
بسم الله الرحمن الرحيم

Treatment of complicated crohn’s disease

1404/01/28. Tabriz



Dr.Daryani

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Dr.Matin



- **A 18 year obese old man has referred to your office with hx of abdominal pain and diarrhea from 1 year ago**
- **During this year he was treated as having IBS with using multiple anti spasmodic drugs**
- **.**



Abdominal picture



In the bush of IBS…



IBS, irritable bowel syndrome.
Image provided by Prof. Danese, Istituto Clinico Humanitas Milan

The long and winding road to CD diagnosis…

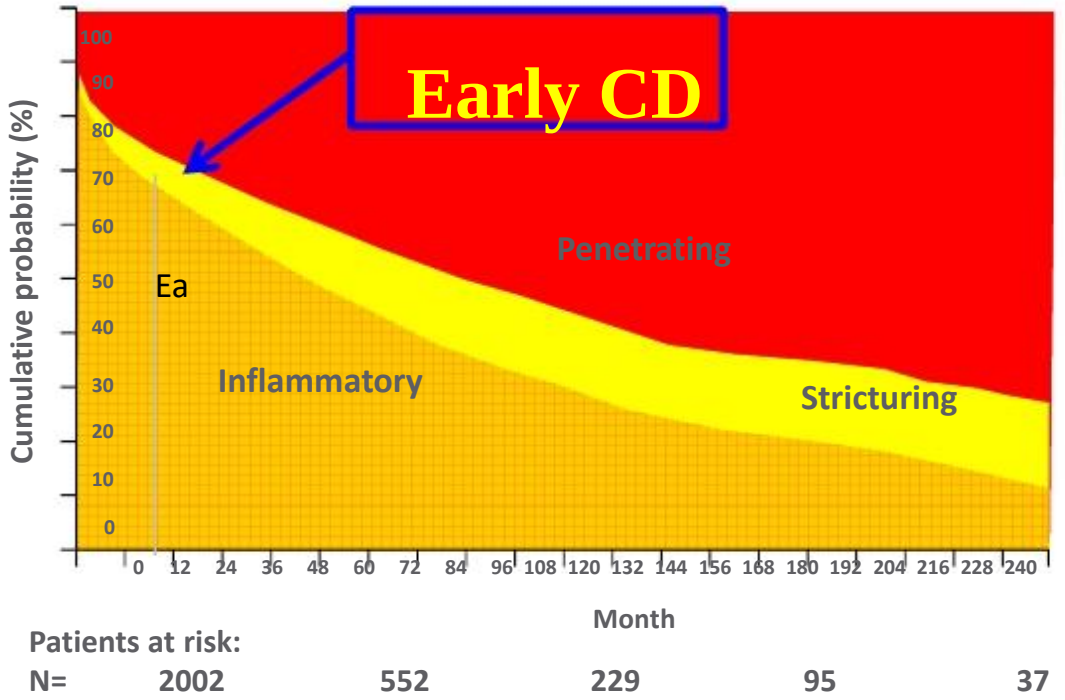


IBD, inflammatory bowel disease.
Image provided by Prof. Danese, Istituto Clinico Humanitas Milan.

Abdominal picture



The natural history of CD



CD, Crohn's disease.
Cosnes J, et al. Inflamm Bowel Dis. 2002;8:244–50.

- **weight loss 4kg up to 4mo ago, BM; non bloody intermittent diarrhea, Hb;11 MCV;71 Ferritin;30 TTG; neg Stool=A few WBC& RBS PPD; 4mm IGRA; neg HBV, HCV; neg, C-diff; neg, CRP: 43 FC:470 Albomin:3**

Colonoscopy; up to TI were seen, and multiple deep ulcerations in TI and involement of proximal area of right side colon

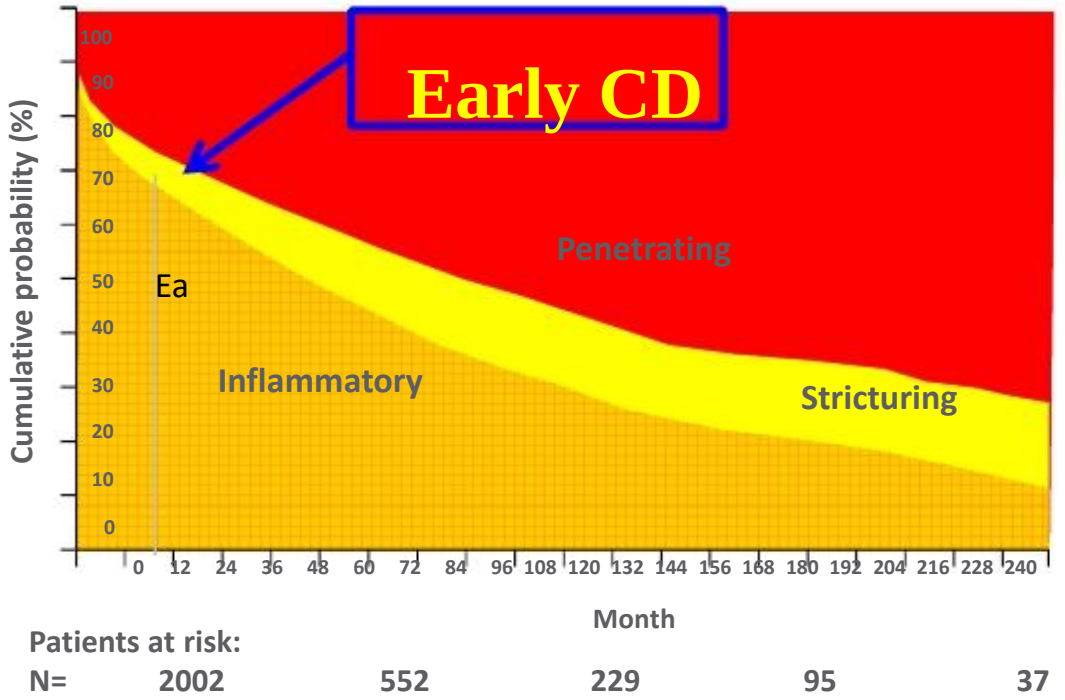
Biopsy report: inflammation and a few granuloma



Abdominal picture



The natural history of CD



CD, Crohn's disease.
Cosnes J, et al. Inflamm Bowel Dis. 2002;8:244–50.

Penetrating disease

Increased risk for surgery and increased surgical risk (compared to inflammatory/obstructive phenotypes)

- 170% increased risk of hospitalization
- 380% increased risk of surgery within 5 years

Burisch-*Gut* 2019

Which of finding in this patient showed severe crohn’s dis.?

- **A 18 year obese old man has referred to your office with hx of abdominal pain and diarrhea from 1 year ago**
- **During this year he was treated as having IBS with using multiple anti spasmodic drugs**
- **With history of drainage periumblical abscess and under antibiotic treatment from afew weeks ago.**

- weight loss 4kg up to 4mo ago, BM; non bloody intermittent diarrhea, Hb;11 MCV;71 Ferritin;30 TTG; neg Stool=A few WBC& RBS PPD; 4mm IGRA; neg HBV, HCV; neg, C-diff; neg, CRP; 43 FC; 470 Albomin:3

Colonoscopy; up to TI were seen, normal colonic mucosa,

and multiple deep ulcerations in TI were seen and involevment of proximal area of right side colon

