Approach to the Newfound Wealth of Medications for IBD

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Disclosures

- Consultant:
  - Janssen, Abbvie, Pfizer, Bristol Meyers Squibb, Eli Lilly
- Speaker:
  - Abbvie, Eli Lilly, Nestle/Aimmune

Objectives

Upon completion of this presentation, participants should be able to:

- Understand the data behind the new medications available for the treatment of IBD
- Conceptualize a framework for choosing the right medication for the right patient

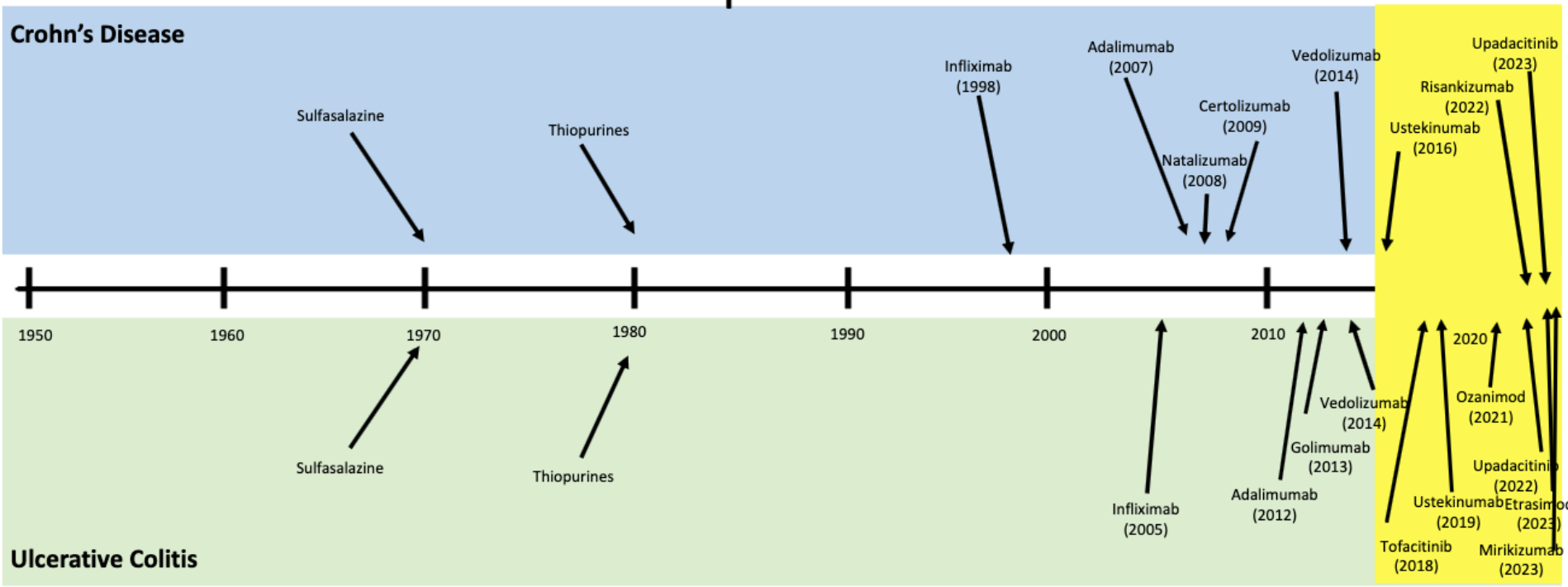
FDA-Approved Targeted Therapies for IBD

Class	CD	UC
TNF inhibitor	Adalimumab[1] Certolizumab[2] Infliximab[3]	Adalimumab[1] Golimumab[8] Infliximab[3]
IL-12/IL-23 inhibitor	Ustekinumab[4] Risankizumab[5]	Ustekinumab[4] Mirikizumab
Integrin inhibitors	Natalizumab[6] Vedolizumab[7]	Vedolizumab[7]
JAK inhibitors	Upadicitinib	Tofacitinib[9] Upadicitinib[10]
S1P receptor modulators	—	Ozanimod[11] Etrasimod

1. Humira (adalimumab) Prescribing Information. https://www.rxabbvie.com/pdf/humira.pdf. 2. Cimzia (certolizumab pegol) Prescribing Information. https://www.cimzia.../themes/custom/cimzia/docs/CIMZIA_full_prescribing_information.pdf. 3. Remicade (infliximab) Prescribing Information. http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/REMICADE-pi.pdf. 4. Stelara (ustekinumab) Prescribing Information. http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/STELARA-pi.pdf. 5. Skyrizi (risakizumab-rzaa) Prescribing Information. https://www.rxabbvie.com/pdf/skyrizi_pi.pdf. 6. Tysabri (natalizumab) Prescribing Information. https://www.tysabrihcp.com/content/dam/commercial/tysabri/hcp/en_us/pdf/tysabri_prescribing_information.pdf. 7. Entyvio (vedolizumab) Prescribing Information. https://general.takedapharm.com/ENTYVIOPI. 8. Simponi (golimumab) Prescribing Information. http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/SIMPONI-pi.pdf. 9. Xeljanz (tofacitinib) Prescribing Information. http://labeling.pfizer.com/ShowLabeling.aspx?id=959. 10.Rinvoq (upadacitinib) Prescribing Information. https://www.rxabbvie.com/pdf/rinvoq_pi.pdf. 11. Zeposia (ozanimod) Prescribing Information. https://packageinserts.bms.com/pi/pi_zeposia.pdf.

