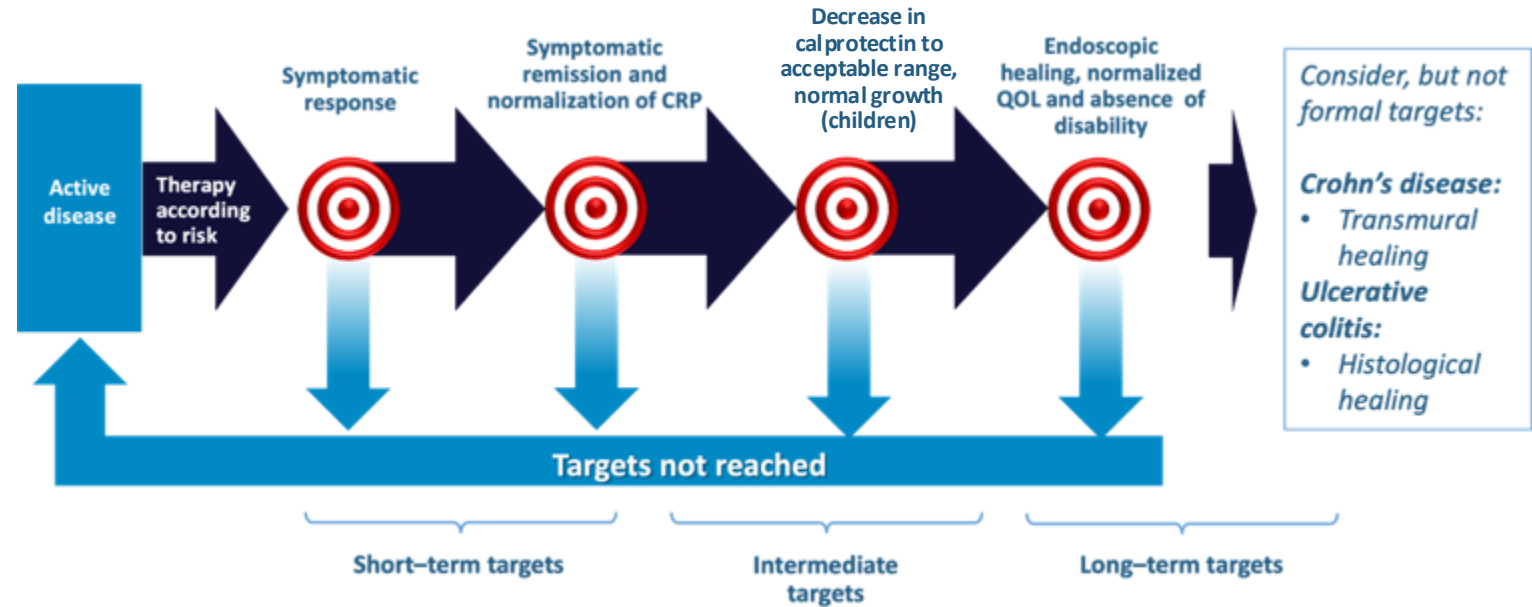
Crohn's Disease Trials

THERAPY	NOT ON STEROIDS AT BASELINE/START OF INDUCTION	
Infliximab	ACCENT-1	48%
	SONIC	59%
Adalimumab	CLASSIC-1	70%
	GAIN	56%
Certolizumab	PRECISE-1 / PRECISE-2	62% / 60%
Vedolizumab	GEMINI-2 / GEMINI-3	55% / 53%
Natalizumab	ENACT-1	61%
Ustekinumab	UNITI-1 / UNITI-2	54% / 60%
Guselkumab	GALAXI-2 / GALAXI-3	63% / 64%
Mirikizumab	VIVID-1	69%
Risankizumab	ADVANCE / MOTIVATE	66% / 67%
Upadacitinib	U-EXCEED / U-EXCEL	65% / 65%