Biopsy report: inflammation and a few granuloma

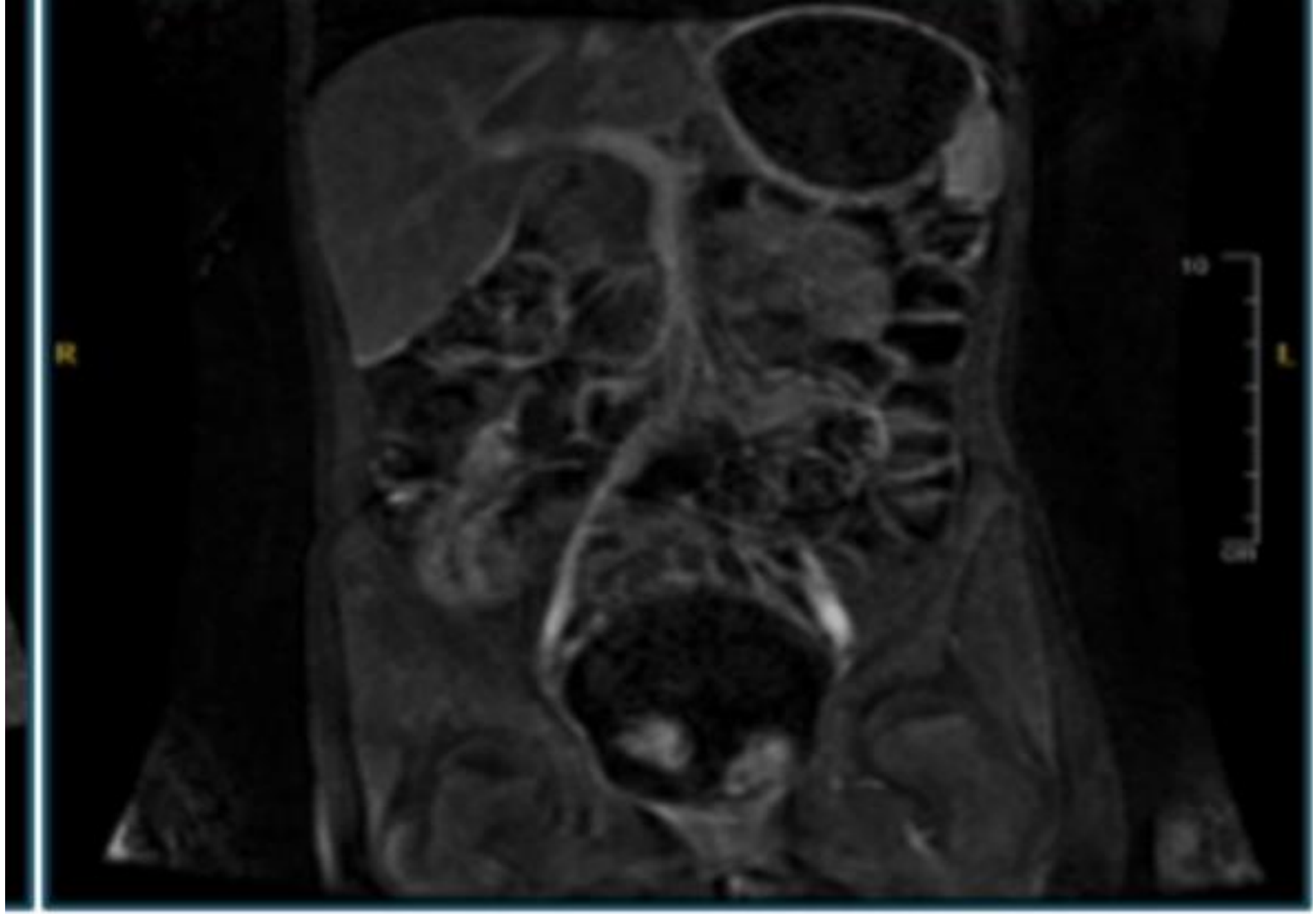
Defining severe Crohn's disease

	Severe Crohn's disease
Structural Damage	• **Large or deep mucosal lesions** • **Fistula and/or perianal abscess** • **Prior intestinal resections, particularly of segments >40cm** • Presence of strictures
Inflammatory burden	• **Extensive disease (ileal involvement >40cm or pancolitis)** • Elevated C-reactive protein • Low albumin
Impact on quality of life	• **Presence of stoma** • **>10 loose stools/week** • **Lack of symptomatic improvement with prior exposure to biologics and/or immunosuppressive agents** • Significant impact of disease on activities of daily living • Presence of anorectal symptoms (anorectal pain, bowel urgency, incontinence, discharge, tenesmus) • Anemia • Daily abdominal pain • Corticosteroid use within last 1 year

Crohn's Disease
• Early age at diagnosis (< 30)
• Extensive anatomic involvement
• Perianal and/or severe rectal disease
• Deep ulcers
• Prior surgical resection
• Strictures and/or penetrating behavior

What is your next step for this patient?

MRE showed involvement of distal area of terminal ileum and ascending colon with active inflammation and ileo-cutaneous fistula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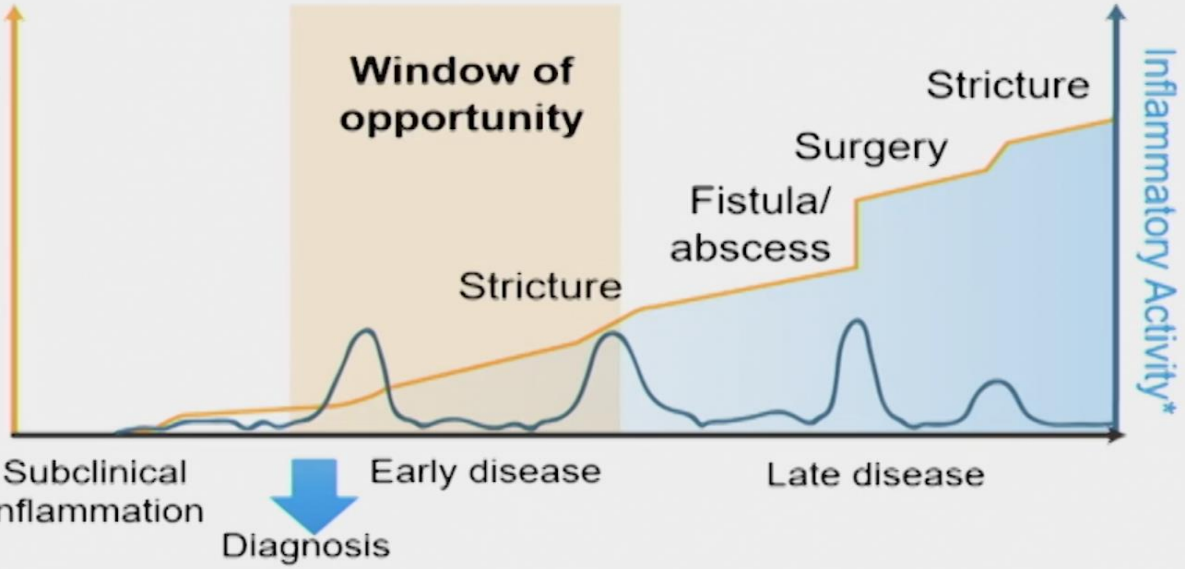
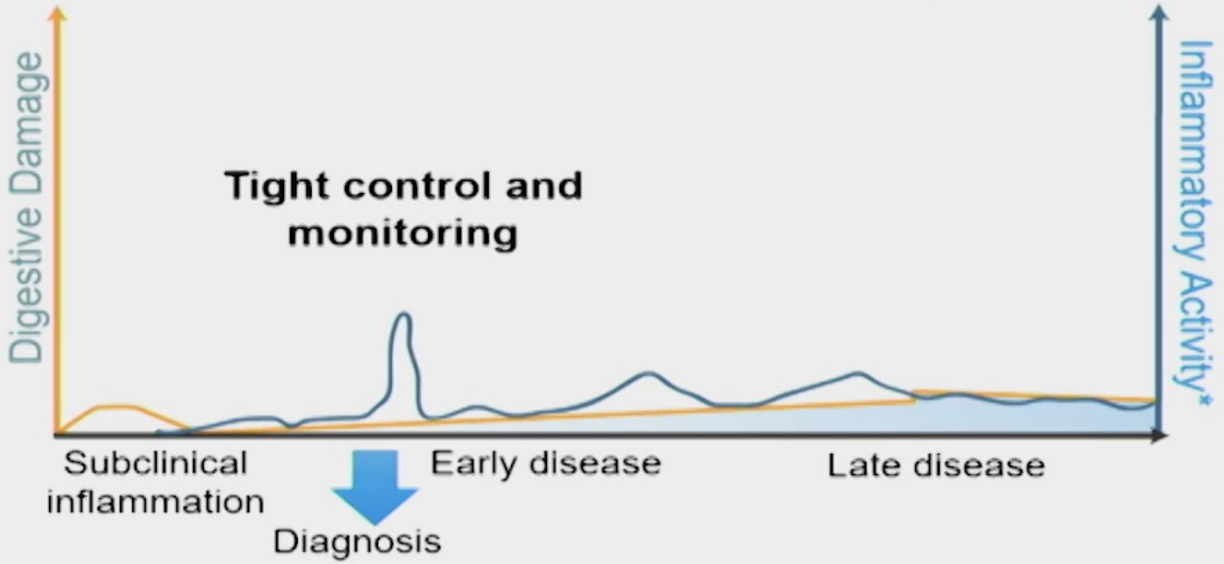
- **Why it is important to start early treatme for crohn’s disease?**

Why Is Early Treatment Important in CD?

Natural Course of Crohn Disease



Theoretical Impact of Early Effective Treatment on Disease Progression



Similar principles hypothesized in UC, but not as clear

Colombel JF et al. *Gastroenterology*. 2017;152(2):351-361.
Pariente B et al. *Inflamm Bowel Dis*. 2011;17(6):1415-1422.

Early Infliximab/IMM Treatment Achieves Better Outcomes Than "Accelerated Step-Up" Strategy in CD, Not Biomarker Risk Status: PROFILE Study

Background: Management strategies and clinical outcomes vary substantially in patients newly diagnosed with CD

Methods

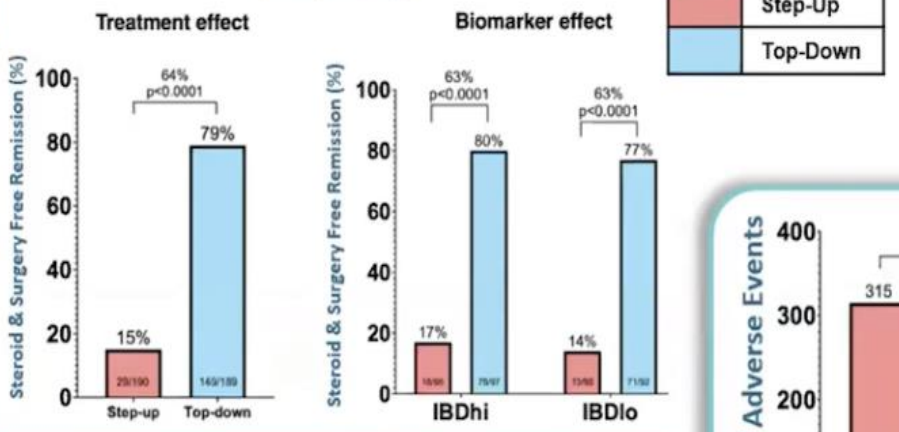
PRedicting Outcomes For Crohn's dIsease using a moLecular biomarkEr (PROFILE)

- Open-label, biomarker-stratified, randomized controlled trial in newly-diagnosed active CD
- HBI ≥7, FC ≥200 and/or CRP >ULN & Endoscopic activity: SES-CD ≥6 or SES-CD ≥4 if ileal-only
- Patients were stratified by a biomarker, validated in prospective studies, to IBDhi or IBDlo and then randomized to early combination or "accelerated step-up" treatment (infliximab+thiopurine)