Slide adapted from Miguel Regueiro

Timeline of IBD Therapies



Slide courtesy of Miguel Regueiro

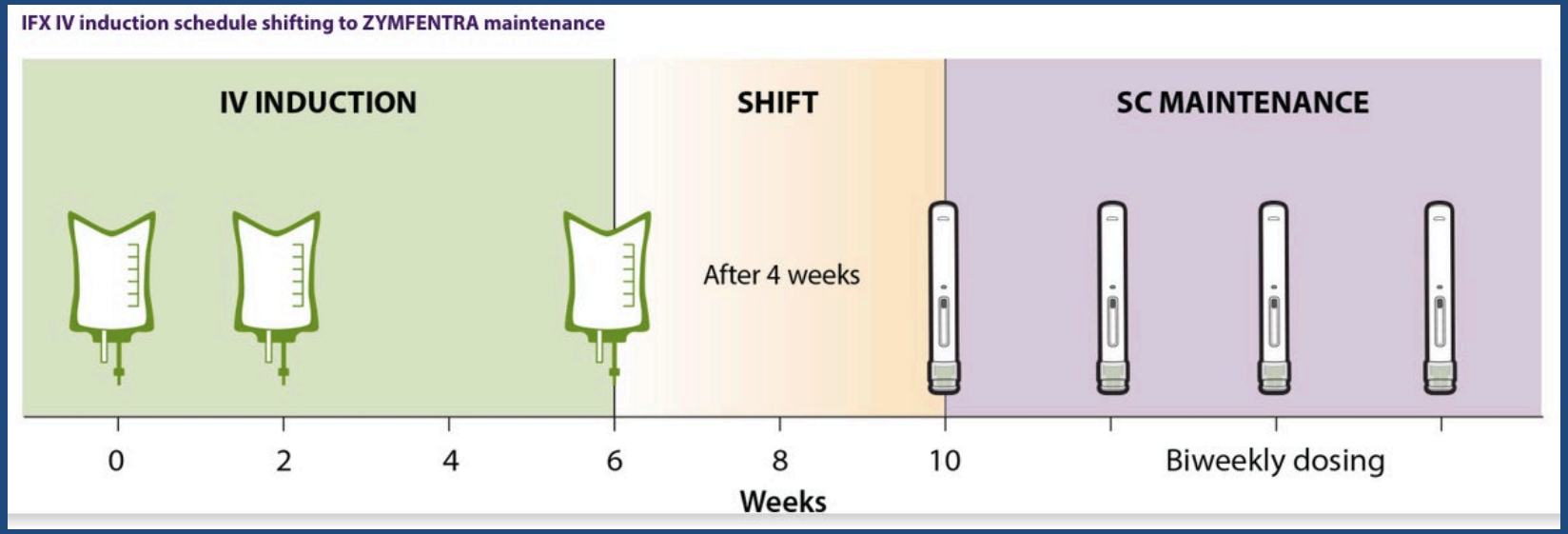
New Therapies in last year

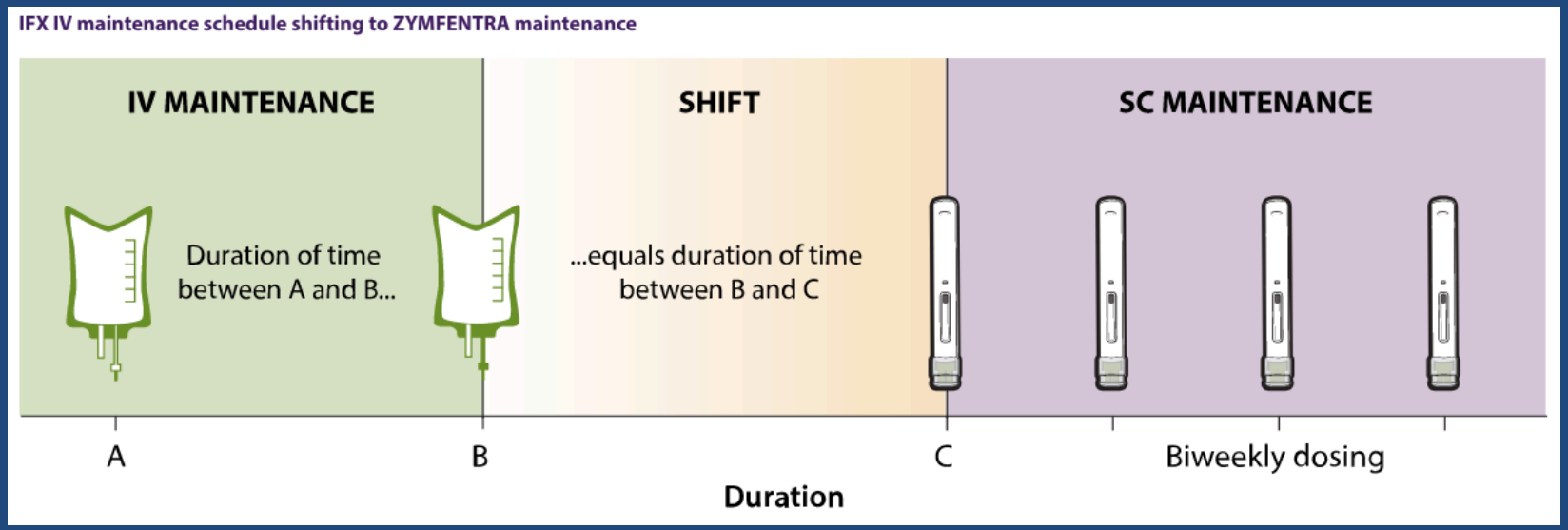
- Infliximab subq (Zymfentra) (CD/UC) – (Oct 2023)
- Mirikizumab (UC) – (Oct 2023)
- Vedolizumab subq (UC only) – (Sept 2023)
- Upadacitinib (Crohn's) – (May 2023)
- Etrasimod (UC) – (Oct 2023)

Infliximab-dyyb (Zymfentra)

- 120 mg pen or syringe

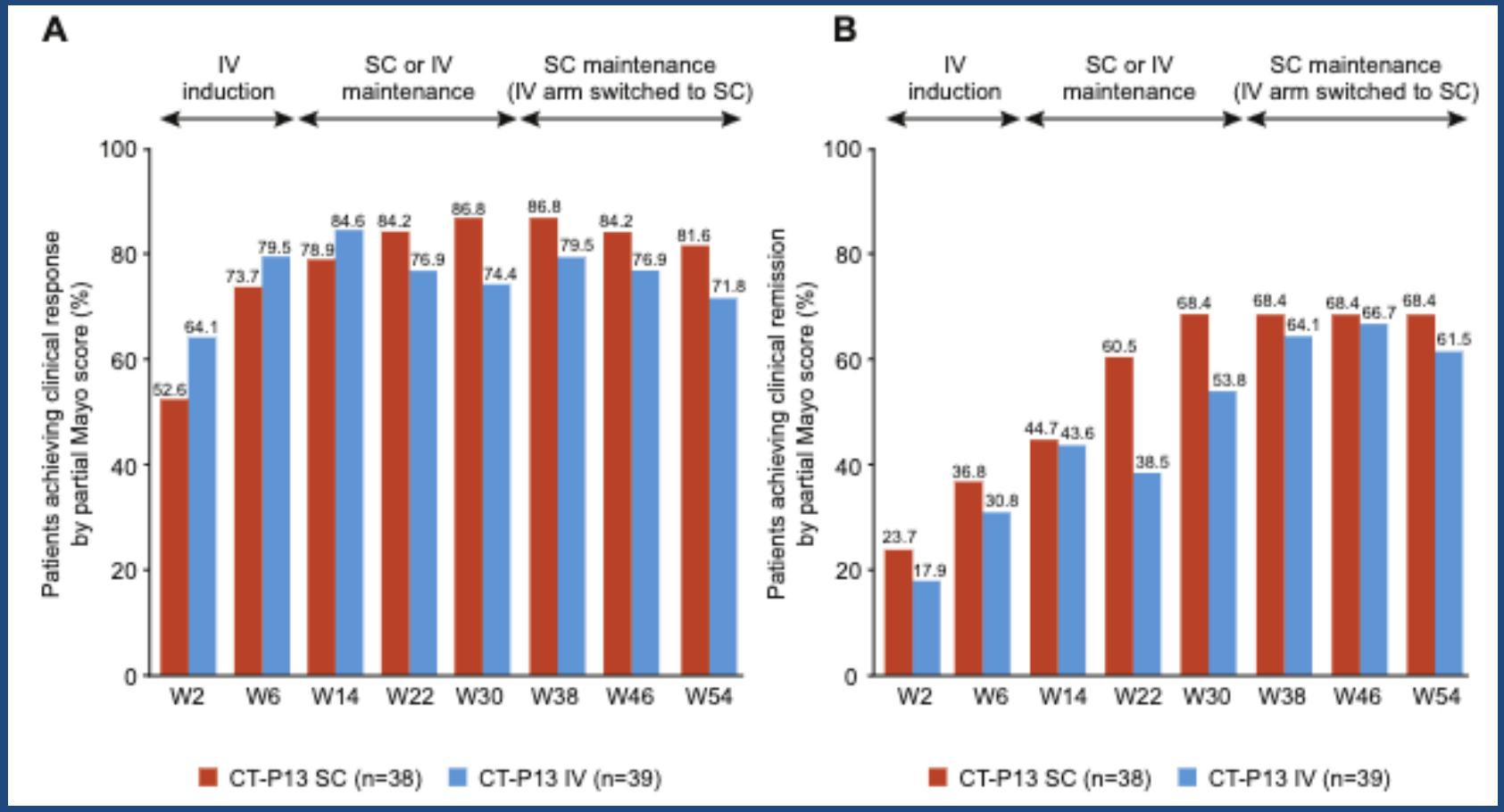
Infliximab-dyyb (Zymfentra)





Infliximab-dyyb (Zymfentra)