4. Treat to a Target

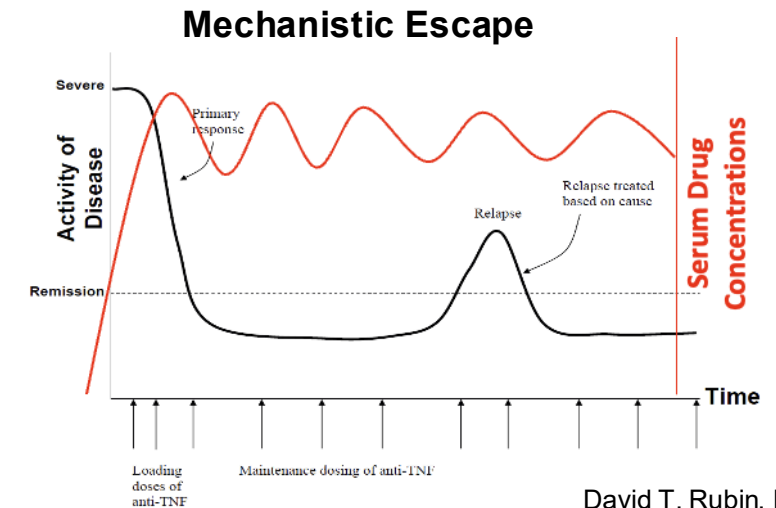
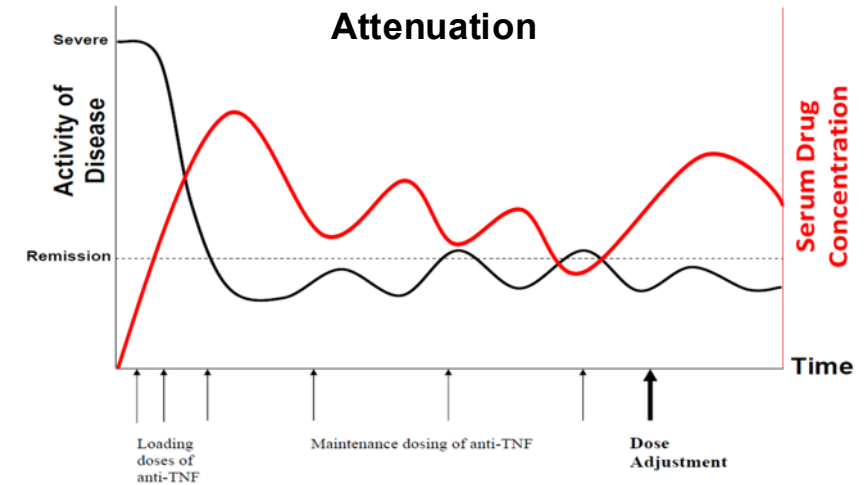


STRIDE II CONSENSUS OF TREATMENT TARGETS IN IBD SELECTING THERAPEUTIC TARGETS IN INFLAMMATORY BOWEL DISEASE ENDPOINTS



5. Develop an Approach to Non-Response

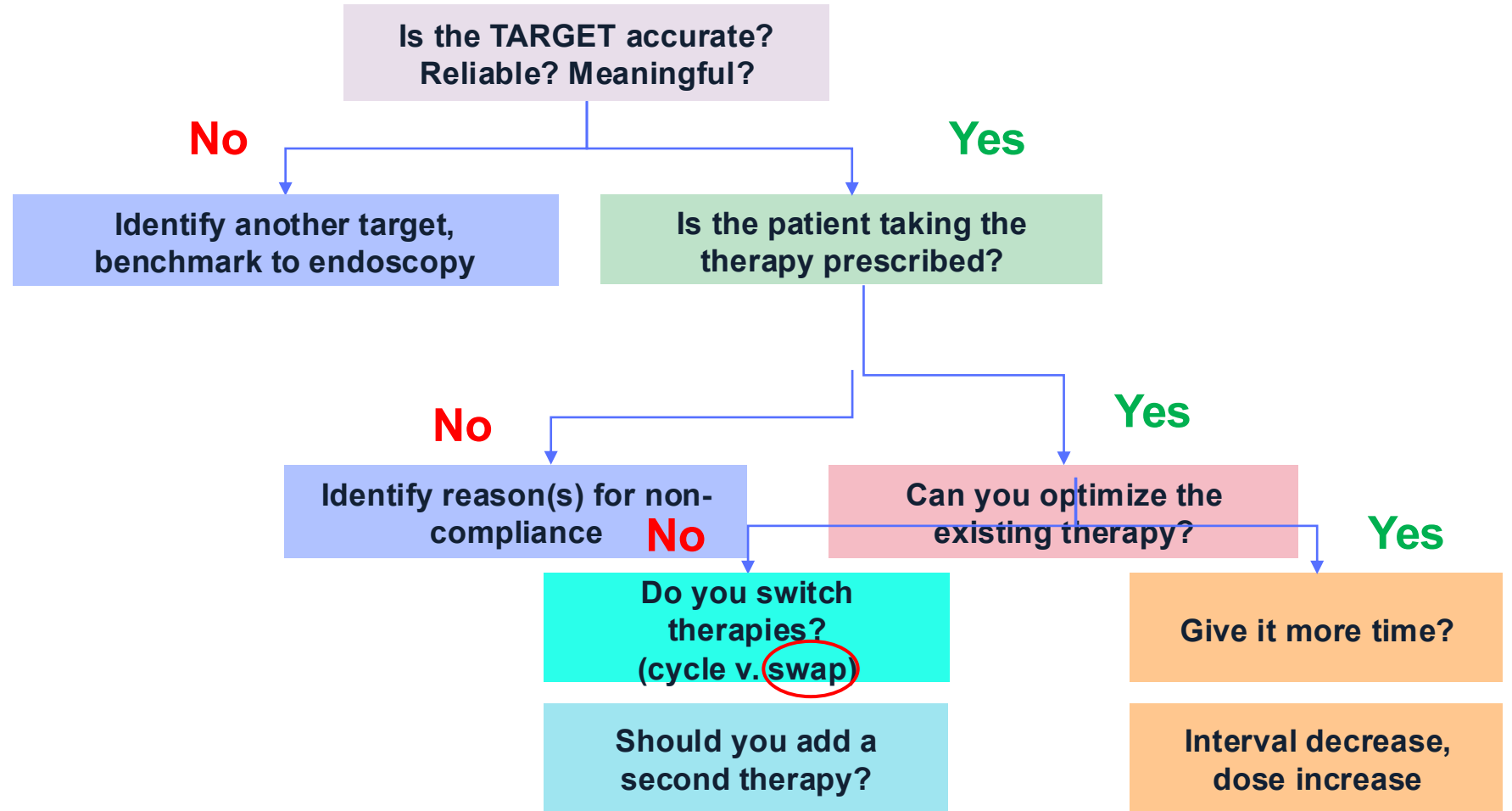
- Anticipate it with proactive disease monitoring
- Where is the drug?
 - Is your patient taking it?
 - Consider serum concentration (reactive TDM)
 - Sort *attenuation* from *mechanism failure*
- Recapture attenuation
 - Shortening the interval better than increasing the dose
 - Consider booster dose when recapturing
- Switch mechanism
 - Switching class of therapy may be better than cycling within class^{1,2}