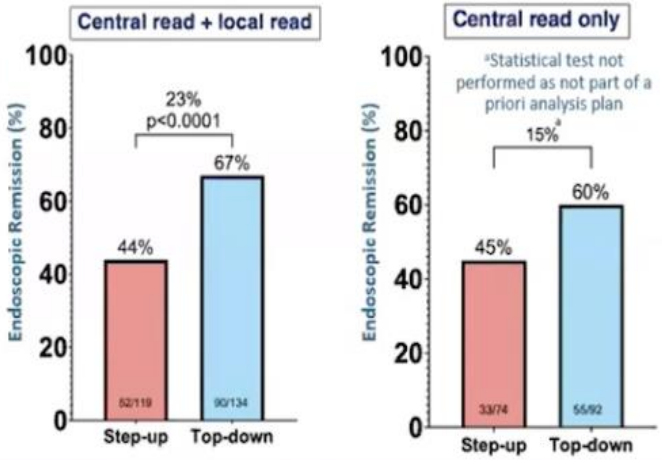
Results

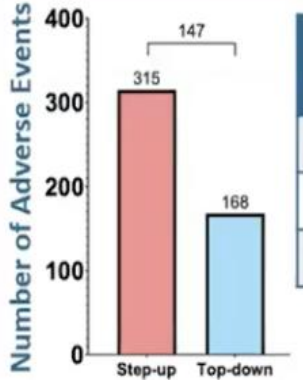
Variable	IBDlo Step Up	IBDhi Step Up
Mean HBI (SD)	9.6 (3.1)	10.0 (2.8)
Median CRP (mg/L; IQR)	10 (4-27)	13 (4-19)
Median FCAL (ug/g; IQR)	600 (249->1800)	905 (396->1800)
Median SES-CD (IQR)	9 (7-13)	9 (7-14)
Median time from diagnosis to enrollment (days; Range)	13.0 (0-138)	17.5 (0-191)

Sustained Steroid-free & Surgery-free Remission
(Primary Endpoint)



Wk48 Endoscopic Remission
(Absence of Ulcers)





Adverse Events	Step Up (N=193)	Top-down (N=193)
Crohn's Flare	225	30
Infection	20	23
Surgery	10*	1**

*indication for surgery was CD
**indication for surgery was gallstone ileus

Conclusion: Very early use of combination treatment with infliximab+thiopurine, irrespective of biomarker risk status, achieved substantially better outcomes compared to "accelerated step-up" therapy

How do you treat this patient with moderat to severe patern and what is important for tratment option?

CLINICAL PRACTICE GUIDELINES

AGA Clinical Practice Guidelines on the Medical Management of Moderate to Severe Luminal and Perianal Fistulizing Crohn's Disease

Gastroenterology 2021;160:2496–2508

A. In adult outpatients with moderate to severe CD, who are *naïve to biologics* the AGA
Recommends the use of infliximab, adalimumab or ustekinumab over certolizumab pegol (Strong recommendation, moderate certainty of evidence)
Suggests the use of vedolizumab over certolizumab pegol (Conditional recommendation, low certainty of evidence)

Ustekinumab vs Infliximab in Crohn's Disease

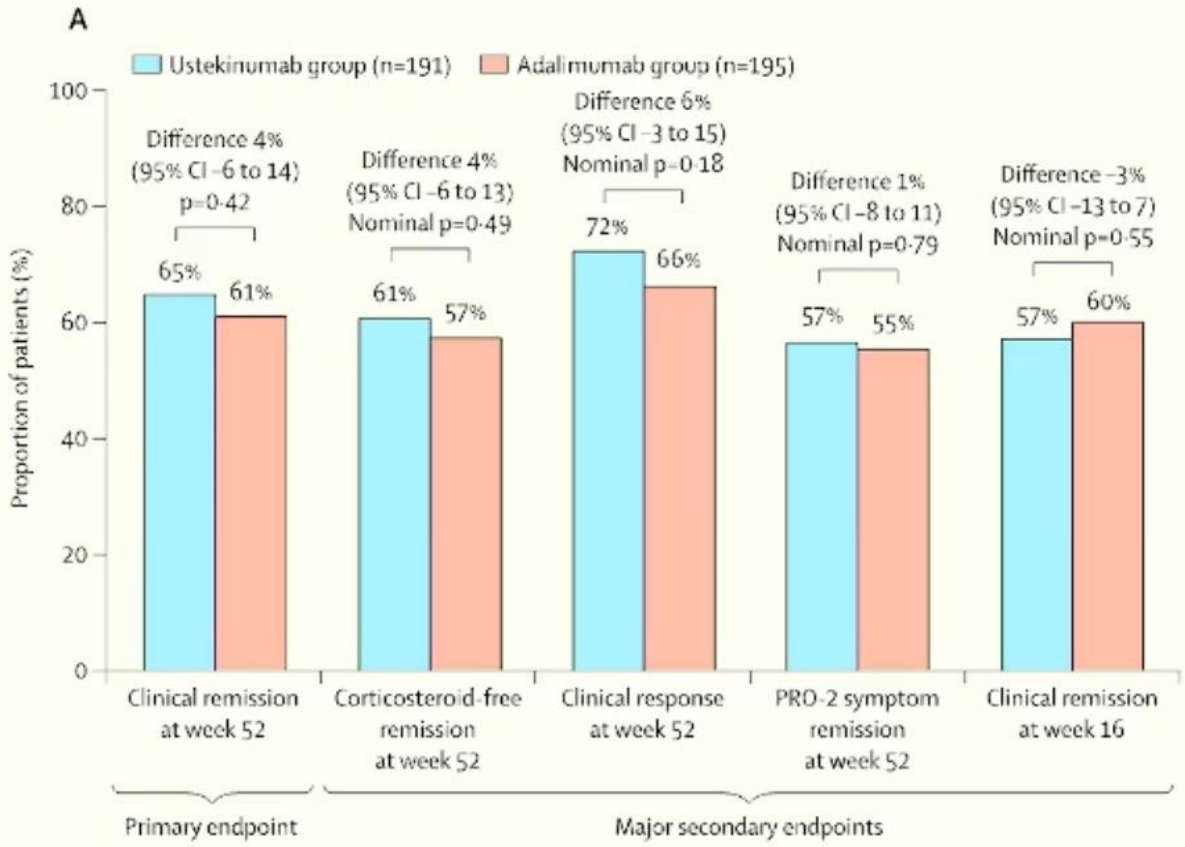
- Post-hoc propensity score matched comparison of pivotal CD trial programs
- 420 biologic naïve CD treated with UST (n=206) or IFX (n=214)
- Week 6 clinical remission: 37.9% vs 44.9%; aOR 1.22, 95% CI 0.79-1.89
- Week 6 clinical response: 54.9% vs 58.4%; aOR 1.25, 95% CI 0.82-1.90
- Week 6 Fcal < 250 ug/g: 34.7% vs 42.3%; aOR 1.34, 95% CI 0.79-2.28
- Ustekinumab and infliximab have similar efficacy in biologic naïve CD

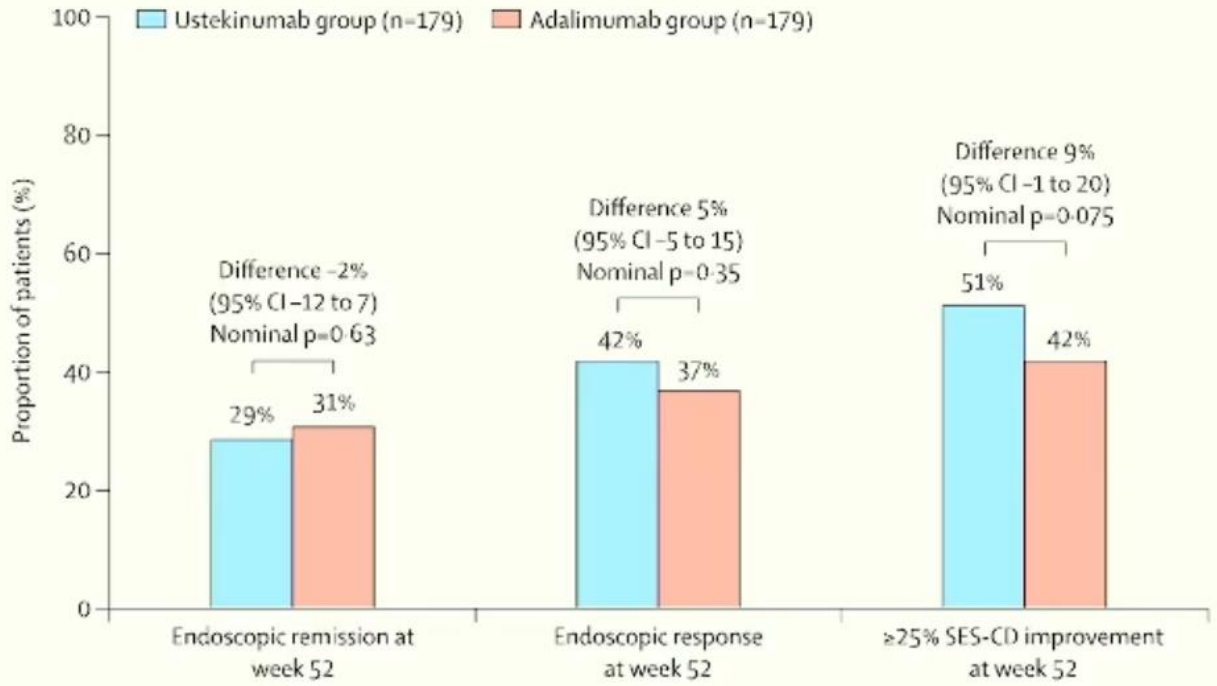
aOR = adjusted odds ratio; Fcal = fecal calprotectin; IFX = infliximab; UST = ustekinumab.
Narula N, et al. *Clin Gastroenterol Hepatol*. 2022;20(7):1579-1597.e.2.