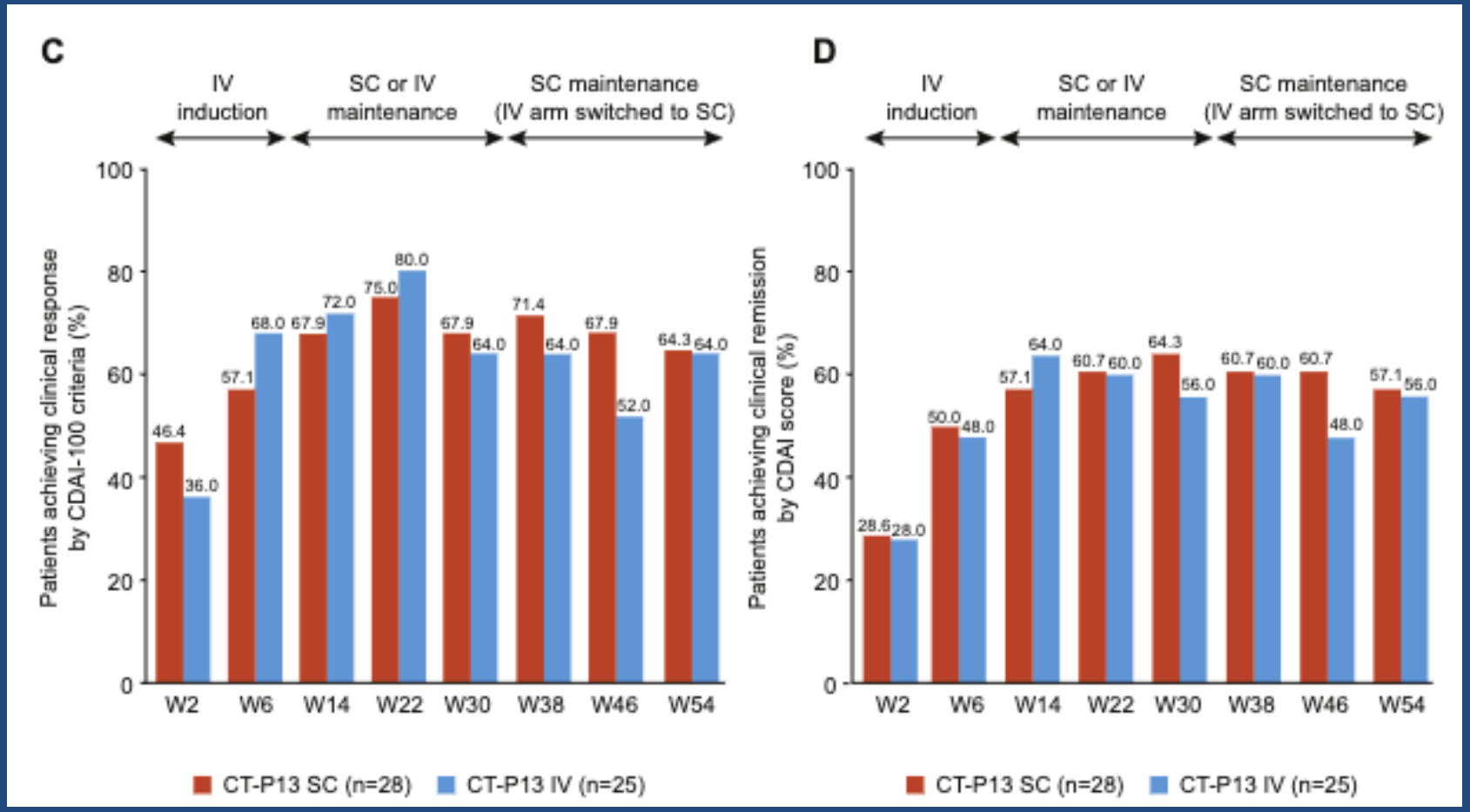
Ulcerative Colitis



Schreiber, et al. Gastro. 2021

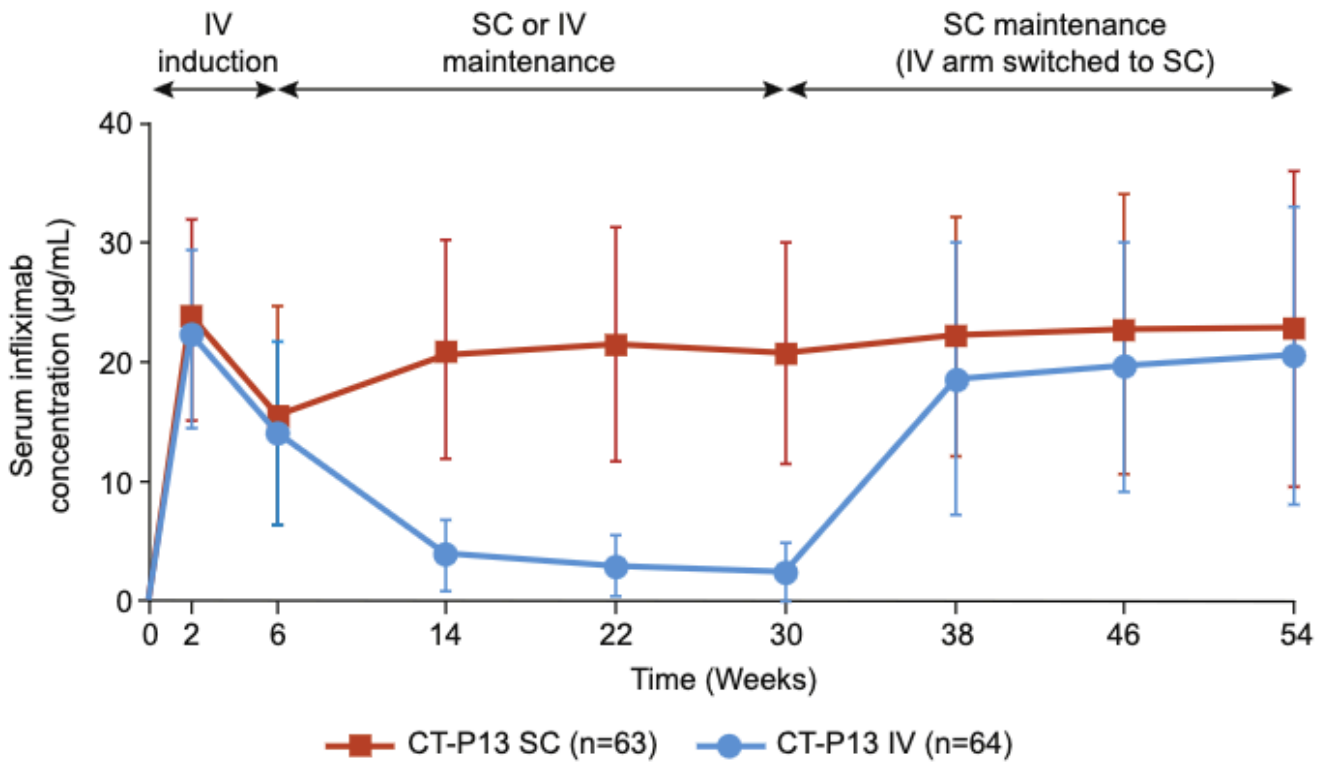
Infliximab-dyyb (Zymfentra)

Crohn's disease



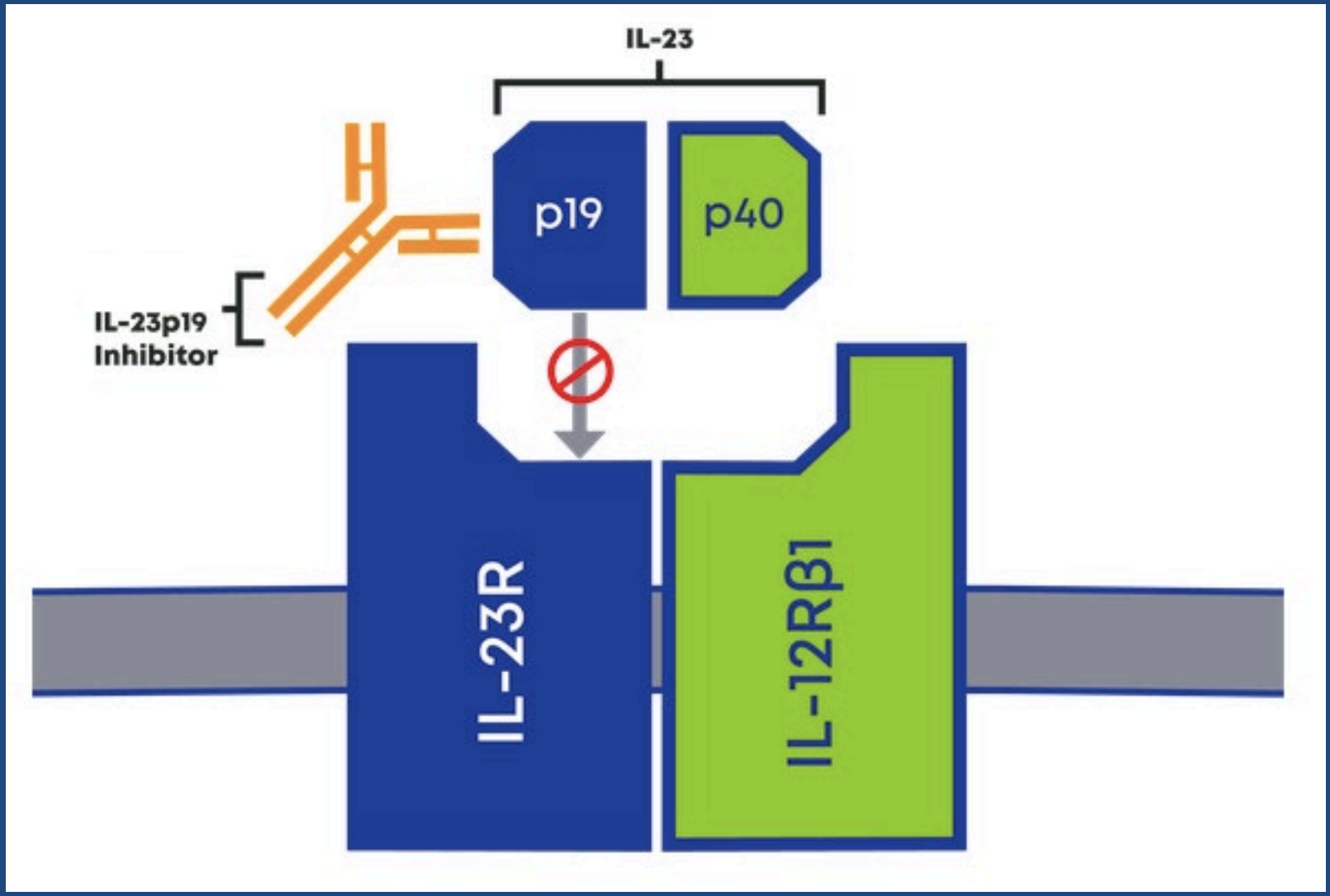
Schreiber, et al. Gastro. 2021

Infliximab-dyyb (Zymfentra)