David T. Rubin, MD

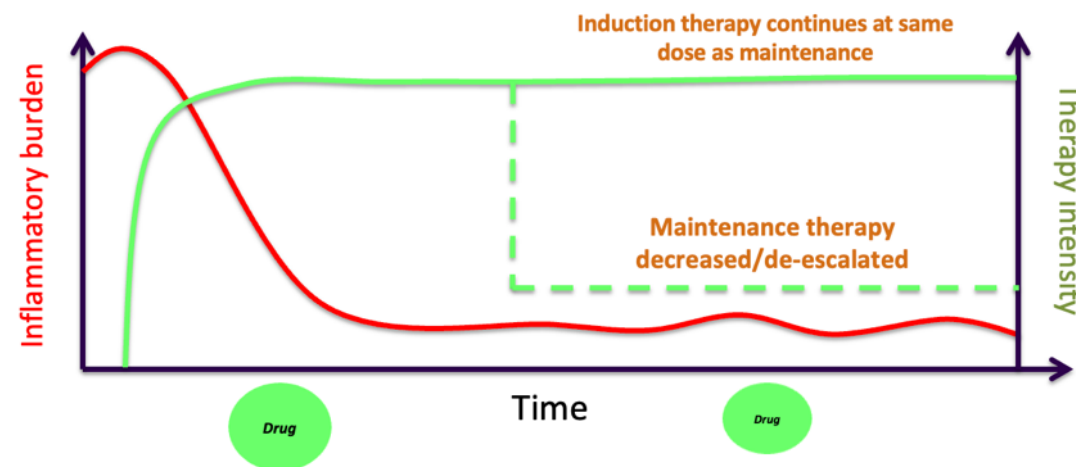
Algorithm for Assessment of Non-Response

Is it IBD?
Rule out Confounders
(C. diff, SIBO, etc.)



Optimize Dosing and Delivery

- Use labeled and approved (proven) doses **INCLUDING LOADING DOSES before MAINTENANCE**
- **Avoid underdosing**
 - Induction of remission THEN maintenance
 - More drug for induction and based on **inflammatory burden** (amount of bowel involved, presence of EIMs, perianal disease)
- **Understand delivery**
 - Extended release vs. immediate release
 - mAb vs. small molecule
- **Increased frequency is pharmacokinetically better than dose increases**



Factors Associated with Increased Clearance/Less Response
Increased BMI
Male sex
High CRP
Low albumin
Prior immunogenicity

Examples of Dose Adjustment Options*

Treatment	Standard Dosing (Maintenance)	Dose Escalation Options	Interval Adjustment Options	Other Comments
Infliximab IV	5 mg/kg Q8 weeks	5mg/kg → 7.5mg/kg or 10mg/kg	Decrease to Q6 or Q4 weeks	TDM helpful based on disease activity, goal level >10 (units)
Vedolizumab IV	300 mg Q8 weeks	-	Q6 or Q4 weeks	-
Ustekinumab SC ¹	90 mg Q8 weeks-Q12 weeks	-	Q6 or Q4 weeks	IV reloading is not effective (POWER study ²)
Guselkumab SC ³	200 mg Q4 weeks 100 mg Q8 weeks	100mg → 200mg	Q8 to Q6 or Q4 weeks	Predictors of dose escalation: More extensive disease, remission at week 12
Risankizumab SC ⁴	180 mg or 360 mg Q8 weeks	-	Q6 or Q4 weeks	-
Upadacitinib PO ^{5,6}	30 mg or 15 mg daily	15mg → 30mg → 45mg (30mg BID)	-	Loss of response may be recaptured ASUC intensive dosing off label
Tofacitinib PO ^{7,8}	5 mg BID	5mg → 10mg BID (10mg TID)	-	ASUC intensive dosing off label

*some off label dosing

¹Ollech JE, et al. *Clin Gastroenterol Hepatol*. 2021;19(1):104-110.