IBD summit FOR FELLOWS

Ustekinumab versus adalimumab for induction and maintenance therapy in biologic-naive patients with moderately to severely active Crohn's disease: a multicentre, randomised, double-blind, parallel-group, phase 3b trial

*Bruce E Sands, Peter M Irving, Timothy Hoops, James L Izanec, Long-Long Gao, Christopher Gasink, Andrew Greenspan, Matthieu Allez, Silvio Danese, Stephen B Hanauer, Vipul Jairath, Tanja Kuehbacher, James D Lewis, Edward V Loftus Jr, Emese Mihaly, Remo Panaccione, Ellen Scherl, Oksana B Shchukina, William J Sandborn, on behalf of the SEAVUE Study Group**





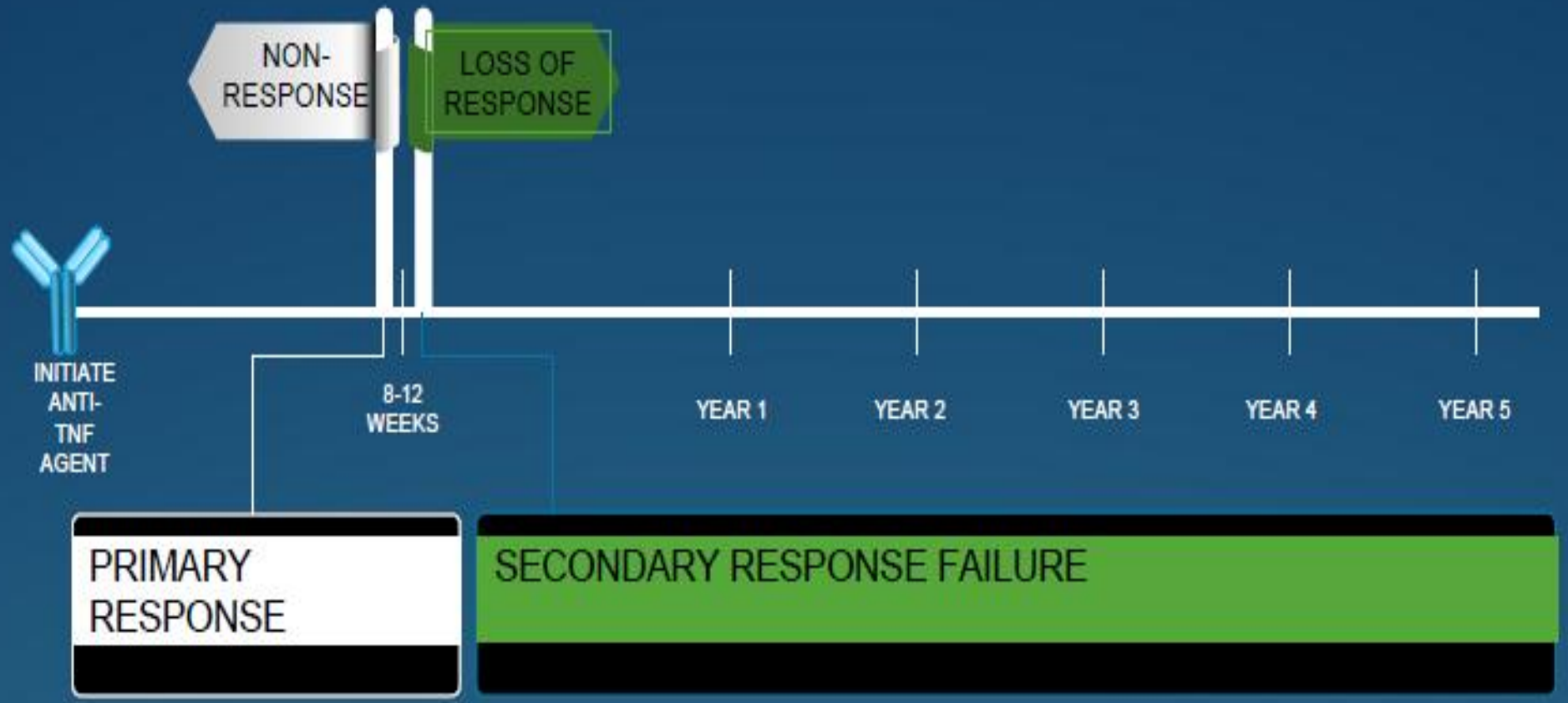
Only **monotherapy** with ADA and UST

Sands, et al. Lancet 2022

We started treatment with Remicade and AZT

How many percen of these patients dosen’t respond to anti –TNF.
What is the meaning of primary & secondary non-responder?

Loss of Response to IBD Medications

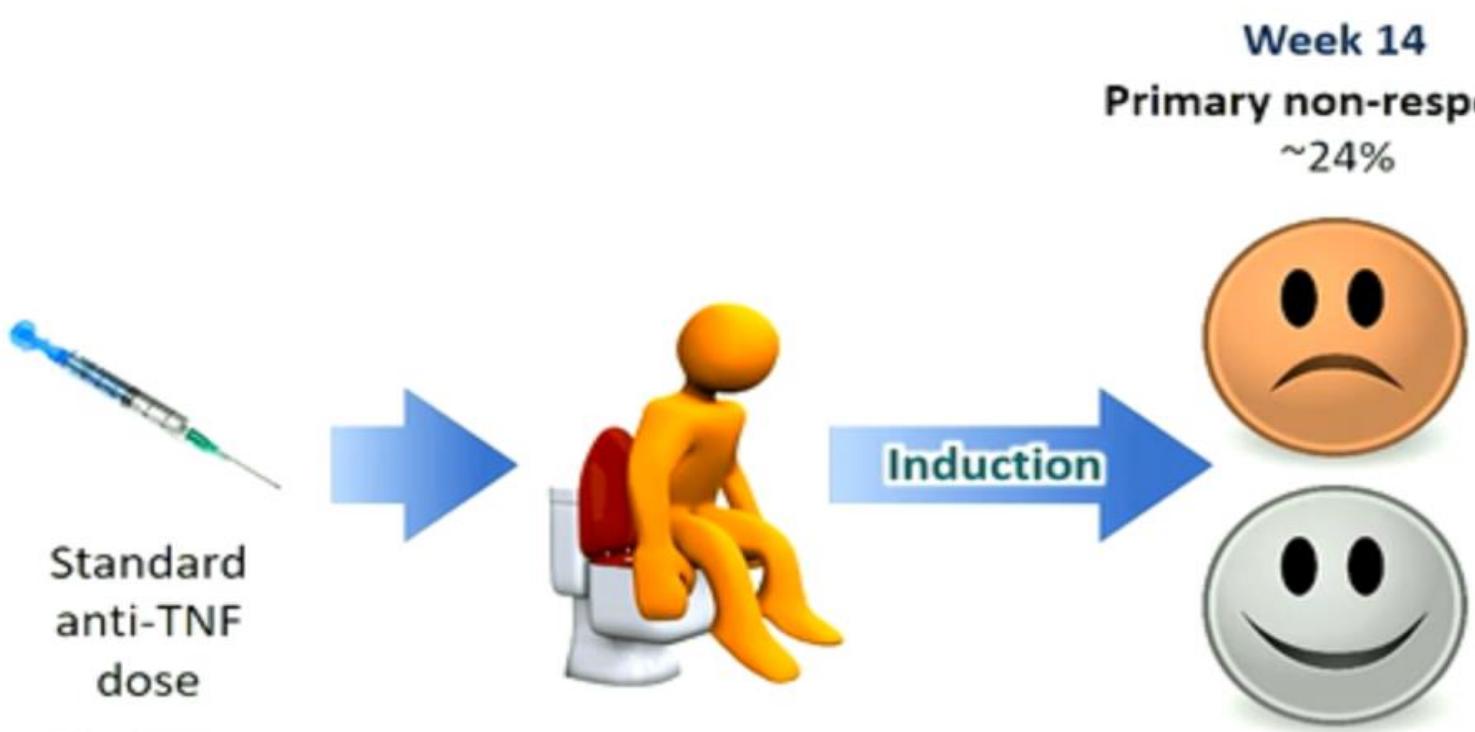


Is there still a place for anti-TNF in 2020?

Anti TNF failure is common in routine clinical practice

Data from 1610 prospective anti-TNF naïve Crohn's patients: UK PANTS study





Is there still a place for anti-TNF in 2020?

Anti TNF failure is common in routine clinical practice



Data from 1610 prospective anti-TNF naïve Crohn's patients: UK PANTS study



Standard anti-TNF dose



Induction

Week 14

Primary non-response

~24%





Maintenance

Week 54

Non-remission

~63%



Loss of response

~35%

Primary Non Response

Failure of CRP to decrease by 50% or to ≤3 mg/L **AND** HBI to fall by 3 points or to ≤4

OR Exit for treatment failure before week 14

OR Failure to completely taper corticosteroids?

Kennedy, et al. *Lancet Gastro Hepatology*. 2019:S2468-1253(19)30012-3.

LIMITATIONS OF CURRENT IBD TREATMENTS

- **~66%** of patients with IBD experience primary or secondary failure to TNF inhibitors[1,2]
  - Development of antibodies against anti-TNF therapies
  - Incidence of primary nonresponse in clinical practice: 13% to 30%
- Secondary nonresponse is a loss of response[2,3]
  - Dose intensification required (23% to 46% [after 12 weeks])
  - Drug discontinuation (5%-13%)
  - Relapse after discontinuation of anti-TNF therapy (28% in UC at 12 months)
- Substantial proportion of patients still require surgery[4]
- AEs, risk of malignancies and infection, mode of administration, IV dosing[5,6]

1. Boland BS, Vermeire S. *Gastroenterol Clin North Am*. 2017;46(3):627-644. 2. Roda G, et al. *Clin Transl Gastroenterol*. 2016;7(1):e135.
3. Gisbert JP, et al. *Am J Gastroenterol*. 2016;111(5):632-647. 4. Sica GS, Biancone L. *World J Gastroenterol*. 2013;19(16):2445-2448.
5. US National Library of Medicine. Infliximab package insert. Updated October 11, 2021. Accessed October 20, 2021. https://dailymed.nlm.nih.gov/dailymed
6. Feuerstein JD, et al. *Gastroenterology*. 2020;158(5):1450-1461.

Abbreviation: AE, adverse effect.

Which factors affecting for non-respond to anti-TNF

Factors Affecting the Pharmacokinetics of Monoclonal Antibodies (Mostly Anti-TNF)

	Impact on Pharmacokinetics	Drug Levels (Exposure)
Presence of ADAs	• Decreases serum mAbs • Threefold-increased clearance • Worse clinical outcomes	↓
Concomitant use of IS	• Reduces formation • Increases serum mAbs • Decreases mAb clearance • Better clinical outcomes	↑
High baseline TNF-α	• May decrease mAbs by increasing clearance	↓
Low albumin	• Increases clearance • Worse clinical outcomes	↓
High baseline CRP	• Increases clearance	↓
Body size	• High BMI may increase clearance	↓
Male Sex	• Men have higher clearance	↓

Ordas I, et al. *Clin Pharmacol Ther*. 2012;91:635.