Schreiber, et al. Gastro. 2021

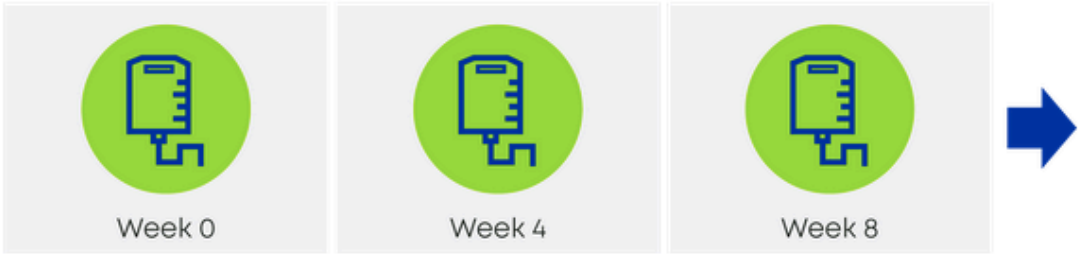
Mirikizumab



Mirikizumab

INDUCTION DOSING: 12 WEEKS[1]

IV infusions of 300 mg[a] at Weeks 0, 4, and 8



[a]Over at least 30 minutes.[1]

Omvoh is intended for use under the guidance and supervision of a healthcare professional. Patients may self-inject after training in proper technique.[1]

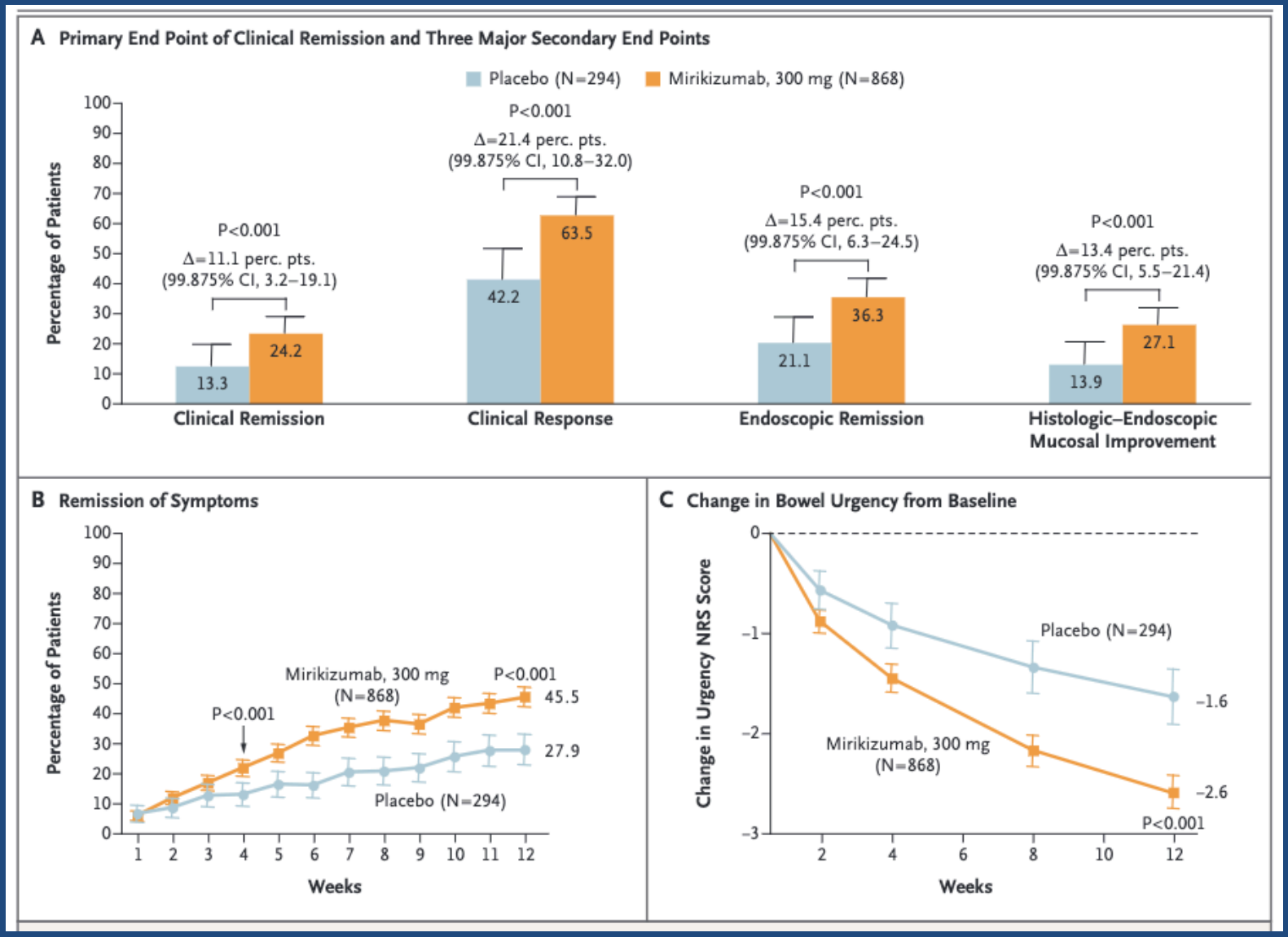
Image description

MAINTENANCE DOSING[1]

Two consecutive 100 mg subcutaneous (SC) injections (200 mg total) every 4 weeks starting at Week 12

