NEW YORK SOCIETY FOR GASTROENTEROLOGY & ENDOSCOPY
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New York Society for Gastroenterology and Endoscopy

# Medical Management of IBD
# So Many Choices

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# Disclosures

- Consultant: Abbvie, Pfizer, Takeda, Johnson&Johnson

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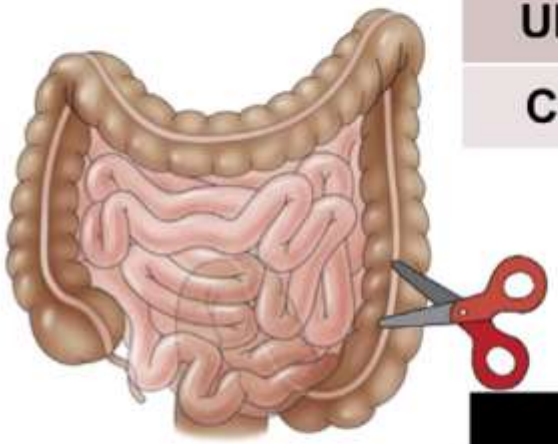
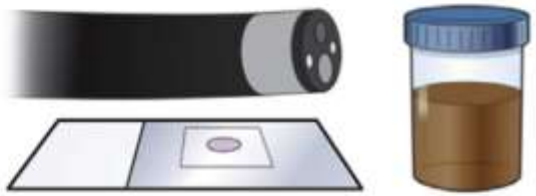
# Surgery Rates Have Improved Over Time But Are Still High

**Risk Associated With Surgery For Ulcerative Colitis Before And After 2000**



| Before 2000 | | | |
|---|---|---|---|
| | 1-y risk of surgery | 5-y risk of surgery | 10-y risk of surgery |
| Ulcerative colitis | 4.8% (3.7-6.1) | 9.5% (7.8-11.4) | 15.2% (12.6-18.2) |
| Crohn's disease | 23.6% (18.3-29.9) | 35.7% (29.2-42.9) | 46.5% (36.7-56.6) |