What is the guide line of AGA for treatment of outpatient with moderate to severe crohn’s dis.

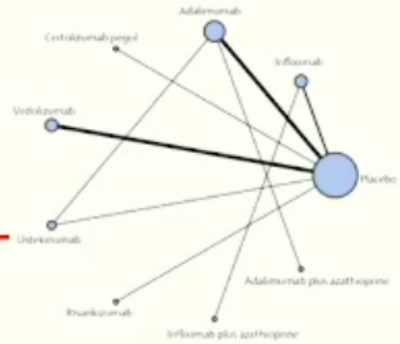
B. In adult outpatients with moderate to severe CD, who have never responded to TNFa antagonists (primary non-response), the AGA
Recommends the use of ustekinumab (Strong recommendation, moderate certainty of evidence)
Suggests the use of vedolizumab (Conditional recommendation, low certainty of evidence)

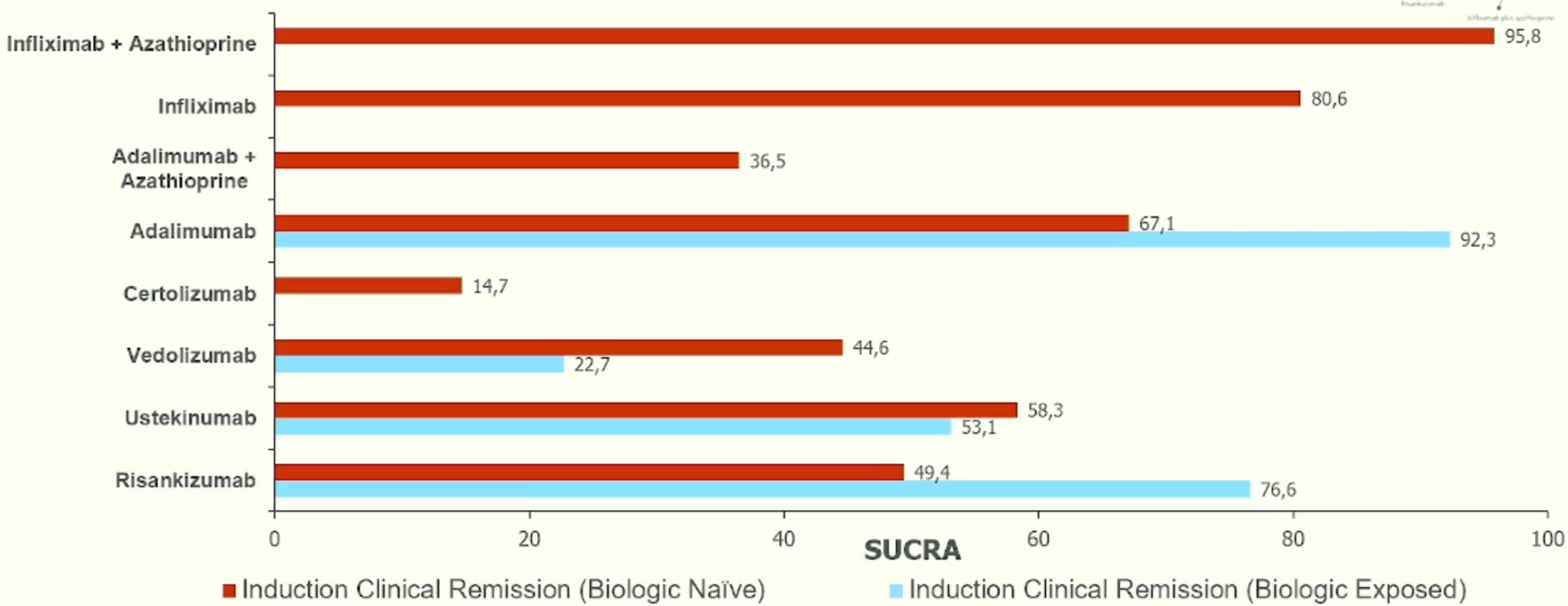
C. In adult outpatients with moderate to severe CD, who have previously responded to infliximab (secondary non-response), the AGA
Recommends the use of adalimumab or ustekinumab (Strong recommendation, moderate certainty of evidence)

Comparative efficacy and safety of biologic therapies for moderate-to-severe Crohn's disease: a systematic review and network meta-analysis

Siddharth Singh, M Hassan Murad, Mathurin Fumery, Rocio Sedano, Vipul Jairath, Remo Panaccione, William J Sandborn, Christopher Ma

Lancet Gastroenterol Hepatol
2021





Singh, …, Ma. *Lancet Gastroenterol Hepatol* 2021

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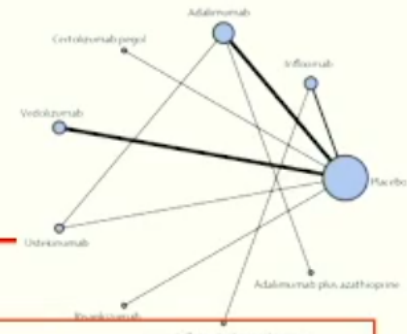

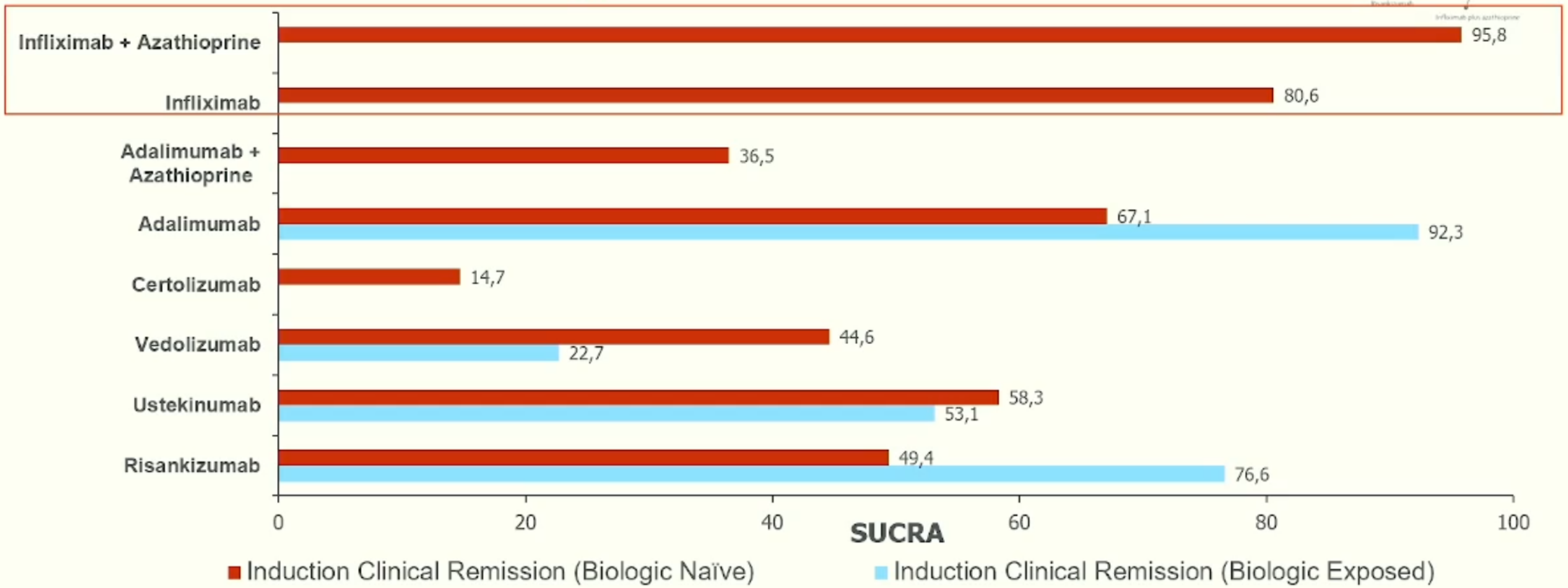

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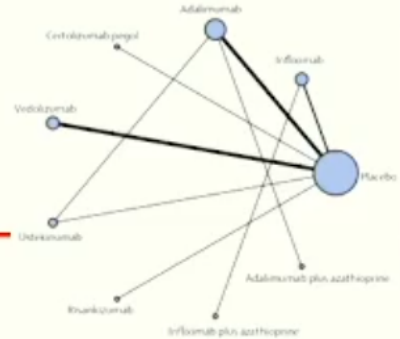
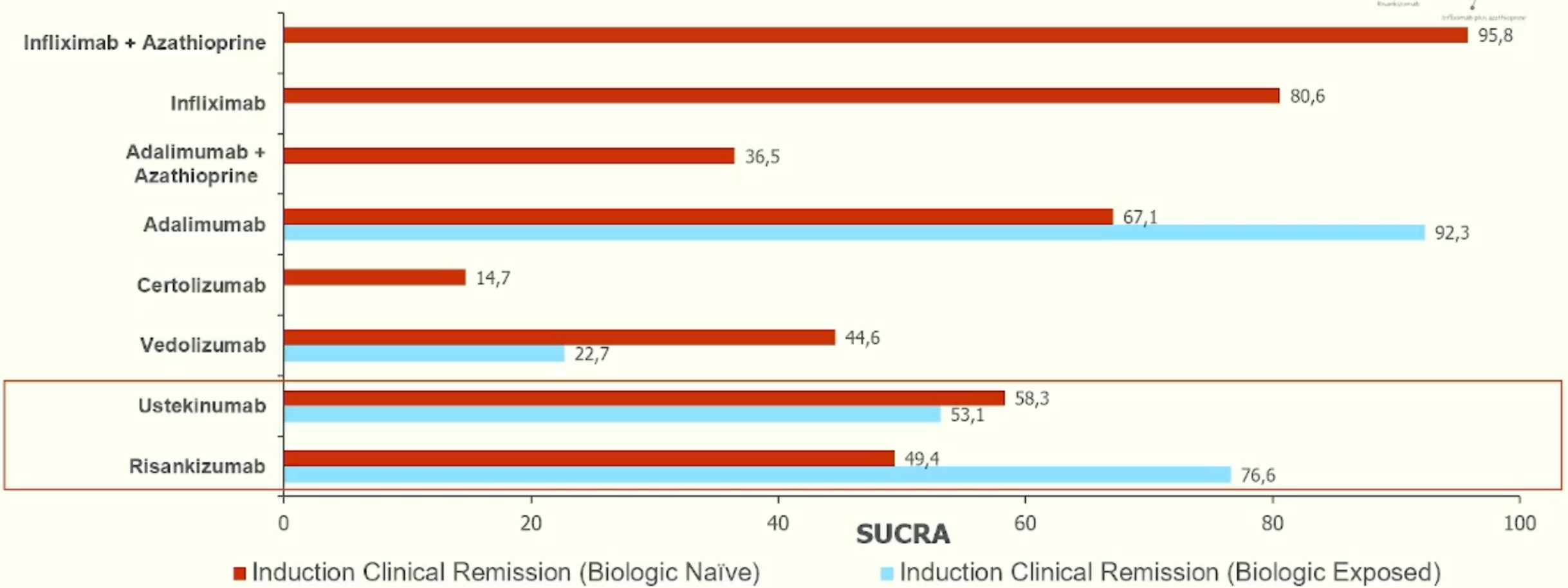
2021