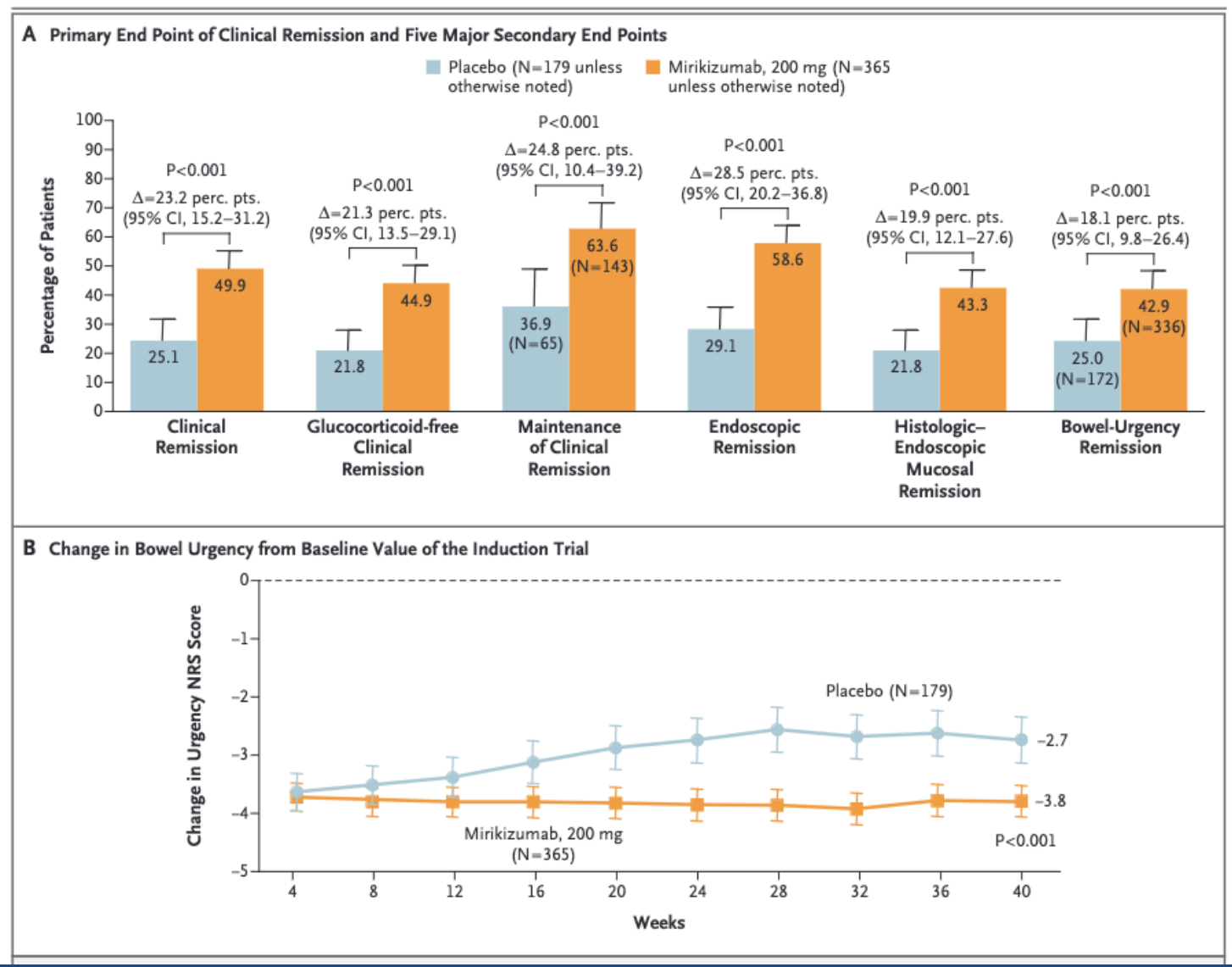
Image description

Mirikizumab



D'Haens, et al. NEJM. 2023.

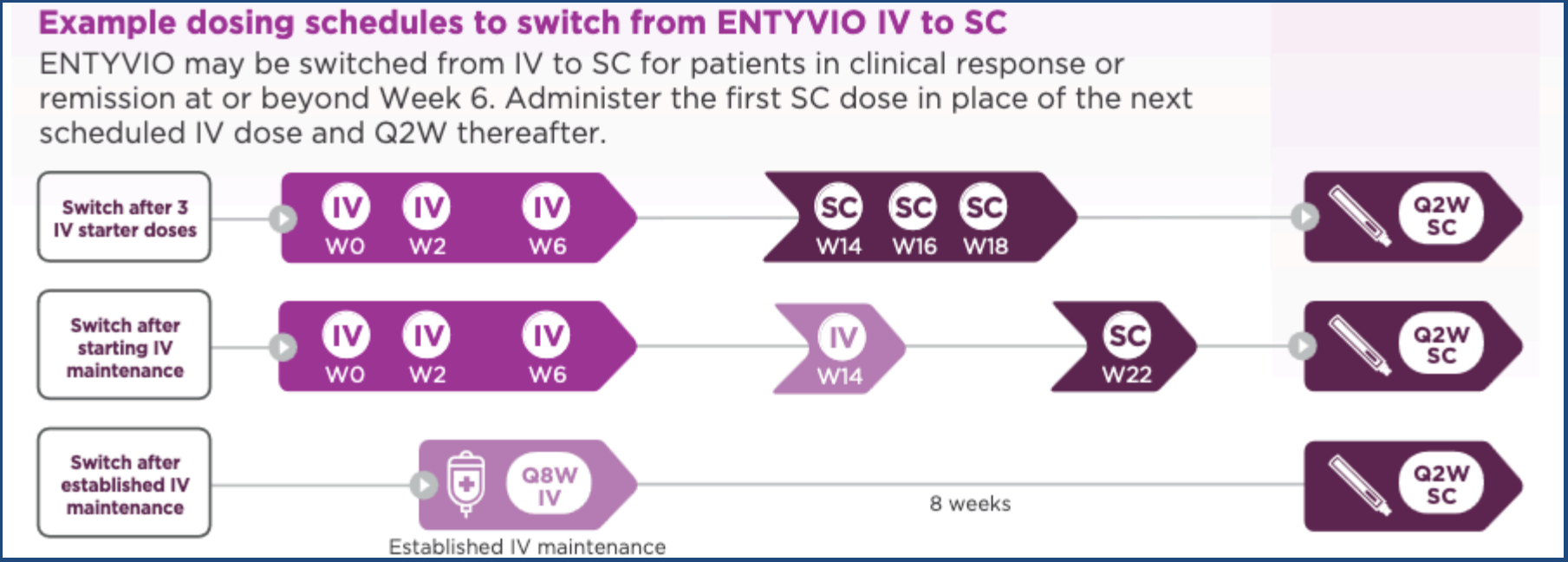
Mirikizumab



D'Haens, et al. NEJM. 2023.

Vedolizumab SubQ

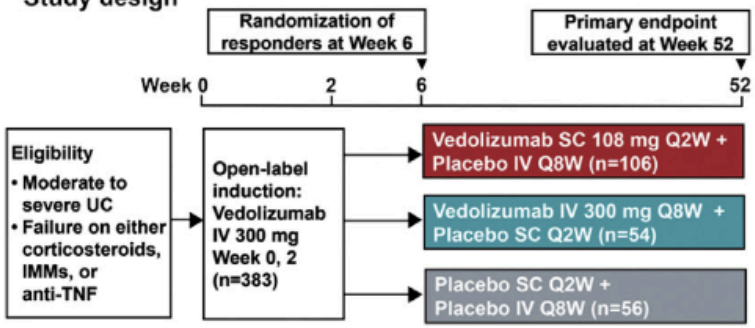
- Vedolizumab SC 108mg pen for UC only



Vedolizumab SubQ

VISIBLE 1 Trial of Vedolizumab Subcutaneous (SC) in Ulcerative Colitis

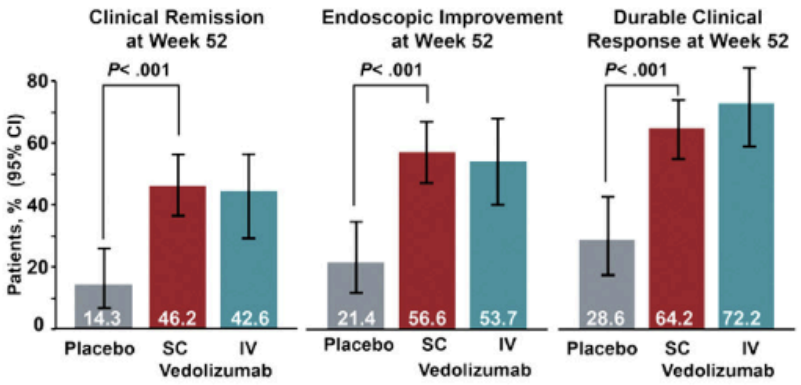
Study design



Safety / tolerability

n (%)	Placebo (N=56)	Vedolizumab SC (N=106)	Vedolizumab IV (N=54)
Adverse events	43 (76.8)	69 (65.1)	41 (75.9)
Serious adverse events	3 (5.4)	6 (5.7)	1 (1.9)
Abdominal and GI infections	5 (4.7)	2 (3.7)	1 (1.8)
Injection site adverse events	0	11 (10.4)	1 (1.9)

Efficacy



Vedolizumab SC effective as maintenance therapy in patients with moderate to severe UC after clinical response to IV induction

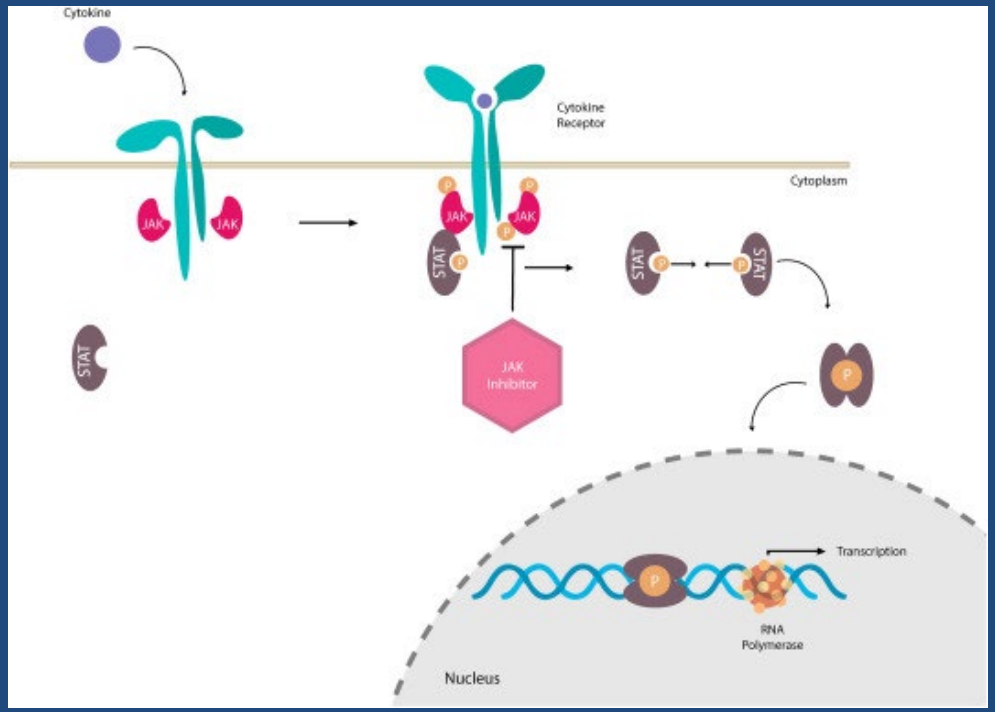
Vedolizumab SC safety / tolerability profile consistent with the well-established profile of vedolizumab IV

Gastroenterology

Sandborn, et al. Gastro. 2020.