²Schreiber S, et al. *Inflamm Bowel Dis*. 2025;31(12):3286-3297.

³Rubin DT, et al. *Lancet*. 2025;405(10472):33-4.

⁴Schreiber-Stainthorp W, Faye AS, Axelrad JE. *Inflamm Bowel Dis*. 2025;31(11):3225-3227.

⁵Ho AHY, et al. *Clin Gastroenterol Hepatol*. 2026;24(3):763-771.

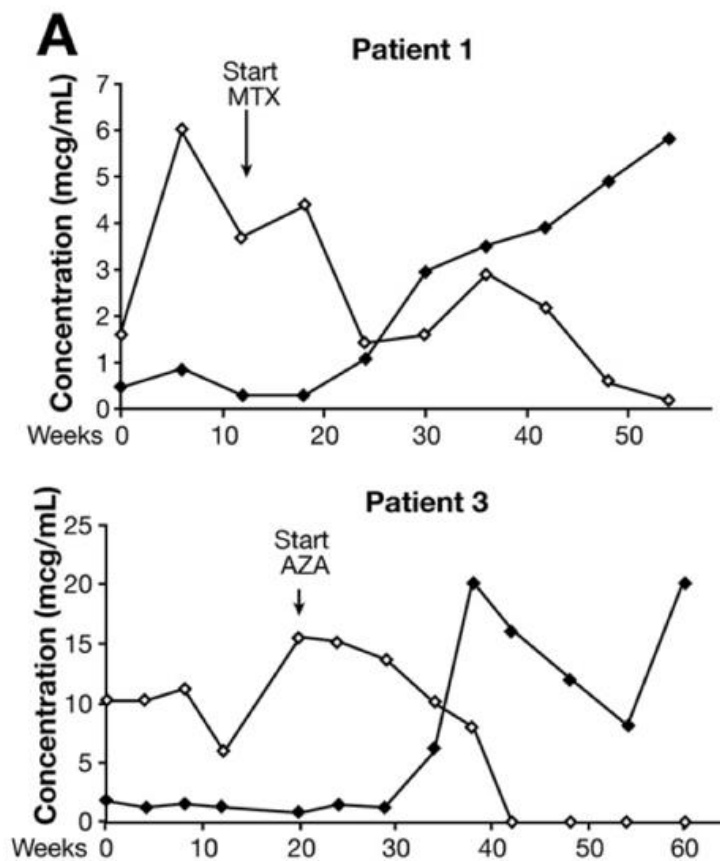
⁶Berinstein JA, et al. *Am J Gastroenterol*. 2024; 119(7): 1421-25.

⁷Vermeire S, et al. *J Crohns Colitis*. 2021;15(7):1130-1141.

⁸Singh A, et al. *Am J Gastroenterol*. 2024; 119(7):1365-72.

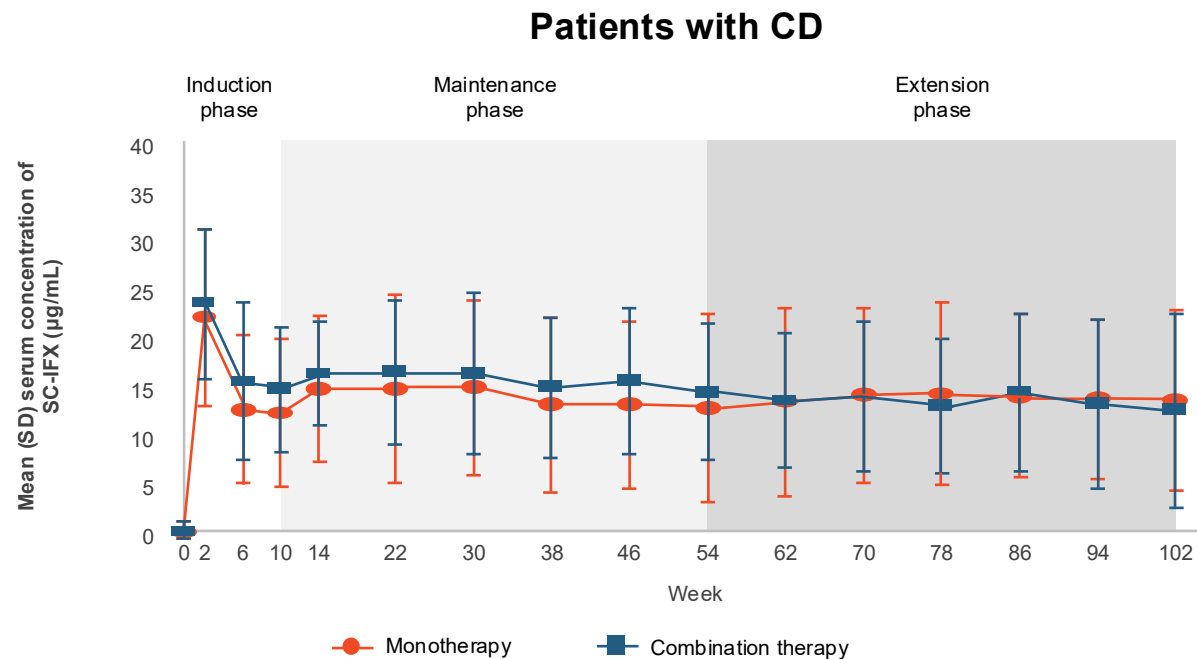
Consideration of Delivery/PK Enhancement