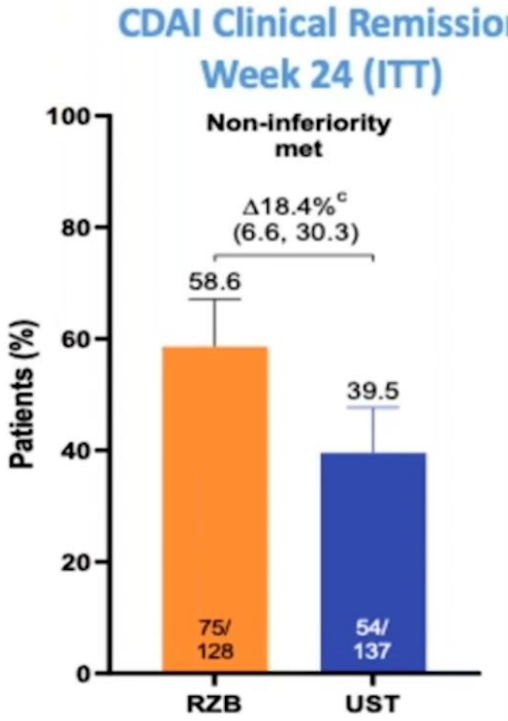


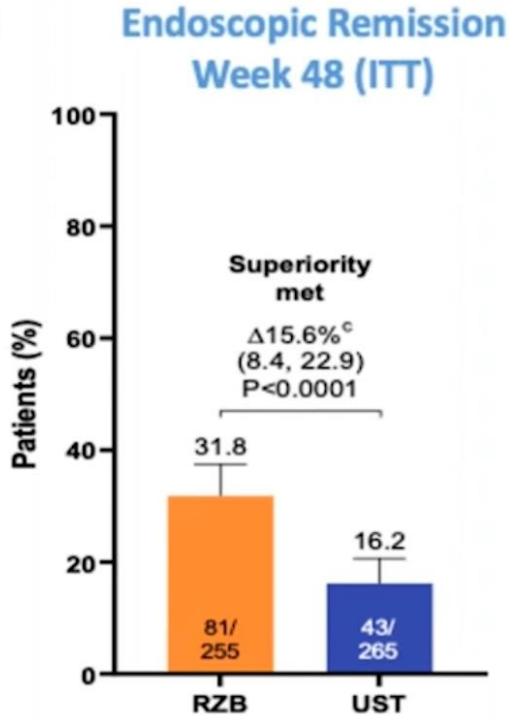


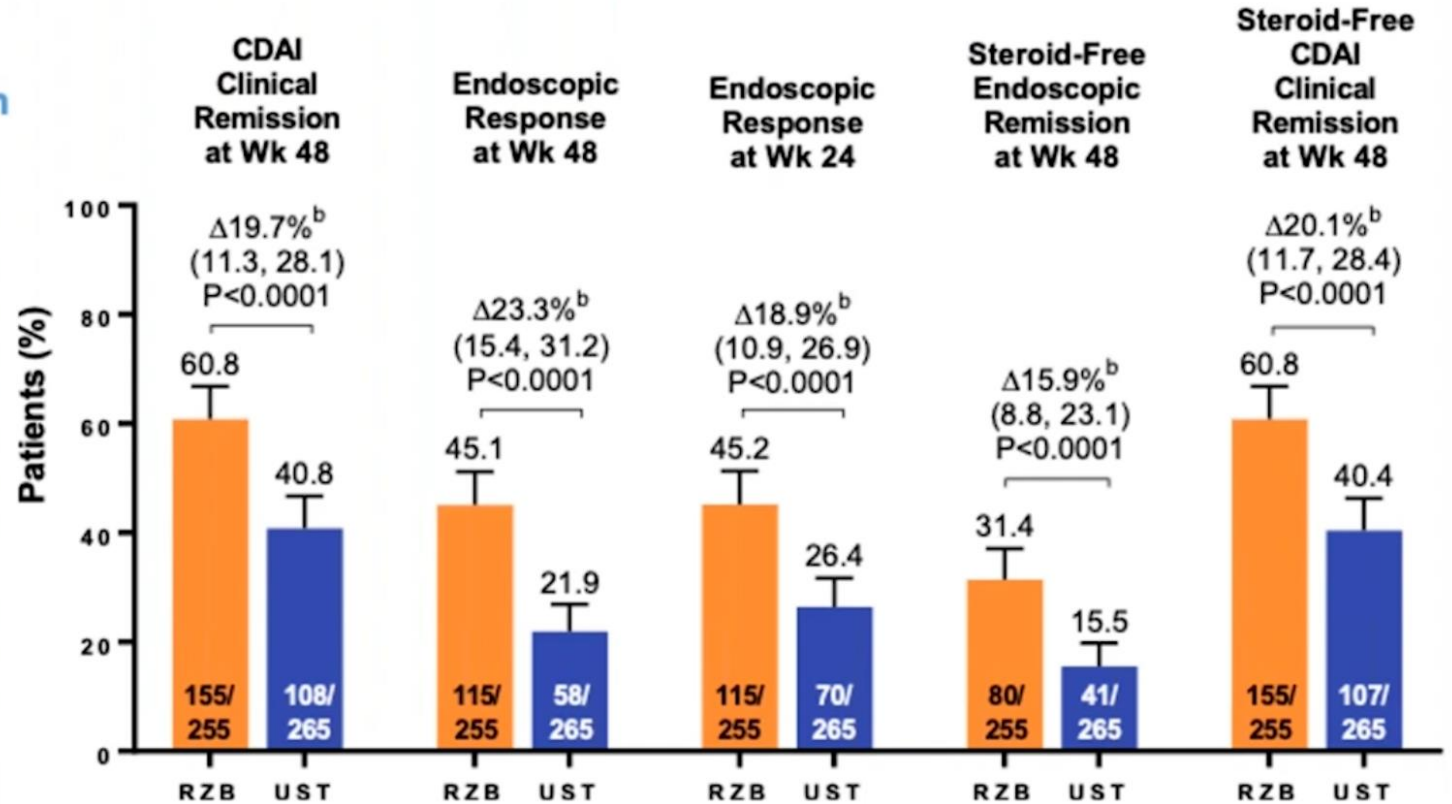
Singh, …, Ma. *Lancet Gastroenterol Hepatol* 2021

Crohn's Disease Second Line:
Risankizumab > Ustekinumab After Anti-TNF (SEQUENCE)









Peyrin-Biroulet L, *et al*. Presented at UEGW. October 2023. LB01.

September 12, 2023

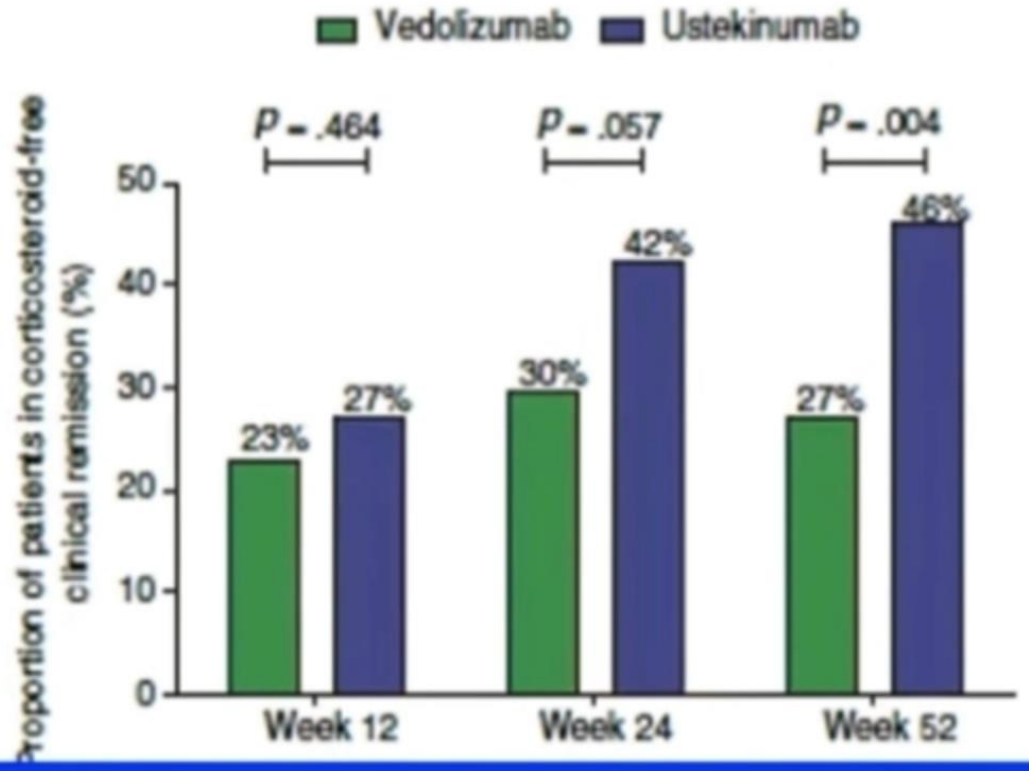
AbbVie's SKYRIZI® (risankizumab) Met All Primary and Secondary Endpoints Versus Stelara® (ustekinumab) in Head-to-Head Study in Crohn's Disease