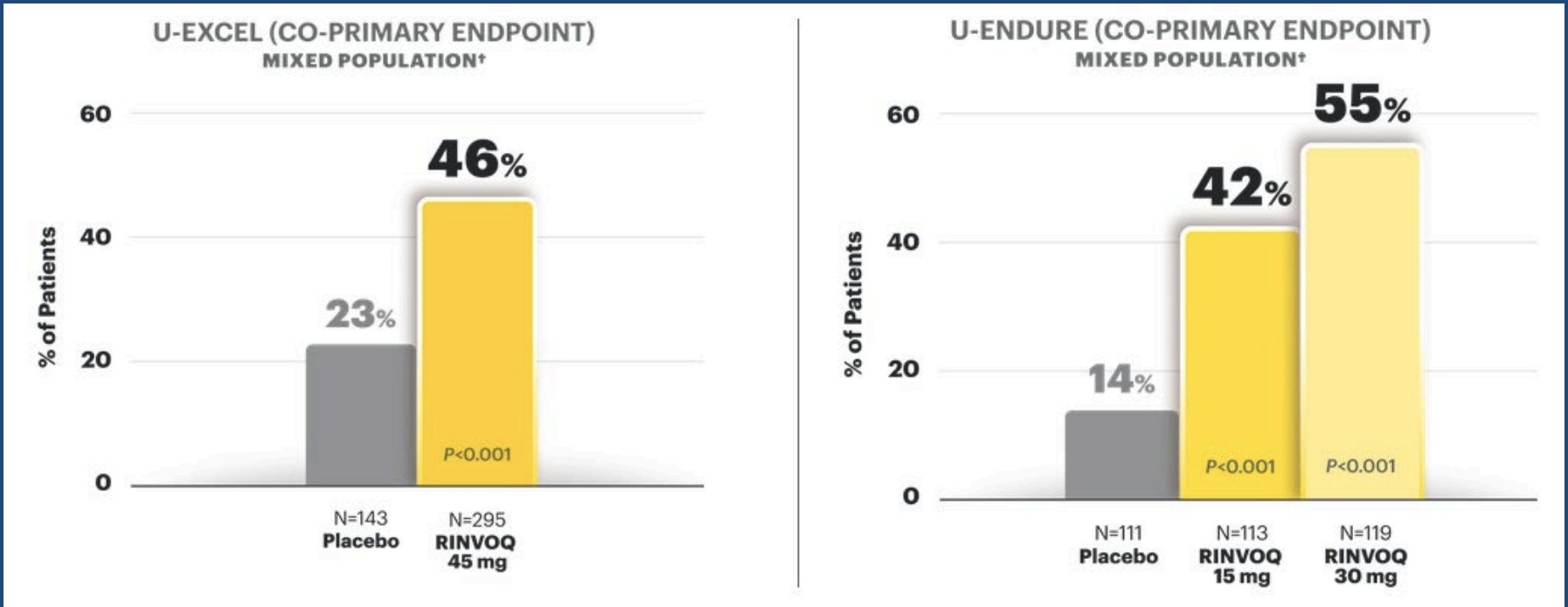
Upadacitinib

- Oral, JAK inhibitor
- Already approved for UC
- Crohn's dosing: 45mg dose x 12 weeks then 30mg or 15mg daily



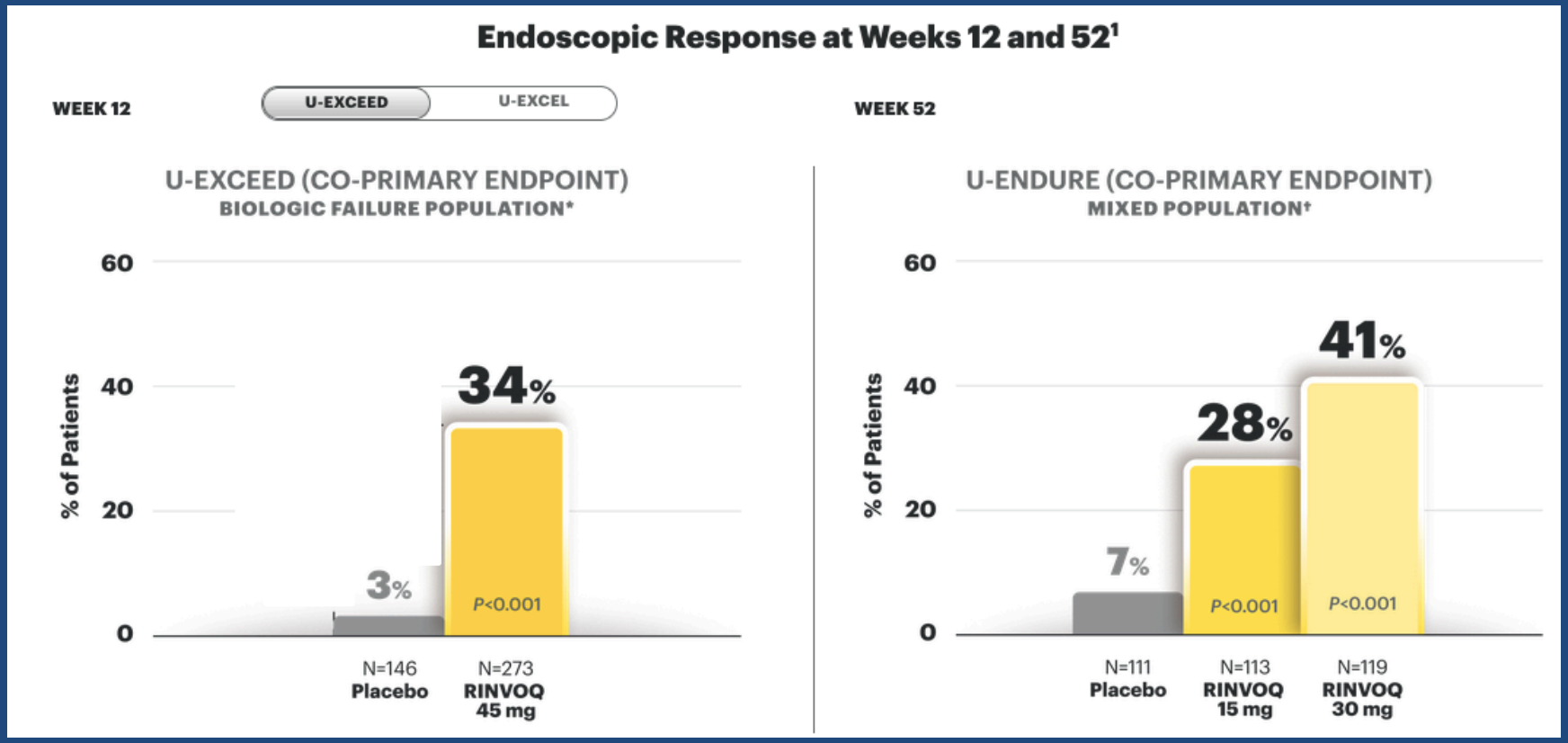
Spiewak, et al. Curr Res Pharm. 2022.

Upadacitinib



Sandborn, et al. Gastro. 2020.