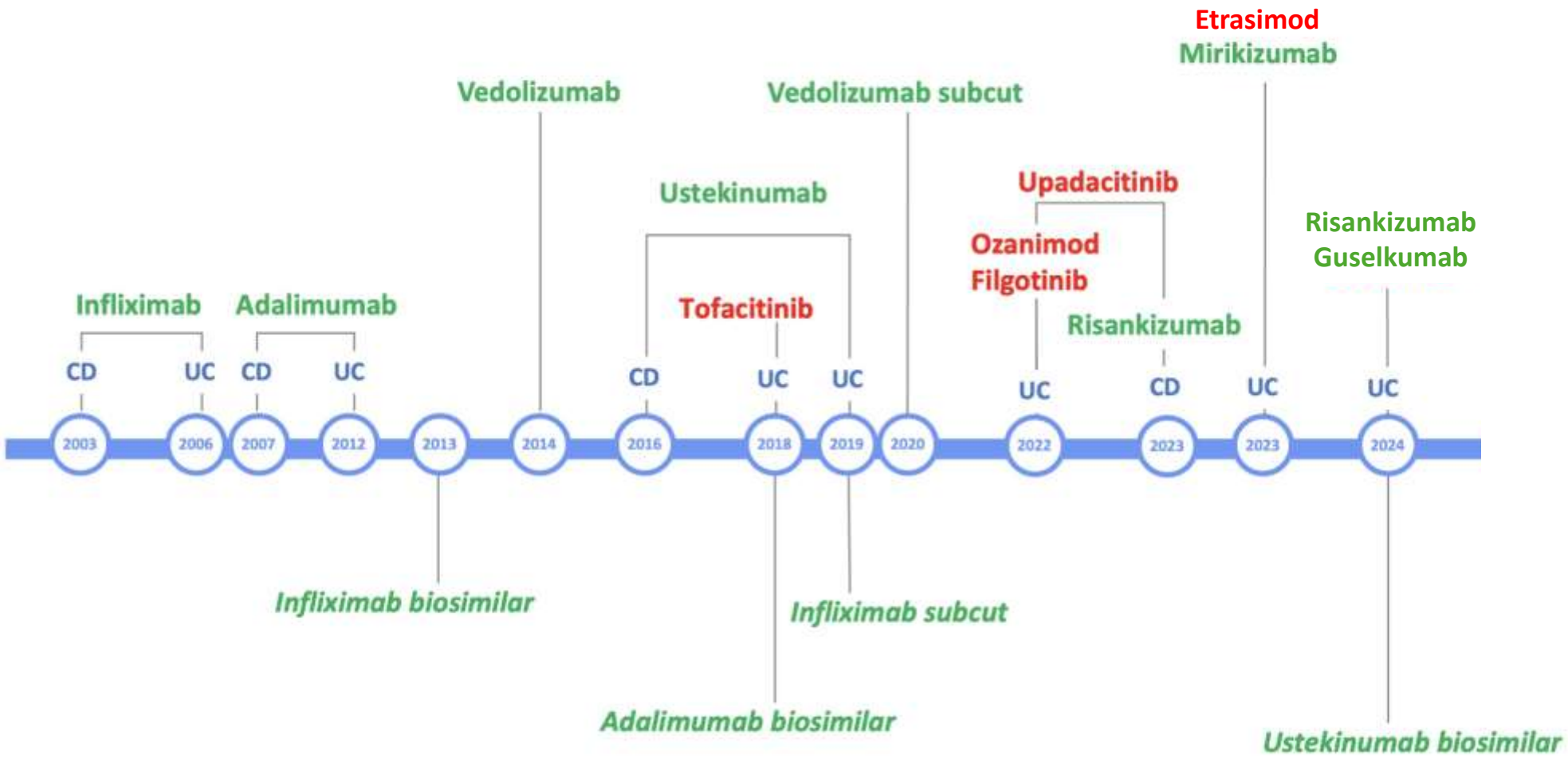


Improved management

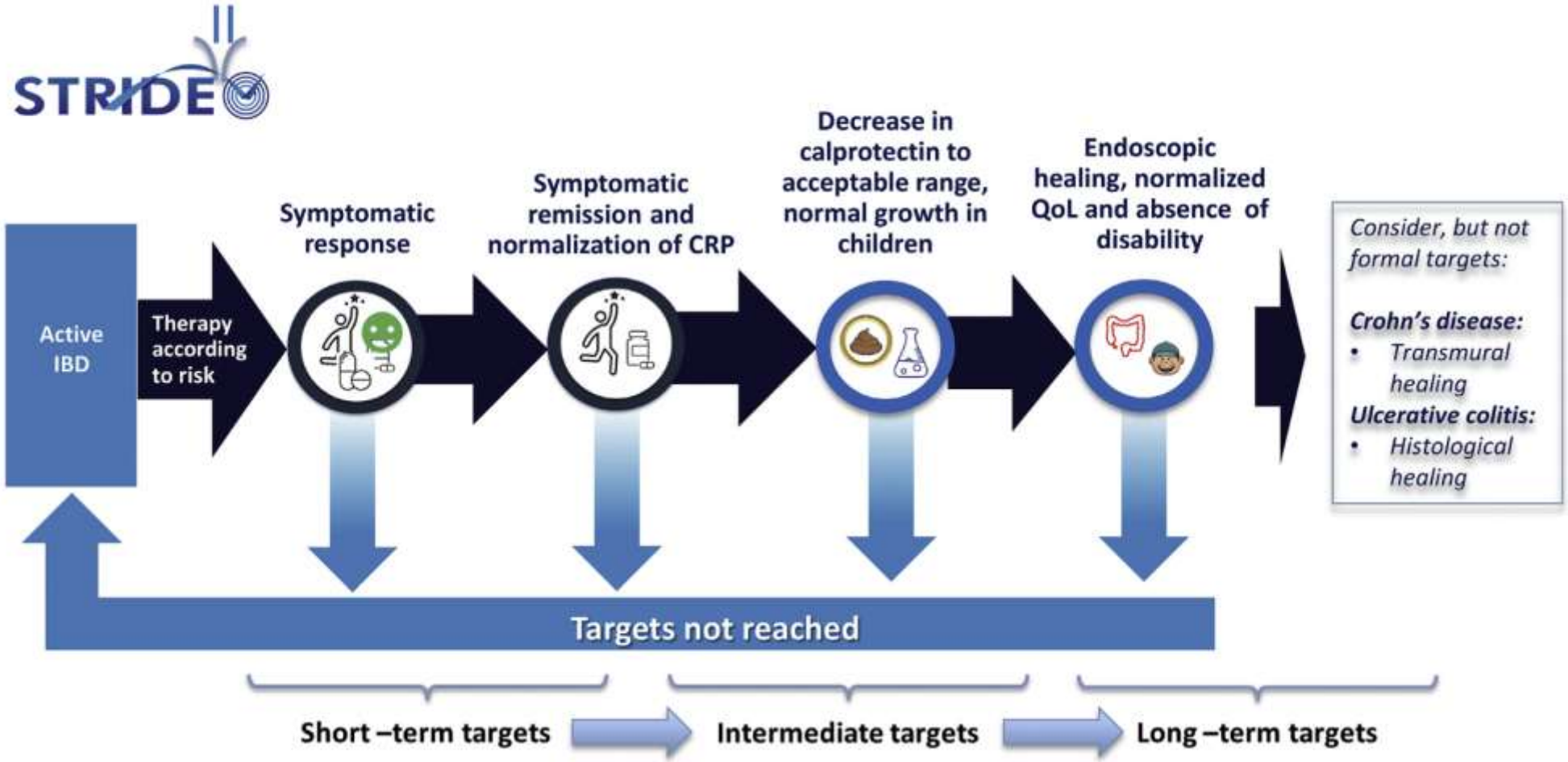
| After 2000 | | | |
|---|---|---|---|
| | 1-y risk of surgery | 5-y risk of surgery | 10-y risk of surgery |
| Ulcerative colitis | 2.8% (2.0-3.9) | 7.0% (5.7-8.6) | 9.6% (6.3-14.2) |
| Crohn's disease | 12.3% (10.8-14.0) | 18.0% (15.4-21.0) | 26.2% (23.4-29.4) |

Tsai L et al. Clin Gastroenterol Hepatol. 2021

# Medical Treatment Options for IBD



# Treat to Target Algorithm in IBD




Turner D, et al. *Gastroenterology*. 2021

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# 5 Factors of Treatment Choice for Patients with IBD

1

**Patient Factors**

- Phenotype
- Comorbidities
- EIMS
- Pregnancy

2

**Efficacy**

- Available evidence
- Clinical trial vs. real-world
-Differences in biologic exposed

3

**Safety**

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

**Convenience**

- Mode of delivery
- Frequency of dose

4

**Access**

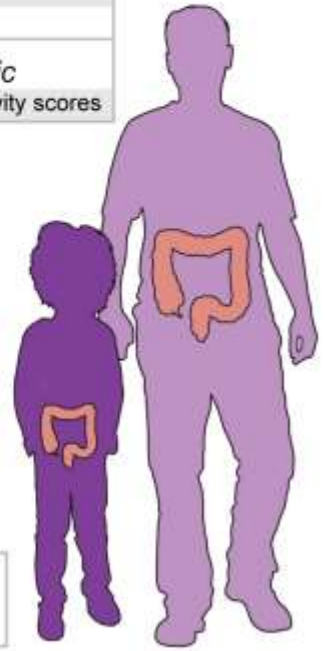
- Insurance coverage
- Cost and time to patient