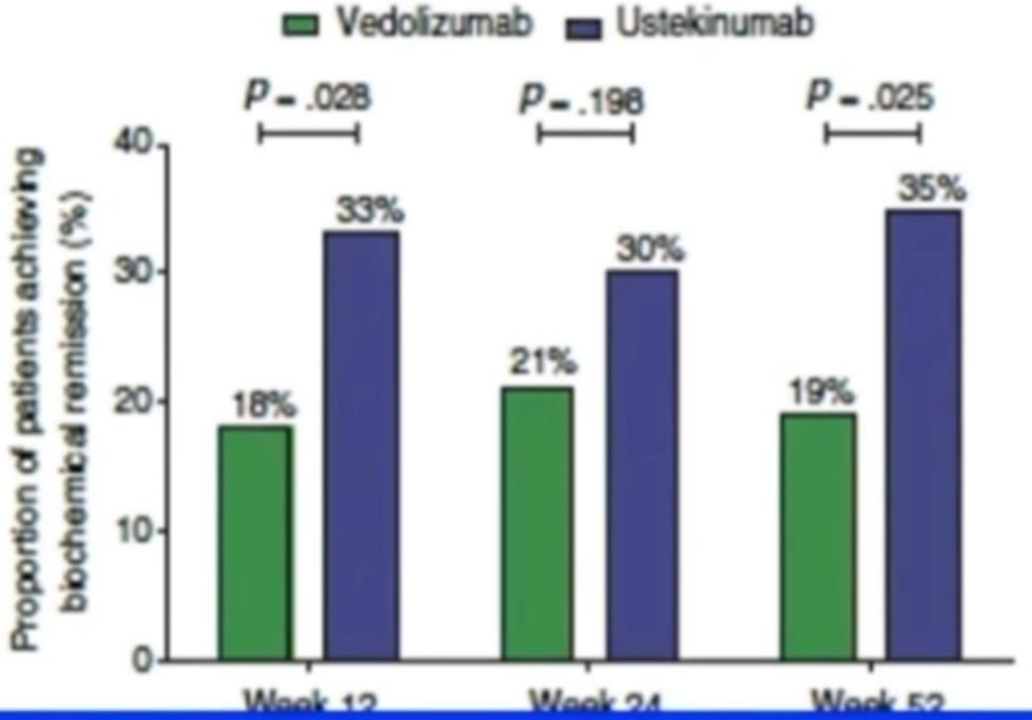
- Non-inferiority trial comparing **Risankizumab vs. ustekinumab**
- Moderate-severe Crohn's disease with **prior failure of TNF antagonists**

Outcomes	Risa vs. UST
Clinical remission @ W24	**59%** vs. 40%
Endoscopic remission @ W48	**32%** vs. 16%

AbbVie Press Release, Sept 12, 2023

Ustekinumab is associated with superior effectiveness outcomes compared to vedolizumab in Crohn's disease patients with prior failure to anti-TNF treatment





Ustekinumab is more effective than vedolizumab in achieving corticosteroid-free clinical remission and/or biochemical remission in TNFα-antagonist refractory patients with Crohn's disease

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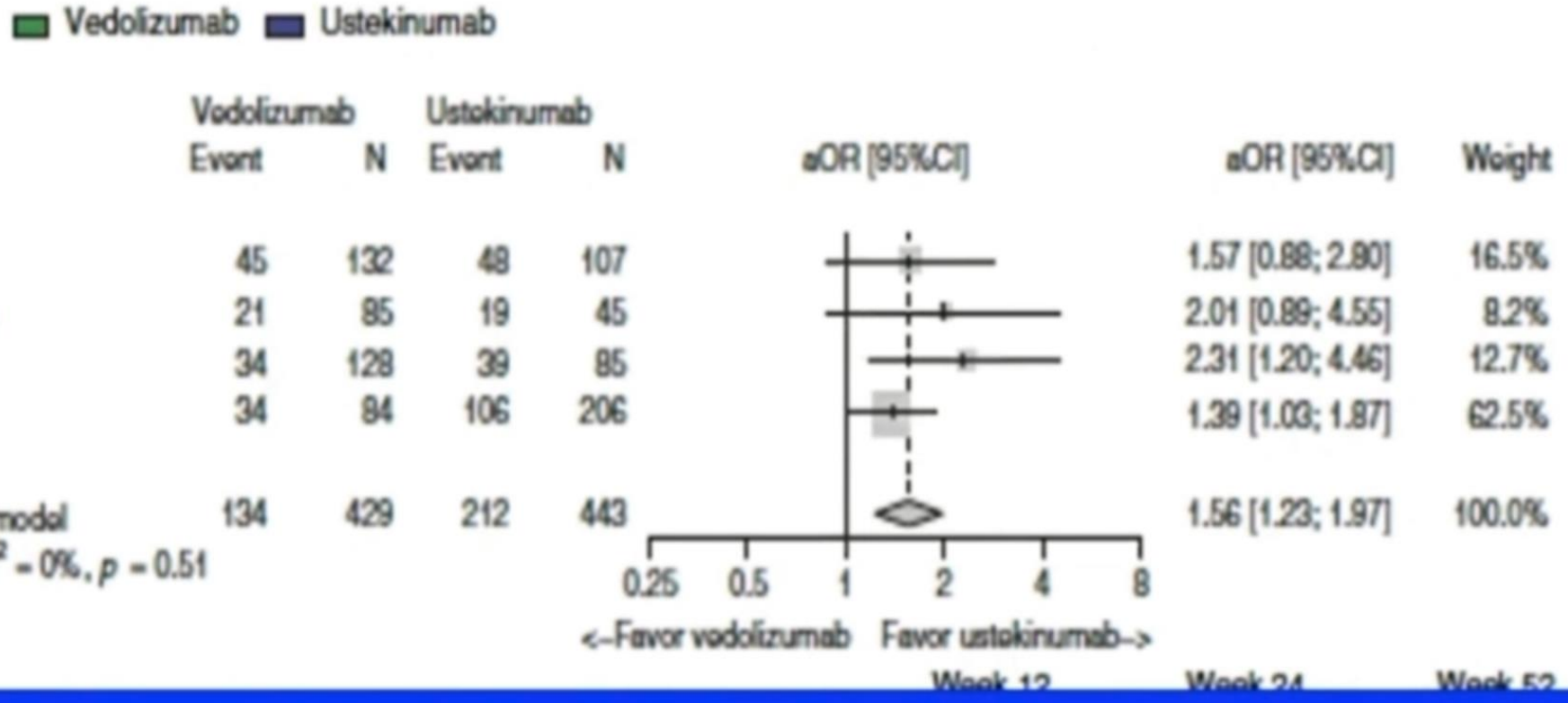

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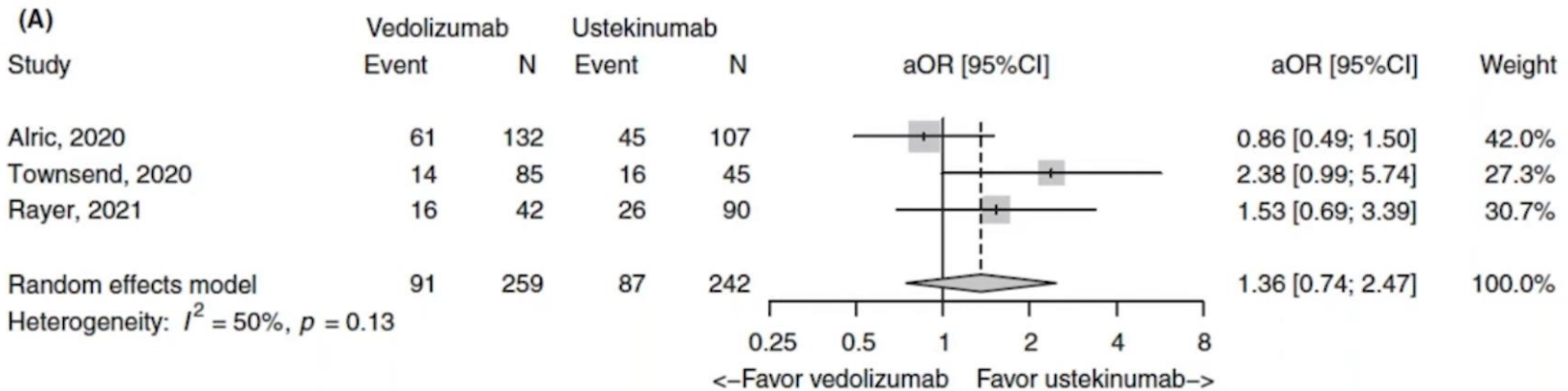
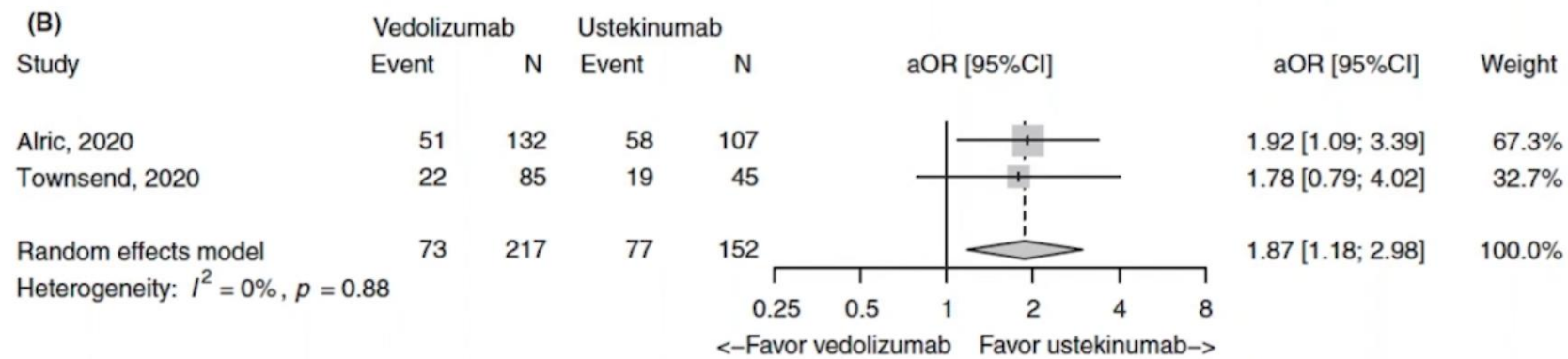
Crohn's Disease Second Line: Ustekinumab > Vedolizumab After Anti-TNF