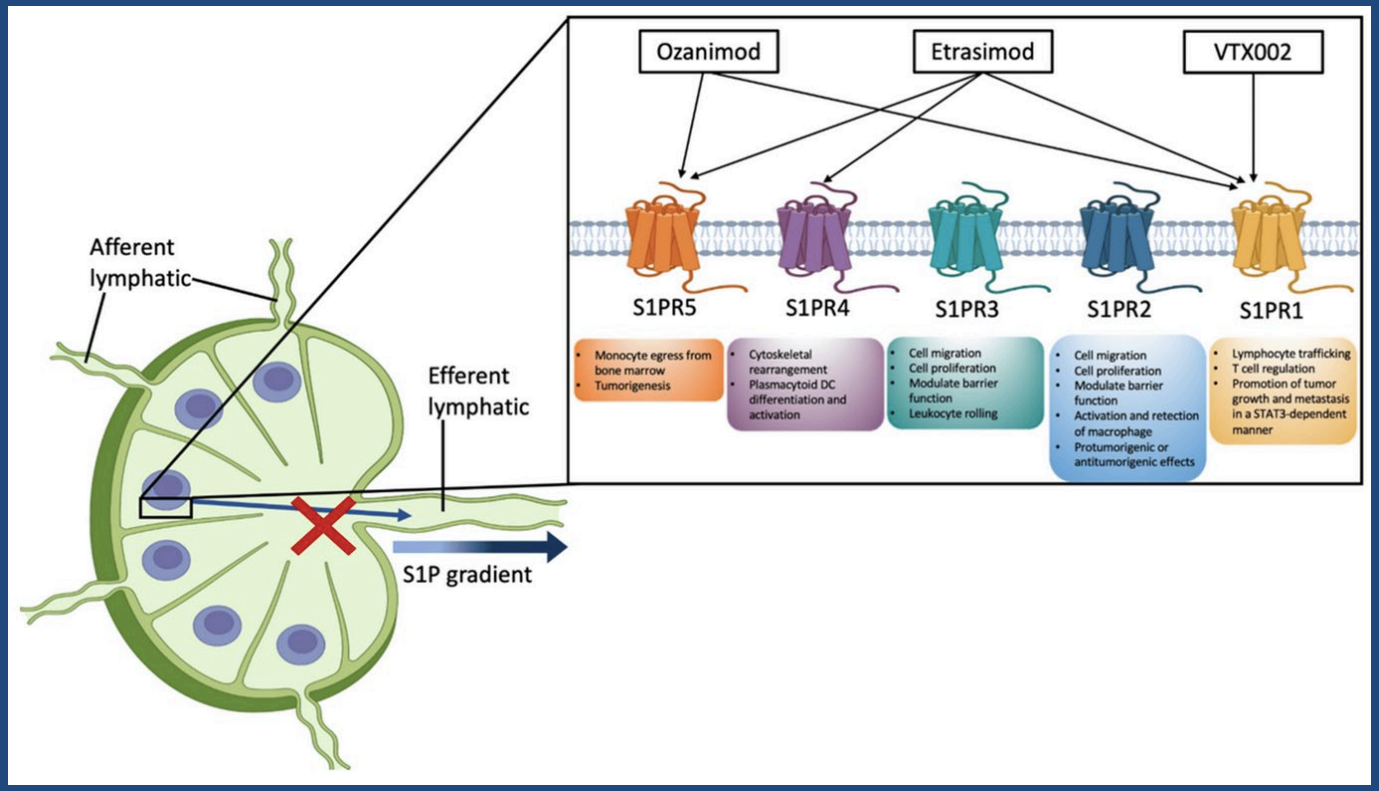
Upadacitinib



Sandborn, et al. Gastro. 2020.

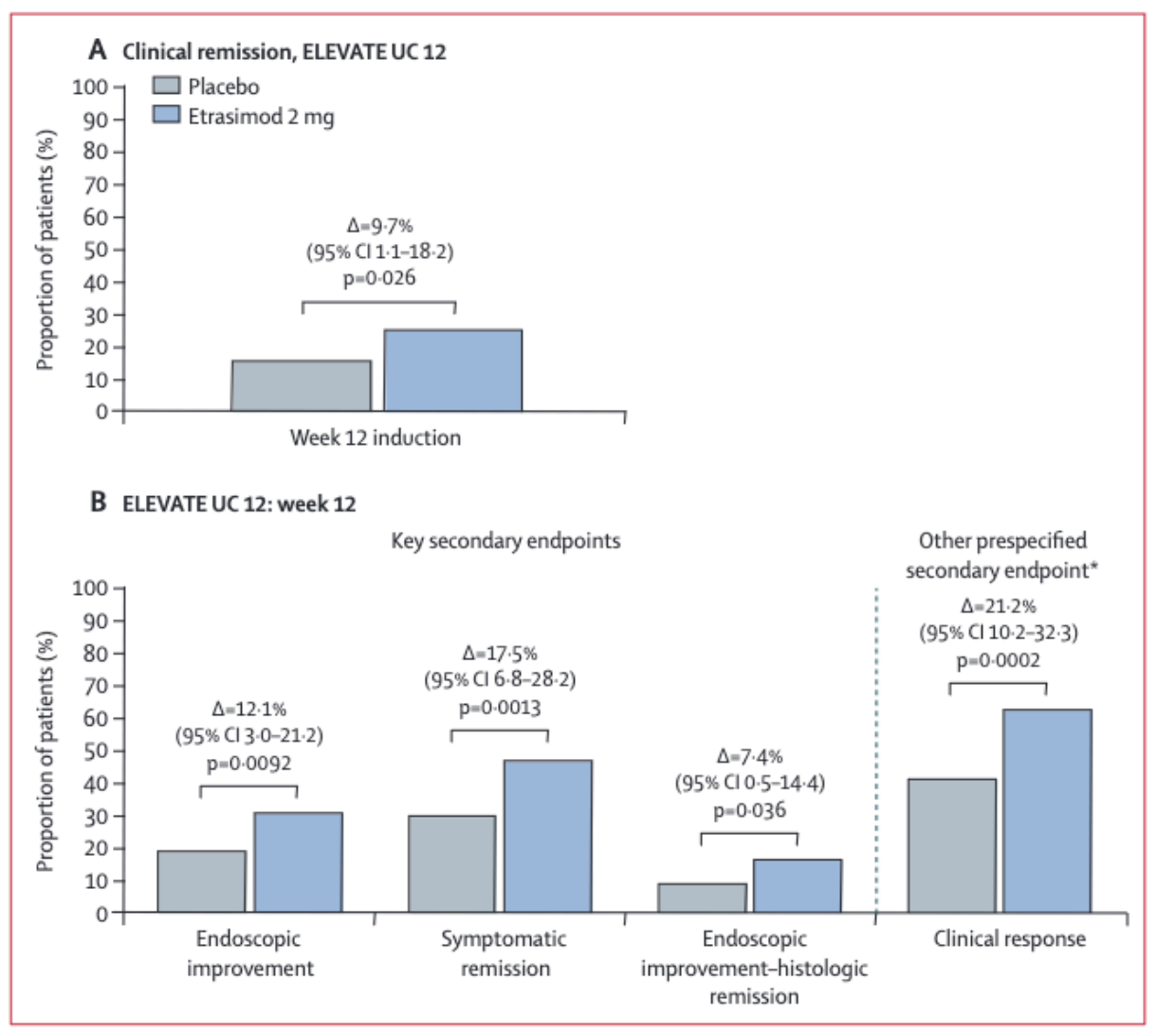
Etrasimod

- Oral, S1P modulator
- UC dosing: 2mg daily



Bencardino, et al. J Clin Med. 2023.

Etrasimod



Sandborn, et al. Lancet. 2023.