Add Immunomodulators to Anti-TNF



Ben-Horin S, et al. *Clin Gastroenterol Hepatol*. 2013;11(4):444-7.

Switch to SC Maintenance
(Infliximab or Vedolizumab)



Schreiber S, et al. *Inflammatory Bowel Diseases*. 2025:1-11.

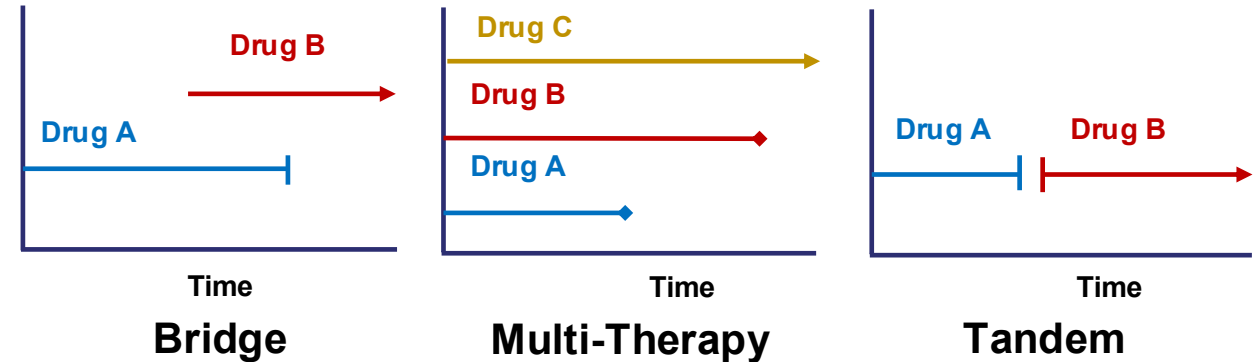
6. Combine Therapies When Rational and Safe

• Mechanism-based

- Multiple targets, more is better
- Theoretically, lower LOR
- Synergy
- One drug makes another work better
- Immune-based vs. PK

• Time-based

- Induction → maintenance
- Bridge vs. Step vs. Tandem
- Pre-treatment
- De-intensification



Clinical Trials of Combination Therapies in IBD

	IL23p19	$\alpha 4/\beta 7$	IL1 α /1 β	IL12/23	TNF	JAK1,2,3	JAK1	TL1A
IL23p19		Target CD (Phase 2)	Target CD (Phase 2)		DUET CD/UC (Phase 2B)			
$\alpha 4/\beta 7$	Target CD (Phase 2)			EXPLORER 2.0 (UC) (Phase 4) SKYLINE-UC (Phase 2)	EXPLORER 2.0 (UC) (Phase 4)	EXIGEM (UC) (Phase 4)	VICTRIVA (CD) (Phase 3b)	SKYLINE-UC (Phase 2)
IL1 α /1 β	Target CD (Phase 2)							
IL12/23		EXPLORER 2.0 (CD) (Phase 4) SKYLINE-UC (Phase 2)						SKYLINE-UC (Phase 2)
TNF	DUET CD/UC (Phase 2B)	EXPLORER 2.0 (CD) (Phase 4)						
JAK1,2,3		EXIGEM (UC) (Phase 4)						
JAK1		VICTRIVA (CD) (Phase 3b)						
TL1A		SKYLINE-UC (Phase 2)		SKYLINE-UC (Phase 2)				