5

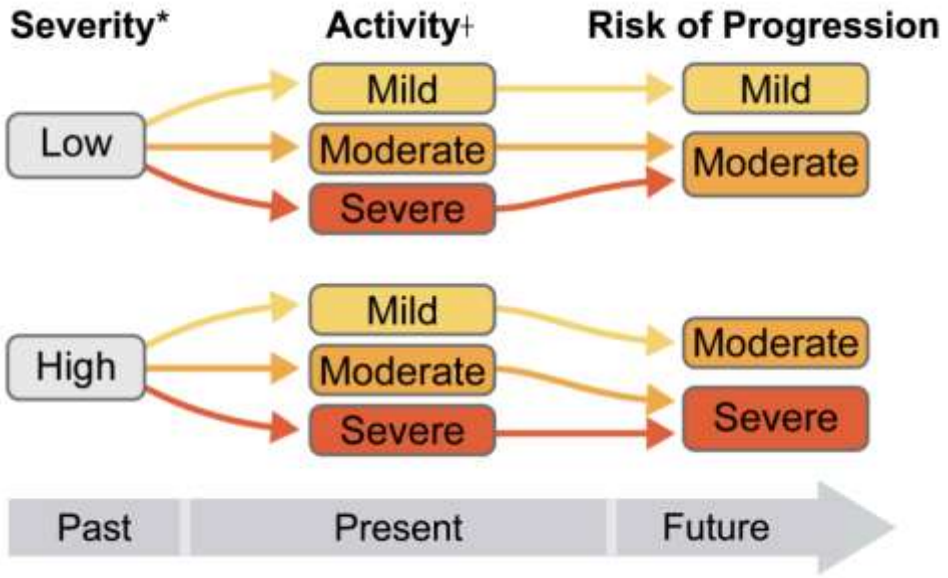
# Disease Severity and Activity Inform Risk Assessment

| Disease Severity Variables | CD | UC |
|---|---|---|
| *Clinical* | | |
| Limited anatomic extent | X | X |
| Growth impairment (pediatric) | X | |
| Age <14 years (pediatric)* | X | X |
| Age <40 years | X | X |
| Perianal or severe rectal disease | X | |
| Penetrating disease | X | |
| Stricturing disease | X | |
| Multi- or long-segment ileal (>20 cm), disease proximal to TI | X | |
| Emergent diagnosis, hospitalization | X | X |
| Need for systemic steroids | X | X |
| Delay in diagnosis | X | X |
| Extensive bowel involvement | X | X |
| *C. difficile*, cytomegalovirus infection | | X |
| *Serologies* | | |
| ASCA (+) | X | |
| ANCA (+) | X | X |
| Anti-Cbir (+) (UC: pediatric) | X | X |
| Anti-GMCSF (+) | X | |
| *Genetic* | | |
| NOD2 mutation | X | |

| Disease Activity Variables* |
|---|
| *Clinical* |
| Symptoms |
| *Biomarkers* |
| C-reactive protein |
| Fecal calprotectin |
| Albumin |
| Hemoglobin |
| *Endoscopic* |
| Disease activity scores |



X Mild
X Severe




Agrawal et al. Gastroenterology 2022

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# Right Drug, Right Patient

## Therapies to Reach For

| Concomitant Immune Conditions/Extraintestinal Manifestations | |
|---|---|
| Plaque Psoriasis | Anti-TNF<br>IL-12/23, IL-23 |
| Psoriatic Arthritis | Anti-TNF<br>IL-12/23, IL-23<br>Jak |
| Rheumatoid Arthritis | Anti-TNF<br>Jak |
| Spondyloarthritis | Anti-TNF<br>Jak |
| Multiple Sclerosis | Ozanimod |
| Uveitis | Anti-TNF |

## Therapies to Avoid

| Safety Considerations | |
|---|---|
| Macular Edema | S1P |
| Type 2 Heart Block | S1P |
| Lymphoma | Anti-TNF |
| Melanoma | Anti-TNF |
| Pulmonary Hypertension | CurQD |
| Pregnancy<br>Breastfeeding | S1P<br>Jak |

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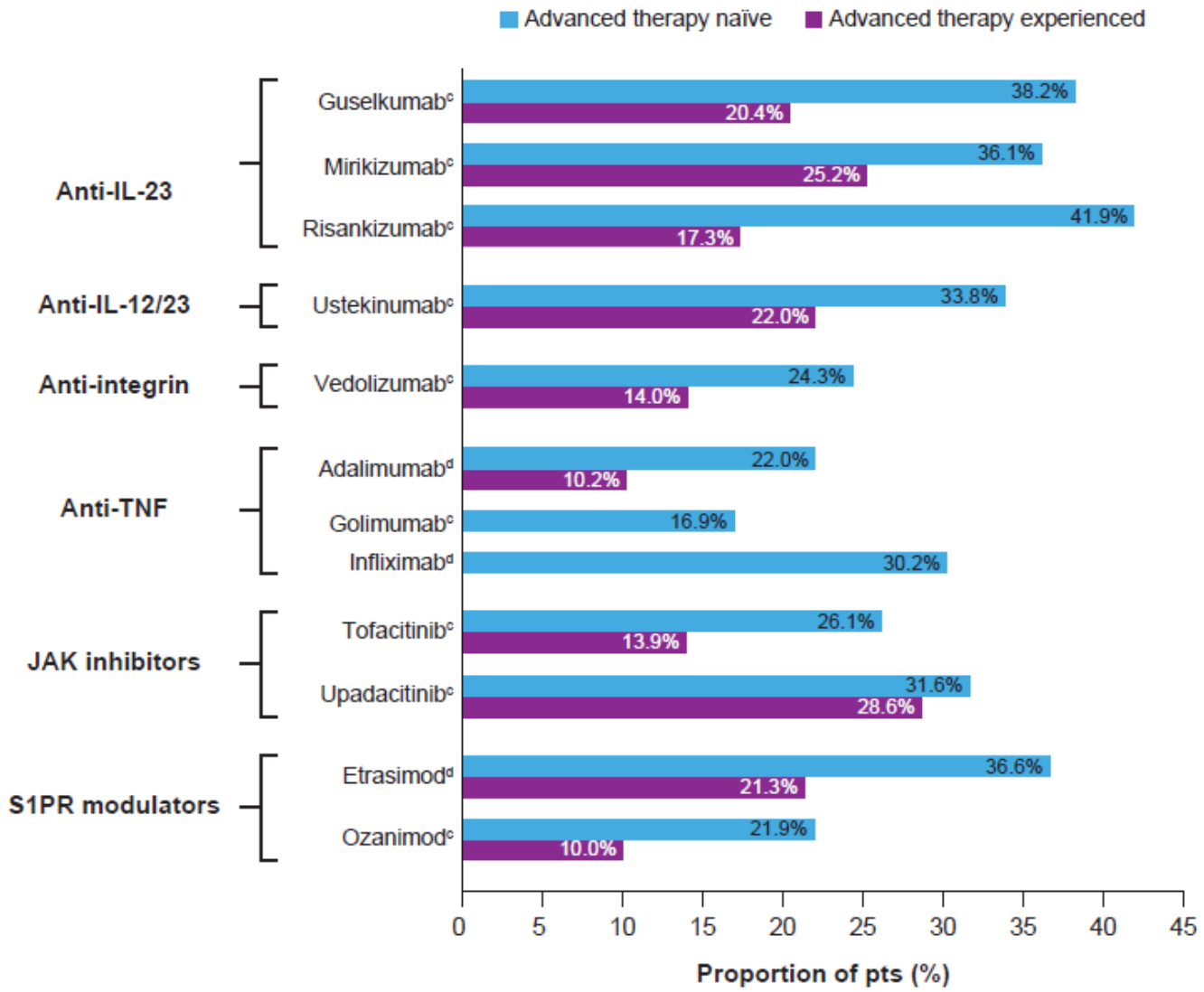
# Right Drug, Right Time