Etrasimod

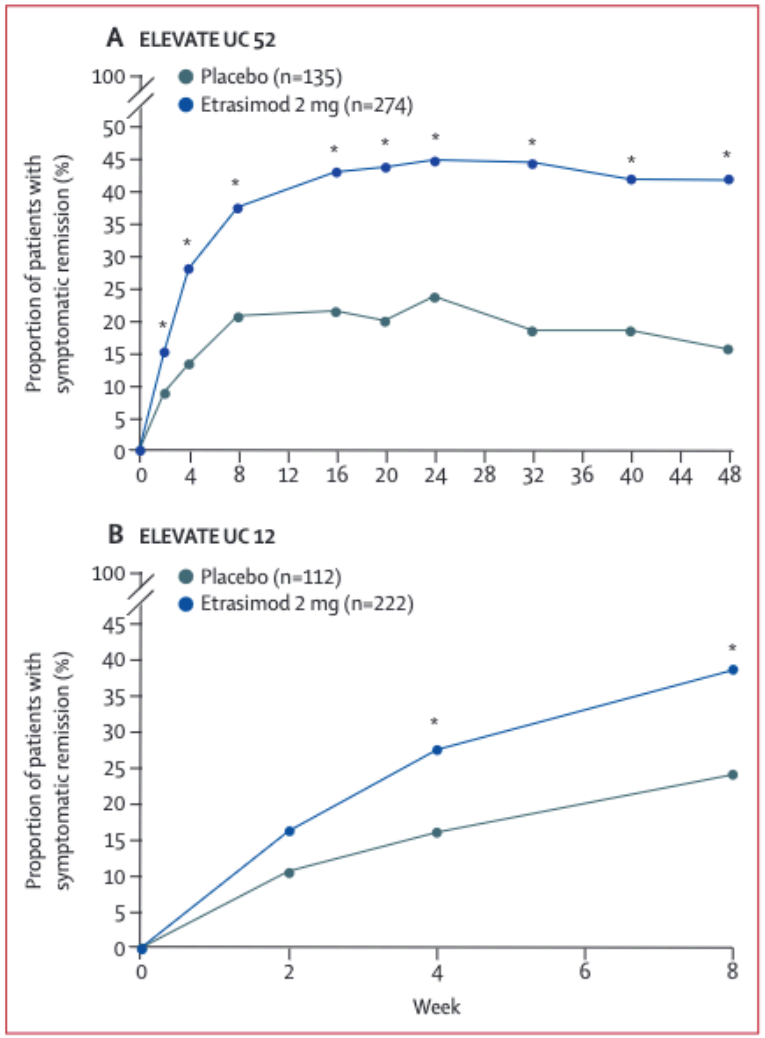


Figure 5: Symptomatic remission over time in ELEVATE UC 52 (A) and ELEVATE UC 12 (B) (non-responder imputation)

Sandborn, et al. Lancet. 2023.

So how do we pick?

What do we KNOW about efficacy?

- All approved medications are better than placebo
- One drug sponsored head-to-head trial in ulcerative colitis (*VARSITY*)
  - Standard dose adalimumab vs standard dose vedolizumab in bio-naïve patients
  - Vedolizumab was better
- One drug sponsored head-to-head trial in Crohn's disease (*SEAVUE*)
  - Standard dose adalimumab vs standard dose ustekinumab in bio-naïve patients
  - No difference in efficacy
- One drug sponsored head-to-head trial in Crohn's disease (*SEQUENCE*)
  - Standard dose risankizumab vs standard dose ustekinumab (open label)
  - Risankizumab non-inferior in clinical endpoint and superior in endoscopic endpoints

- Other observational data, network meta-analyses
- No direct comparisons of other drugs

Some factors used in making a decision

- Prior IBD history
- Assessment of IBD severity
- Efficacy
- Safety
- Mode of administration
- Concomitant medical problems
- Extraintestinal manifestations
- Insurance access

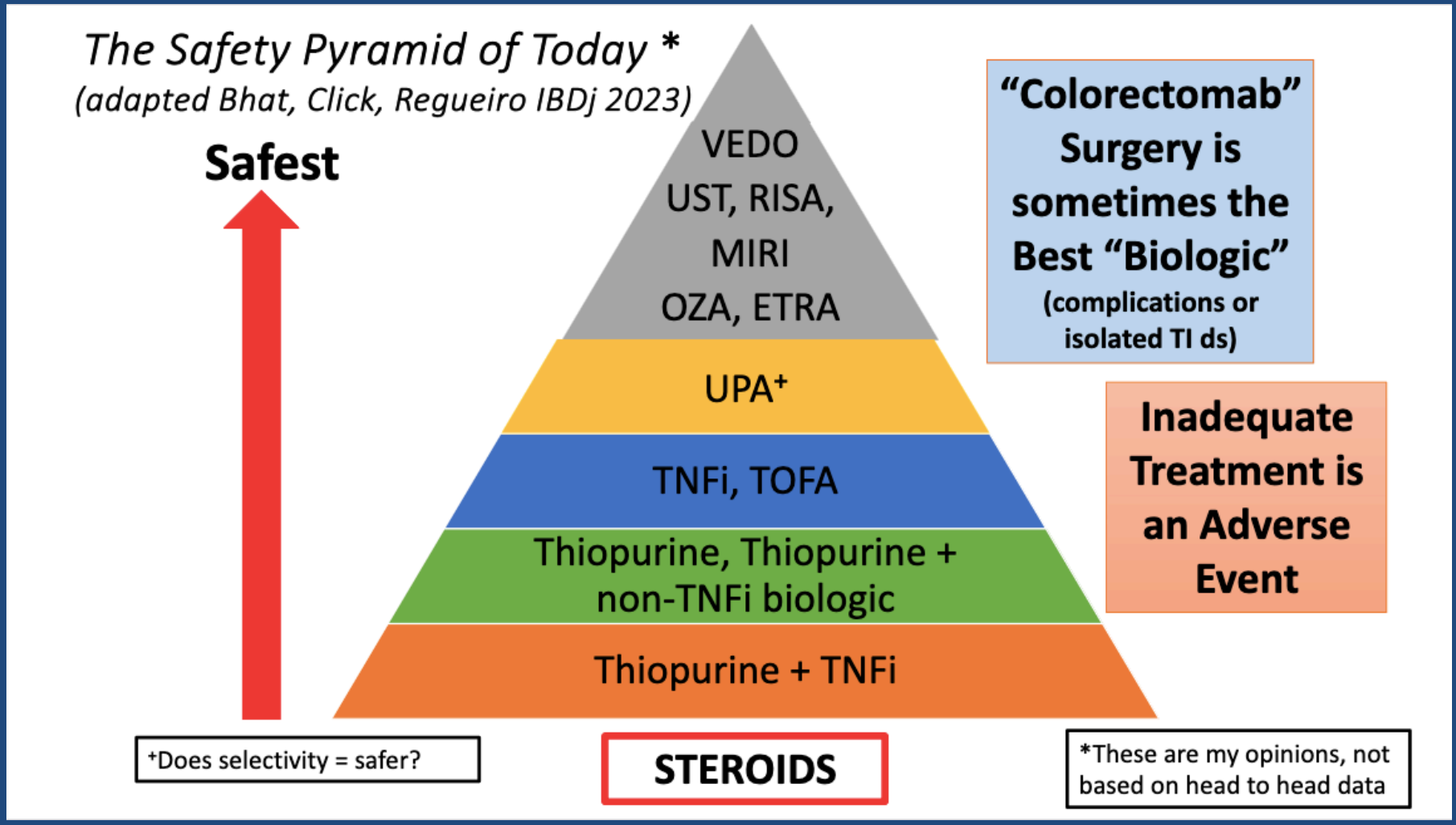
Efficacy

- Limited direct head to head data
- Increasing observational data that may or may not apply to your personal situation
- Some general guidance
  - No medication works for everyone
  - No medication works immediately (though some work faster than others)
  - First biologic/advanced therapy may be most effective
  - In the real world, many patients do not fit into the strict criteria of a clinical trial

Safety

- In general, we think the benefits of these medications outweigh the risks
- Infusion reactions, injection site reactions
- Allergic reactions
- Most advanced therapies work by suppressing the body's natural immune response
  - Increased risks of infection
  - Increased risks of cancer
- Cardiac risks
- Risks of medications need to be balanced with risks of not being on medication
- Special populations to be considered
  - Pregnancy/lactation
  - Elderly
  - Immunocompromised

Safety



Slide courtesy of Miguel Regueiro, 2024

Mode of administration

- Patients have different opinions which works best for them
- Intravenous
  - Every 8 weeks
  - Loading doses
  - Hospital infusion center, outpatient infusion center, home infusion
- Self injection
  - Every 2 weeks
  - Every 4 weeks
  - Every 8 weeks
  - Loading doses
- Oral
  - Daily or multiple times per day

Concomitant medical problems

- Medical conditions that exclude certain medications
  - Examples: heart failure, blood clots, (pregnancy)
- Medical conditions that may favor a certain medication
  - Examples: rheumatoid arthritis, psoriasis
- Immunosuppressed state
- Medical conditions that limit mode of administration
  - Examples: needle phobia, IV drug use, vision loss

Extraintestinal manifestations

- Perianal Crohn's disease
- Ankylosing spondylitis (and other rheumatologic problems)
- Pyoderma gangrenosum
- Uveitis

Insurance access

- An unfortunate reality of our healthcare system
- Often is the largest reason for choosing a medication
- Most insurers have preferred medications and formulary medications
- Often a need for appeals and extra reviews (also for off-label dosing)
- Creates additional hassles, paperwork, treatment delays
- Even with “approval”, there may be significant costs
- Pharma companies often have patient assistance programs (particularly for new therapies) but are limited to commercial insurance

Summary

- Multiple new therapies in just last year
  - Some modifications to old therapies
  - Some new mechanisms
- There is no “one size fits all” strategy for IBD medications
- Many factors to consider besides just efficacy
- Shared decision making will result in better buy-in from patients
- Caution about always prescribing the “easy” drug

Thank you!

Questions?

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