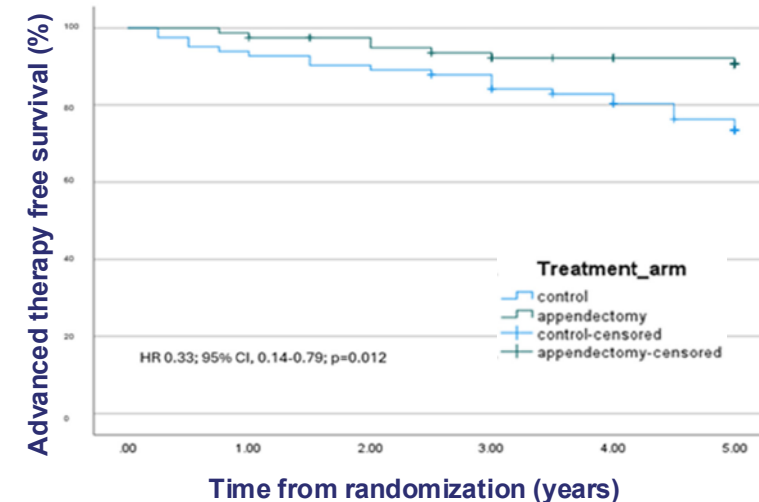
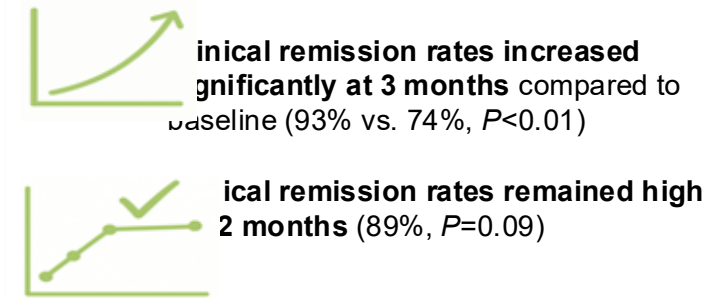
	Under Investigation
	Potential combinations

7. Change the Patient!

- **Add incretin (GLP-1) or twincretin (GLP-1 + GIP):**
 - Improved weight, metabolic, and disease-related outcomes¹⁻³
 - CAUTIONS: changes in inflammatory burden, gut transit (delivery), potential drug-drug interactions, and drug dosing and safety⁴
 - Ongoing prospective trials evaluating disease activity and outcomes (COMMIT trials of mirikizumab + tirzepatide^{5,6})
- **Remove the appendix?**
 - Appendectomy reduced advanced therapy escalation (8.8% vs. 25.3%; HR 0.33, p=0.012)^{7,8}
 - Showed association with lower colectomy rates (p=0.09)^{7,8}

Mount Sinai, NYC (n=~900)

IMPACT ON IBD¹



¹Gold SL, et al. Presented at DDW. May 2025. Tu1968.

²Maracle B, Quan S, Hamilton P, et al. *Aliment Pharmacol Ther.* 2026;63(1):17-39.

³St-Pierre J, Rubin DT, et al. *Dig Dis Sci.* 2024.

⁴Klein J, et al. *ACG Case Rep J.* 2024.

⁵Clinicaltrials.gov/NCT06937086.

⁶Clinicaltrials.gov/NCT06937099.

⁷Van Dijk I, et al. Presented at ECCO. February 2026. OP34.

⁸ACCURE Study Group. *Lancet Gastroenterol Hepatol.* 2025;10(6):550-561

8. Eat to Target?

- **Augmenting Biologic Effectiveness**
 - Exclusive enteral nutrition (EEN) + anti-TNF improves outcomes [OR 2.93 (95% CI (1.66-5.17))]^{1,2}
- **Dietary Therapeutics**^{3,4}
 - Anti-inflammatory dietary patterns (AID, Mediterranean)
 - Symptom improvements, milder disease⁵
 - Low emulsifier diet may improve disease control⁶
- **Role of Diet in Perioperative Management⁷ & Disease Modification**
 - Address malnutrition
 - Preoperative optimization (EEN/PEN in CD) reduces complications, may reduce bowel length of involvement

Mediterranean Diet



Accessed from VectorStock.com/37057030.