Kayal M et al. Clin Gastroenterol Hepatol. 2023.

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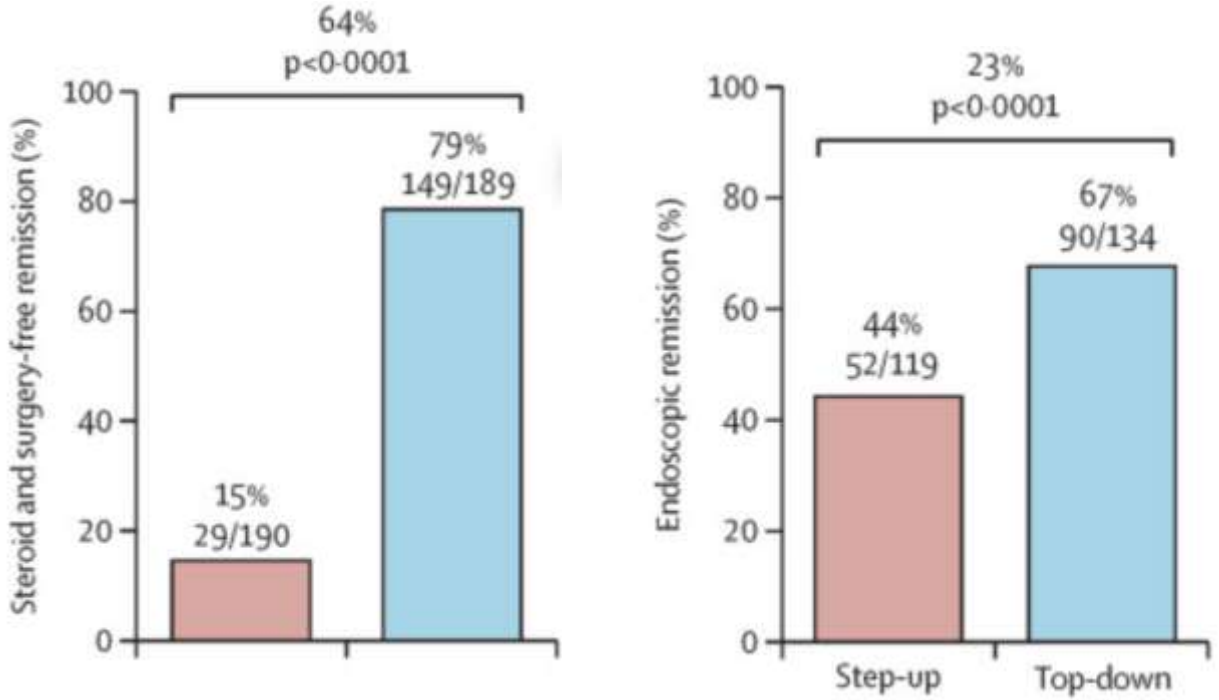
# PROFILE
# Step-up Therapy vs Top-down Therapy in CD

| Accelerated step-up | Top-down |
|---|---|
| Start steroid induction for active Crohn's disease | Start steroid induction for active Crohn's disease |
| Following randomisation, continue steroid taper | Following randomisation, start infliximab and immunomodulator, and continue steroid taper |
| If in remission, continue on current step of treatment<br>If flare 1, start steroids and immunomodulator<br>If flare 2, start infliximab alongside immunomodulator | If in remission, continue infliximab and immunomodulator<br>If flare 1, additional course of steroid medication<br>If flare 2, consider non-response and trial withdrawal |