Emulsifier-containing foods

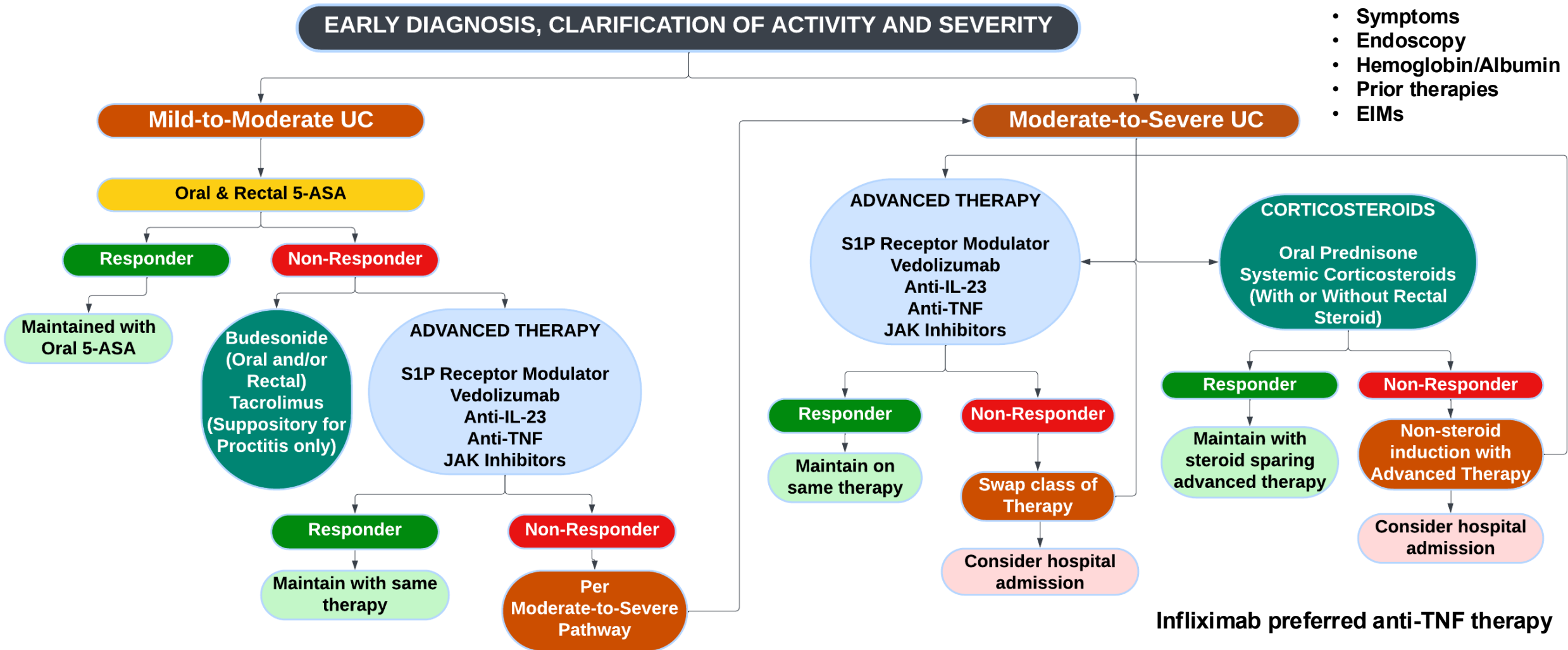


9. Personalize Your Approach to Each Patient in Your Practice (N=1 Strategy)

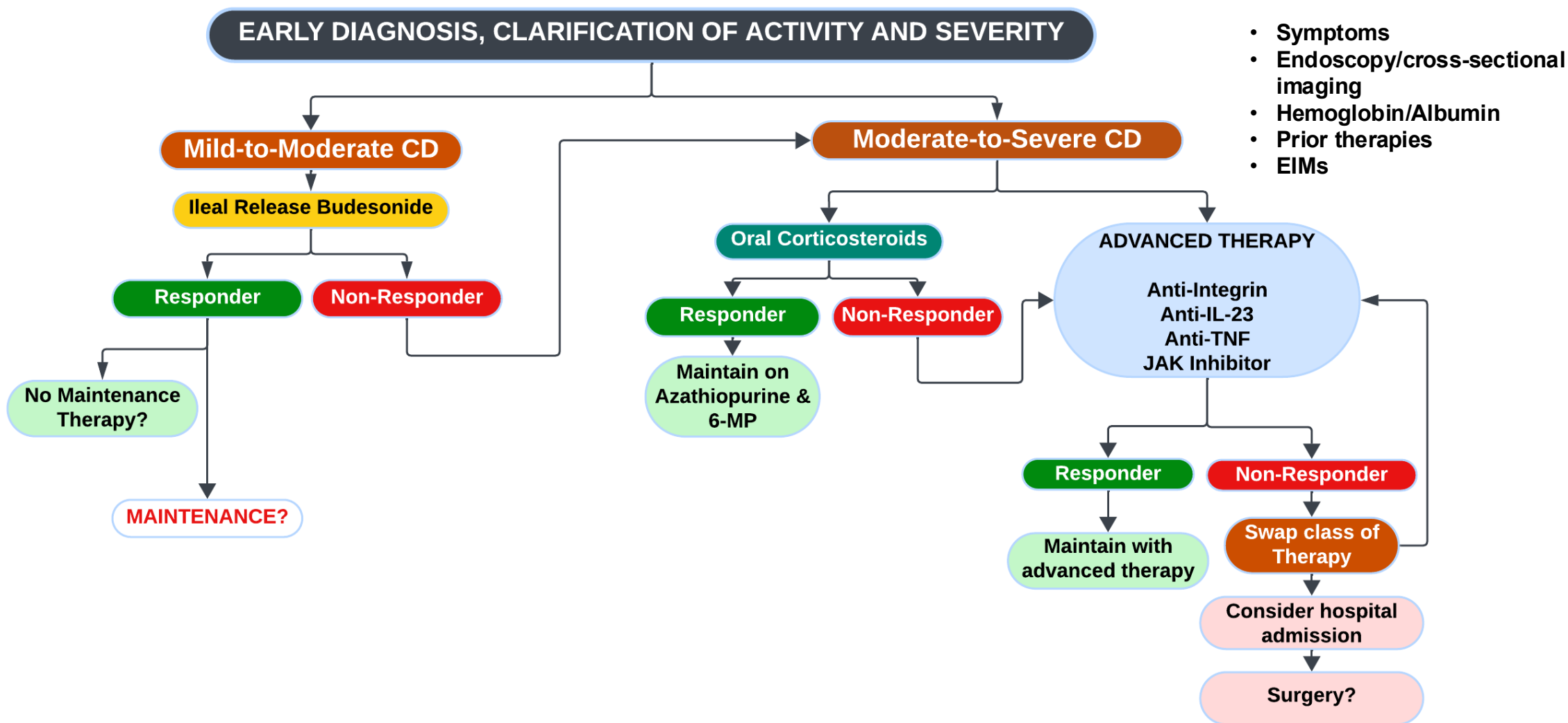
- **System issues (insurance coverage, access) still trump best intentions**
- **Early intensive therapy enables conceptual de-intensification considerations later**
 - Requires proactive disease monitoring
- **Need pragmatic trials of mechanistic switching from induction to maintenance and proactively in maintenance phase**



Management of Ulcerative Colitis

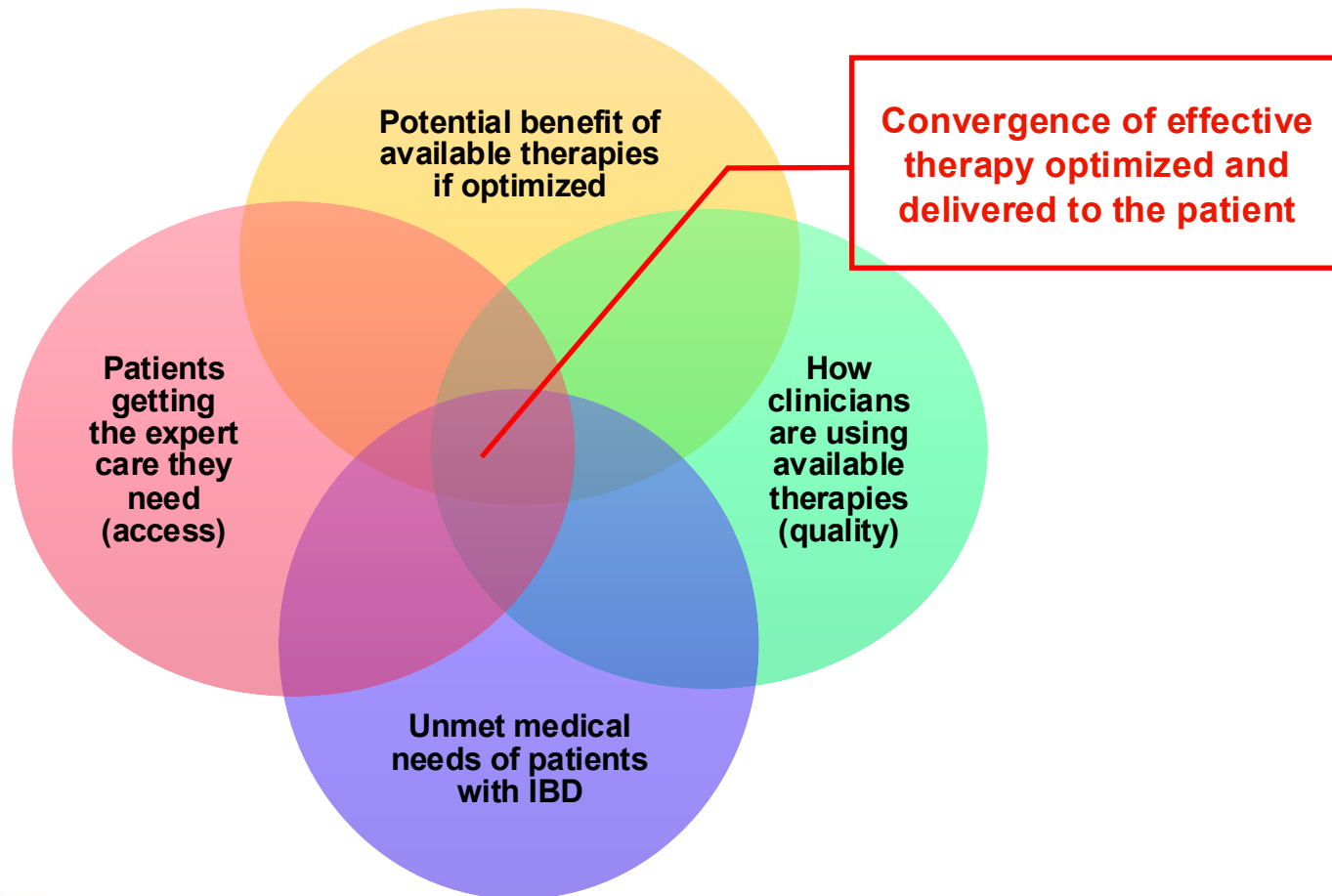


Management of Crohn's Disease



Summary: Managing IBD in 2026

Most Patients Should be in Remission Now!



1. Treat EARLY
2. Choose Wisely: First Line Therapy
3. Avoid Corticosteroids!
4. Treat to a Target
5. Develop an Approach to Non-Response
6. Combine Therapies When Rational and Safe
7. Change the Patient!
8. Eat to Target?
9. Personalize Your Approach (N=1)

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