**Top-down treatment with combination infliximab and immunomodulator is superior to step-up therapy**

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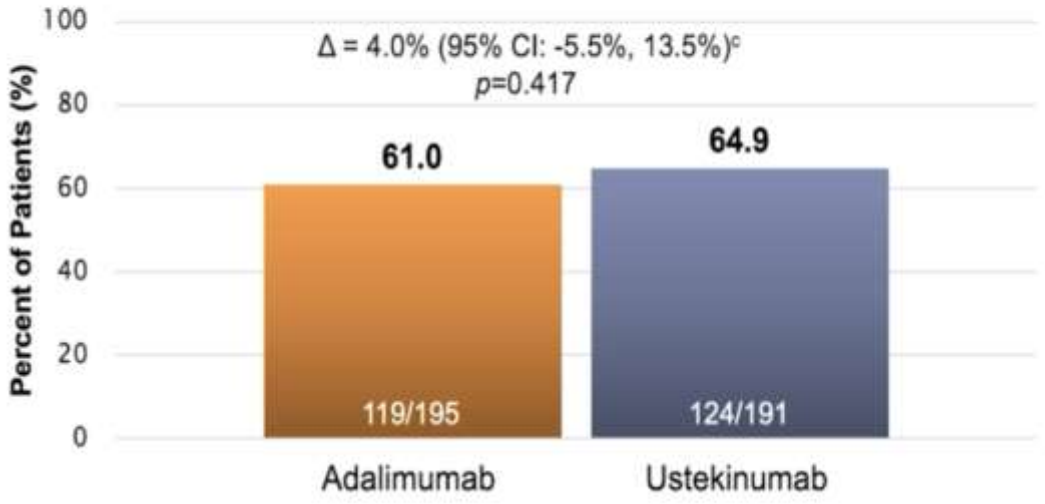
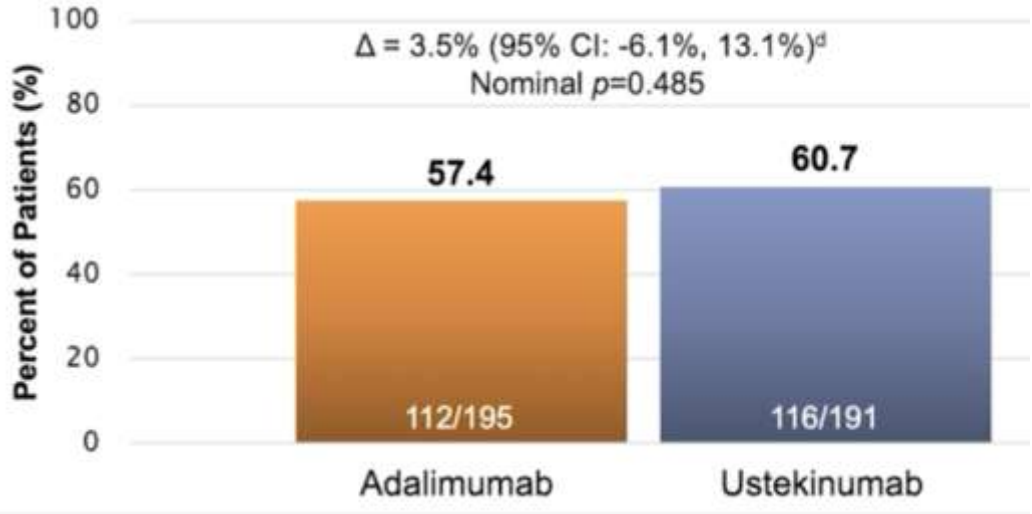
Noor NM et al. Lancet Gastroenterol Hepatol. 2024

# SEAVUE
# Adalimumab vs Ustekinumab in CD

**Clinical remission**




**Corticosteroid free clinical remission**




**No difference between ustekinumab and adalimumab in moderate-severe CD**

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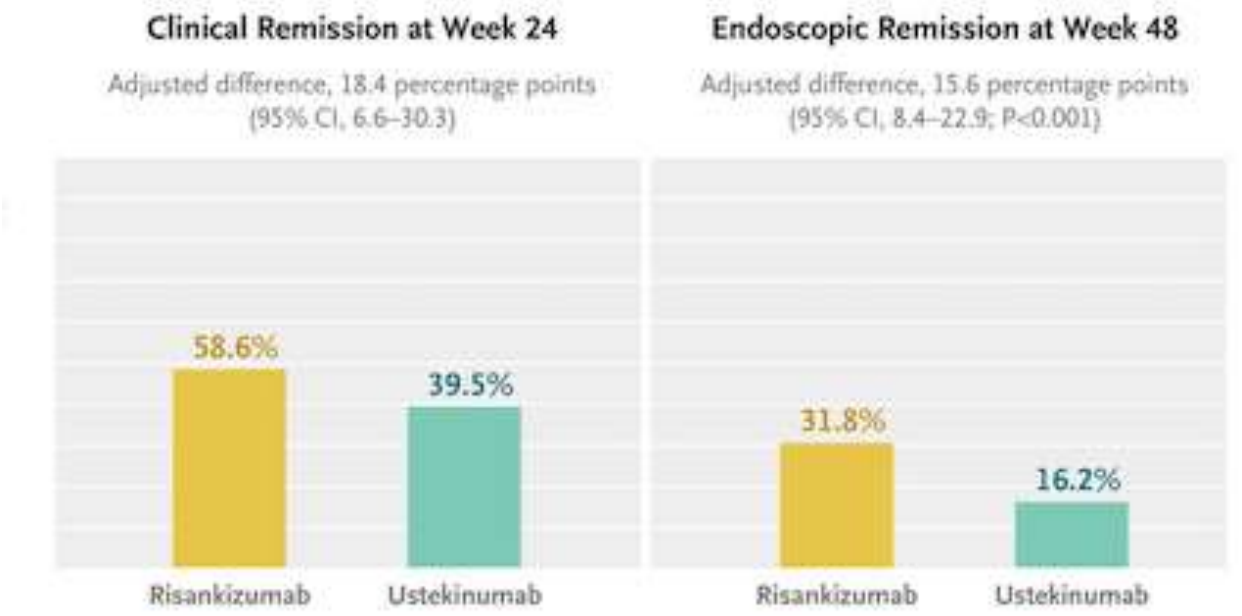
Sands BE, et al. *Lancet.* 2022.

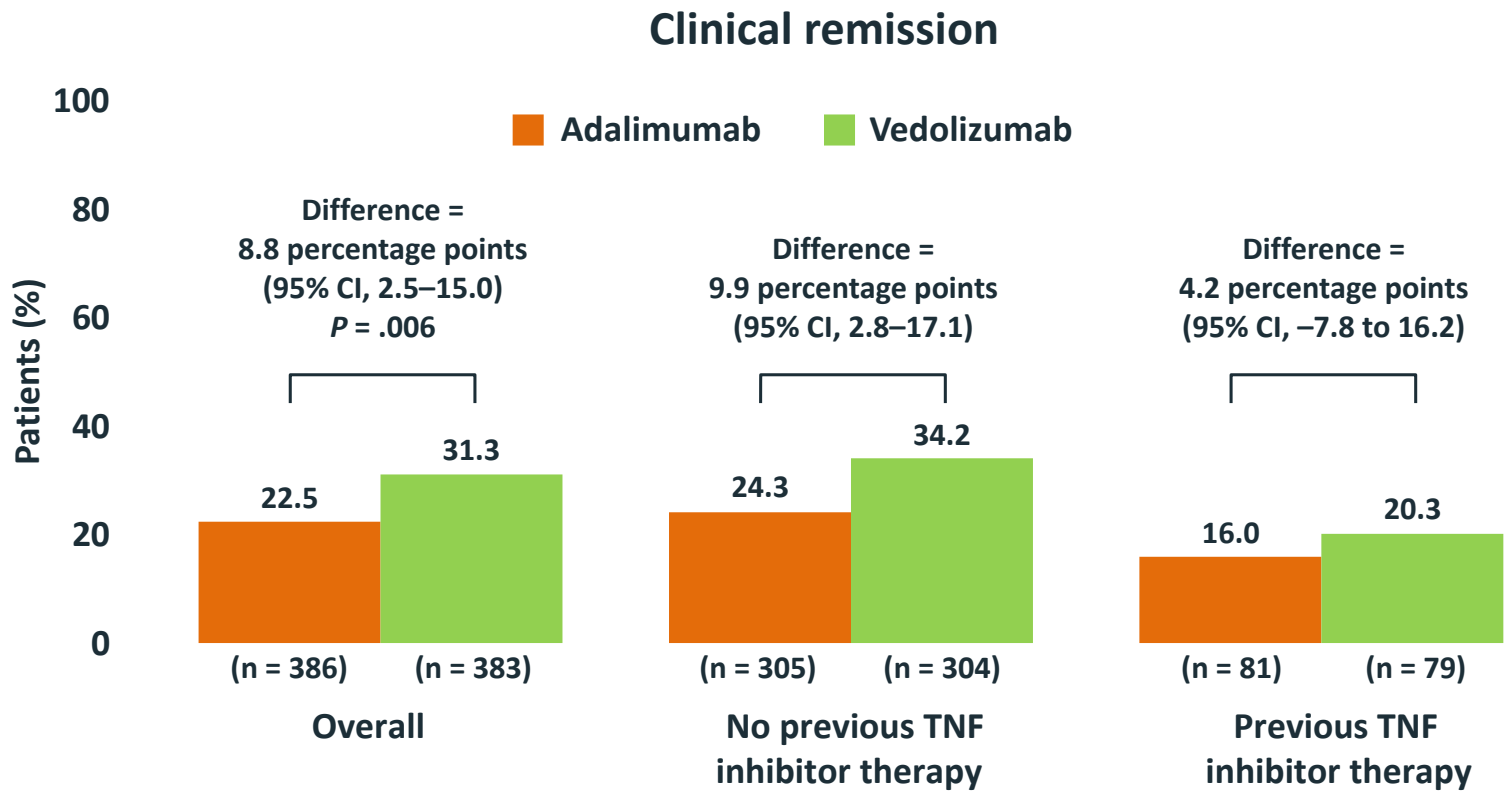
# SEQUENCE
# Risankizumab vs Ustekinumab As Second Line in CD




**Risankizumab was noninferior to ustekinumab for clinical remission and superior for endoscopic remission**

Peyrin-Biroulet L. N Engl J Med. 2024

# VARSITY
# Adalimumab vs Vedolizumab in UC




**Vedolizumab is superior to adalimumab in moderate-severe UC**

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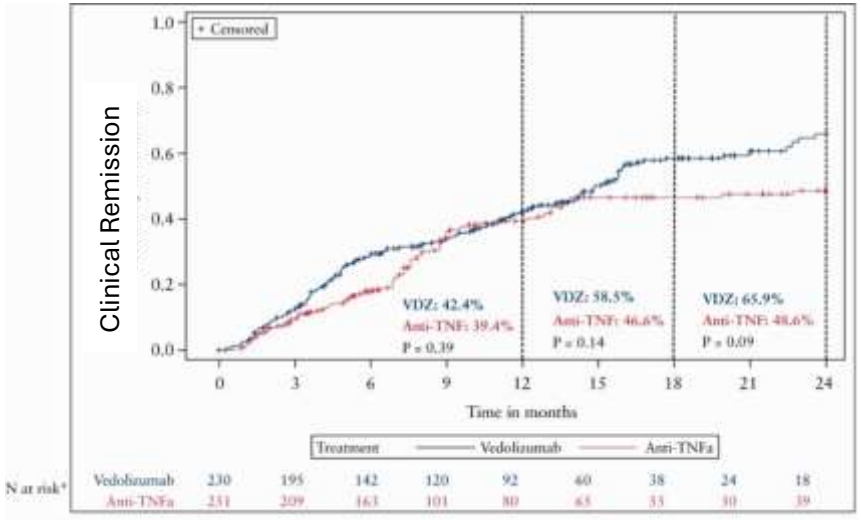
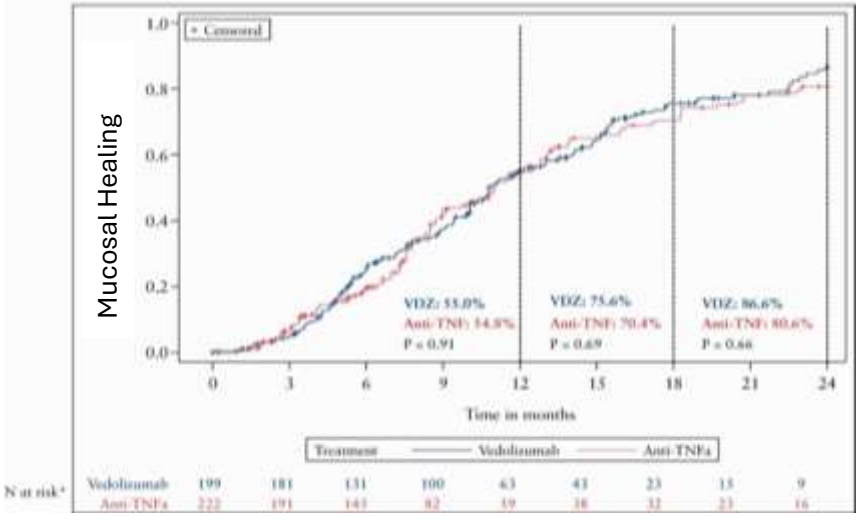
Sands BE, et al. *N Engl J Med*. 2019

# EVOLVE
# Vedolizumab is Equivalent to Infliximab in UC

- EVOLVE: multicenter retrospective study comparing anti-TNF as 1st or 2nd line after vedolizumab, N=604 biologic naïve patients with UC
- Vedolizumab and anti-TNFα treatments were equally effective at controlling disease symptoms as first line therapies, but vedolizumab has a more favorable safety profile

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Bressler B, et al. *J Crohns Colitis.* 2021

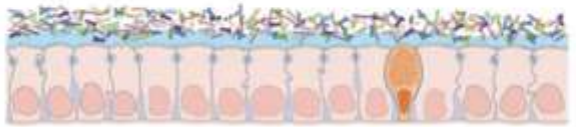
# Risankizumab and Guselkumab Rank High in Achieving Clinical and Endoscopic Remission in UC

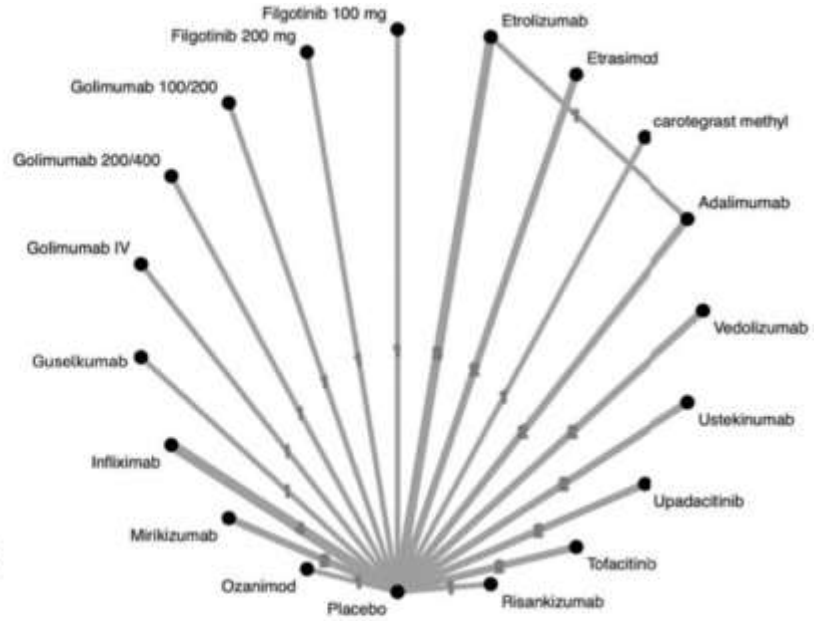
36 studies
Included, with 14,270 patients with UC

Upadacitinib was superior to most biologics and small molecules drugs in inducing and maintaining clinical remission.
Novel biologics such as risankizumab and guselkumab also ranked high in achieving clinical remission.

Upadacitinib was superior to most biologics in inducing and maintaining endoscopic improvement and remission.

Risankizumab ranked highest in the induction of histological remission, whereas upadacitinib was superior in maintenance of histological remission.



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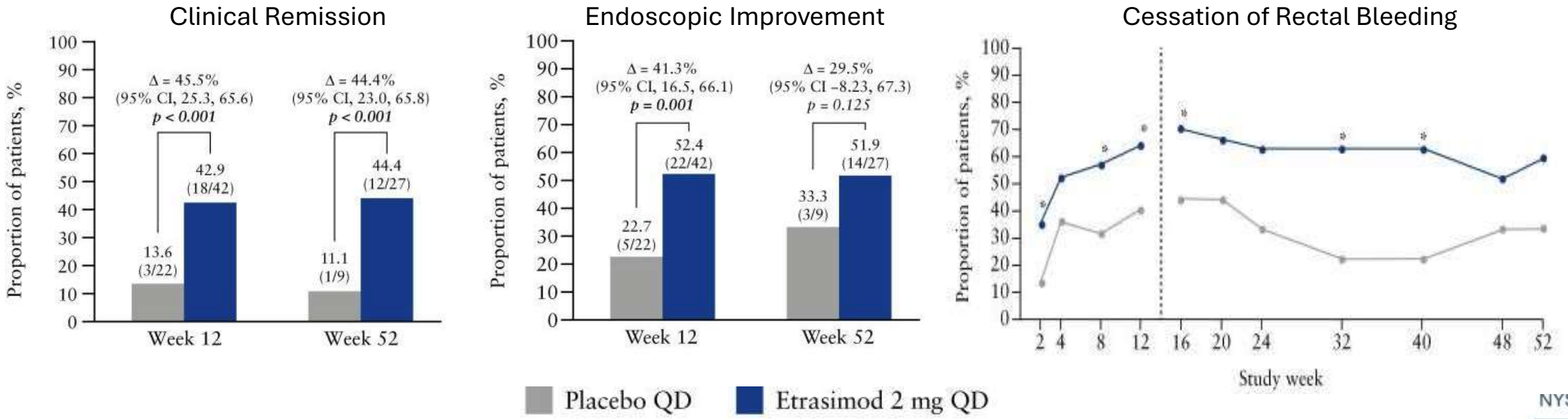
Shehab M et al. Clin Gastroenterol Hepatol. 2024.

# Etrasimod Is Effective in Isolated Proctitis

- Post-hoc analyses of week 12 and 52 ELEVATE data of patients with isolated proctitis defined as <10cm of active rectal involvement
- Significant improvements in clinical remission rates at weeks 12 and 52, endoscopic improvement at week 12, cessation of rectal bleeding at week 2




Peyrin-Biroulet L, et al. *J Crohns Colitis.* 2024

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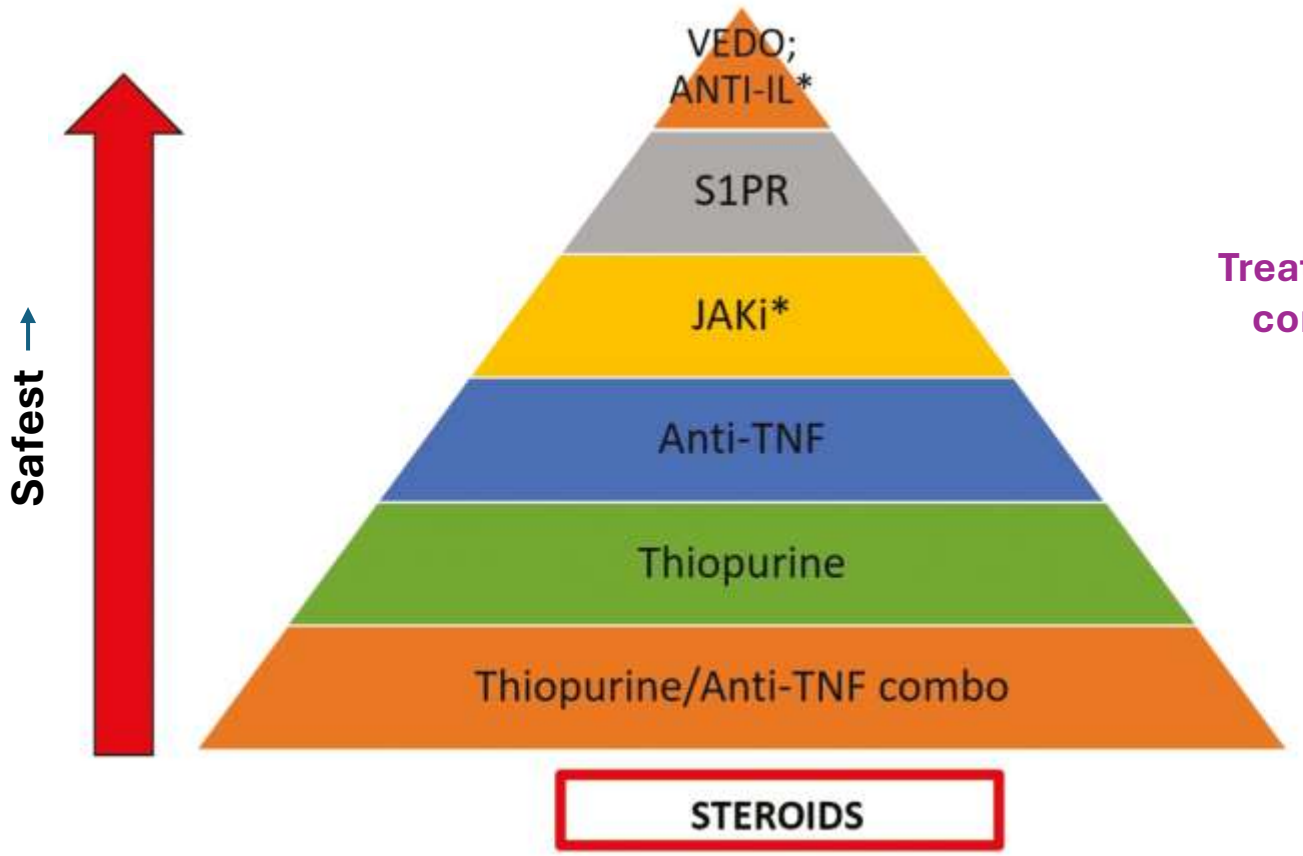
# Safety of Medical Therapies for IBD





**Inadequate treatment of Crohn's disease and ulcerative colitis is an adverse event**

Bhat S et al. Inflamm Bowel Dis. 2024.

# Therapeutic Options and Route of Administration

| Biologic Agents | | Route of Admin | CD | UC |
|---|---|---|---|---|
| TNF inhibitors | Adalimumab | SC | ✓ | ✓ |
| | Certolizumab | SC | ✓ | |
| | Golimumab | SC | | ✓ |
| | Infliximab | IV, IV to SC | ✓ | ✓ |
| Integrin inhibitors | Natalizumab | IV | ✓ | |
| | Vedolizumab | IV, IV to SC | ✓ | ✓ |
| IL-12/23 inhibitor | Ustekinumab | IV to SC | ✓ | ✓ |
| IL-23 inhibitors | Risankizumab | IV to SC | ✓ | ✓ |
| | Mirikizumab | IV to SC | | ✓ |
| | Guselkumab | IV to SC | | ✓ |
| **Small Molecule Agents** | | | | |
| S1P modulators | Ozanimod | PO | | ✓ |
| | Etrasimod | PO | | ✓ |
| JAK inhibitors | Tofacitinib | PO | | ✓ |
| | Upadacitinib | PO | ✓ | ✓ |

# Considerations for Positioning Therapies

## Ulcerative Colitis

- Therapy Naive:
  - Infliximab
  - Vedolizumab
  - Ozanimod
  - Etrasimod
  - Risankizumab
  - Guselkumab
- Therapy Exposed:
  - Tofacitinib
  - Upadacitinib
  - Ustekinumab

## Crohn's Disease

- Therapy Naive:
  - Infliximab
  - Vedolizumab
  - Ustekinumab
  - Risankizumab
- Therapy Exposed:
  - Upadacitinib
  - Risankizumab

Special Considerations:
- Acute severe UC: Infliximab or upadacitinib/tofacitinib
- CD with multiple segments involved +/- fistula: Infliximab + IMM
- Pregnancy: Any monoclonal antibody

Singh S, et al. *Gastroenterology.* 2024

# Conclusions

- Choice of therapy should be based on:
  - Disease activity and severity with a balance of efficacy and safety
  - Concomitant immune conditions and extraintestinal manifestations

- Comparative effectiveness data suggests:
  - Vedolizumab > adalimumab in UC
  - Adalimumab = Ustekinumab in CD
  - Risankizumab > Ustekinumab as second line in CD

- Employ treat to target strategies to achieve objective endpoints for control