Clinical Remission at Week 14



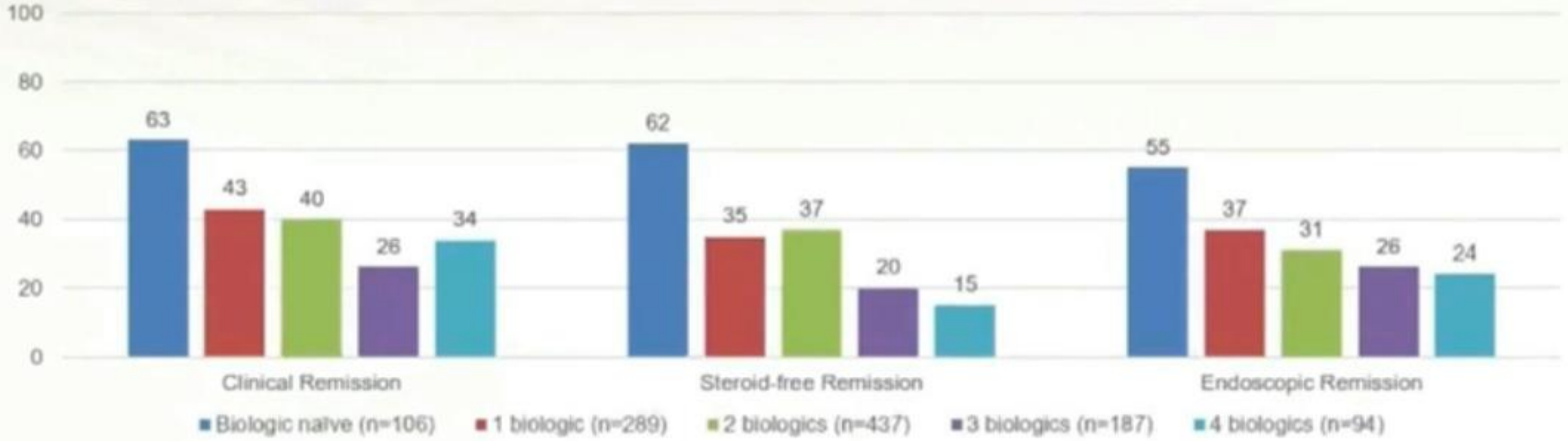
Clinical Remission at Week 52



- 5 studies (4 retrospective and 1 prospective) in CD patients with prior anti-TNF failure
- **Ustekinumab is more effective than vedolizumab as maintenance therapy**

Parrot L et al. *Aliment Pharmacol Ther*. 2022;55(4):380-388.

Ustekinumab After Biologic Exposure

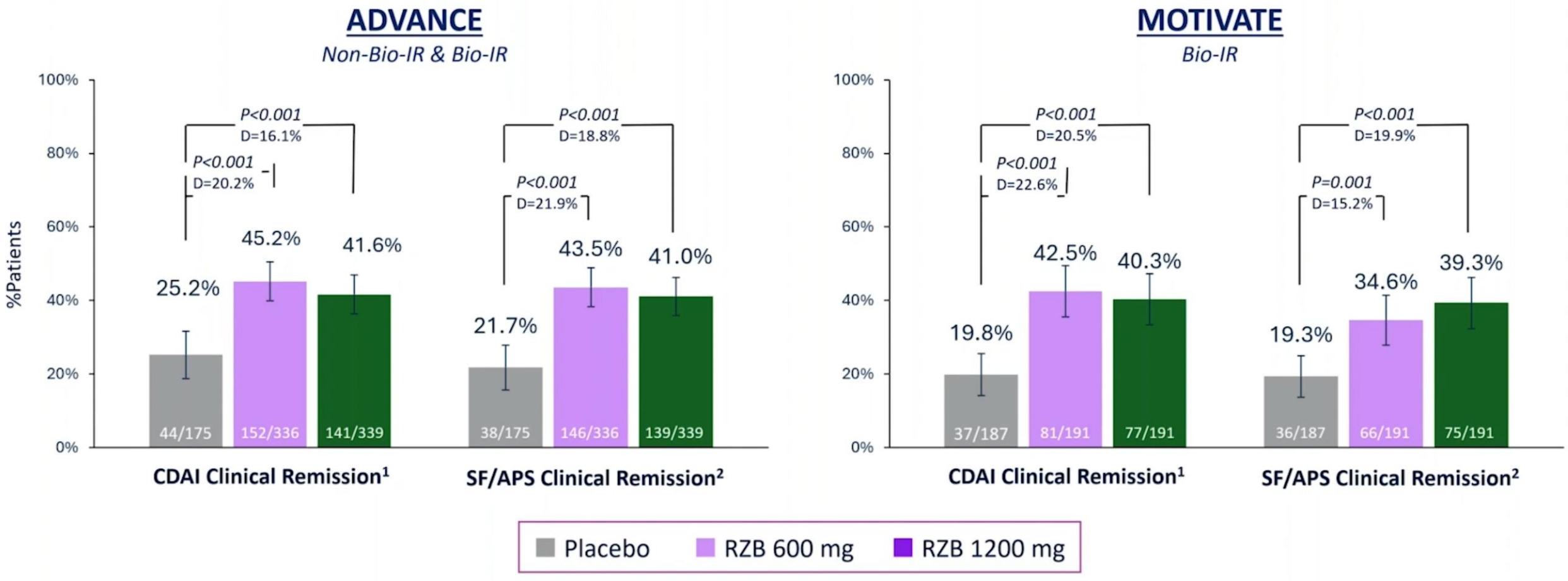


- Multicenter retrospective study of over 1000 CD patients (SUCCESS Consortium)
- **Lower effectiveness for ustekinumab with increasing biologic exposures**

Johnson AM, et al. *Am J Gastroenterol.* 2023;118(2):317-328.

IBD summit FOR FELLOWS

Risankizumab (p19: IL-23) for Crohn's Disease



D'Haens GR et al, Lancet 2022;399:2015-30.

Summary 2:
Practical Approach to Positioning Therapies for CD

- Mild: Budesonide induction, monitoring
- Moderate-to-severe:
  - Anti-TNF + thiopurine for severe disease
  - Risankizumab or ustekinumab for moderate disease
  - Vedolizumab for moderate inflammatory CD
  - SECOND LINE adv therapy: upadacitinib effective after anti-TNF
  - SECOND LINE adv therapy: risankizumab > ustekinumab
  - Anti-TNF and upadacitinib for joint EIMs
  - Risankizumab and ustekinumab for skin EIMs
  - Any biologic preferred for pregnancy

ORIGINAL ARTICLE

Upadacitinib Induction and Maintenance Therapy for Crohn's Disease

E.V. Loftus, Jr., J. Panés, A.P. Lacerda, L. Peyrin-Biroulet, G. D'Haens, R. Panaccione, W. Reinisch, E. Louis, M. Chen, H. Nakase, J. Begun, B.S. Boland, C. Phillips, M.-E.F. Mohamed, J. Liu, Z. Geng, T. Feng, E. Dubcenco, and J.-F. Colombel

ABSTRACT

BACKGROUND

Upadacitinib, an oral selective Janus kinase (JAK) inhibitor, is under investigation for the treatment of Crohn's disease.

METHODS

In two phase 3 induction trials (U-EXCEL and U-EXCEED), we randomly assigned patients with moderate-to-severe Crohn's disease to receive 45 mg of upadacitinib or placebo (2:1 ratio) once daily for 12 weeks. Patients who had a clinical response to upadacitinib induction therapy were randomly assigned in the U-ENDURE maintenance trial to receive 15 mg of upadacitinib, 30 mg of upadacitinib, or placebo (1:1:1 ratio) once daily for 52 weeks. The primary end points for induction (week 12) and maintenance (week 52) were clinical remission (defined as a Crohn's Disease Activity Index score of <150 [range, 0 to 600, with higher scores indicating more severe disease activity]) and endoscopic response (defined as a decrease in the Simple Endoscopic Score for Crohn's Disease [SES-CD; range, 0 to 56, with higher scores indicating more severe disease] of >50% from baseline of the induction trial [or for patients with an SES-CD of 4 at baseline, a decrease of ≥2 points from baseline]).

RESULTS

A total of 526 patients underwent randomization in U-EXCEL, 495 in U-EXCEED, and 502 in U-ENDURE. A significantly higher percentage of patients who received 45-mg upadacitinib than those who received placebo had clinical remission (in U-EXCEL, 49.5% vs. 29.1%; in U-EXCEED, 38.9% vs. 21.1%) and an endoscopic response (in U-EXCEL, 45.5% vs. 13.1%; in U-EXCEED, 34.6% vs. 3.5%) (P<0.001 for all comparisons). At week 52 in U-ENDURE, a higher percentage of patients had clinical remission with 15-mg upadacitinib (37.3%) or 30-mg upadacitinib

The authors' full names, academic degrees, and affiliations are listed in the Appendix. Dr. Colombel can be reached at jean-frederic.colombel@mssm.edu or at the Henry D. Janowitz Division of Gastroenterology, Department of Medicine, Icahn School of Medicine at Mount Sinai, 1470 Madison Ave., New York, NY 10029.

A list of the trial investigators is provided in the Supplementary Appendix, available at NEJM.org.

Drs. Loftus and Panés contributed equally to this article.

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CME at NEJM.org

Real-World Effectiveness and Safety of Upadacitinib in Crohn's Disease: A Multicenter Study

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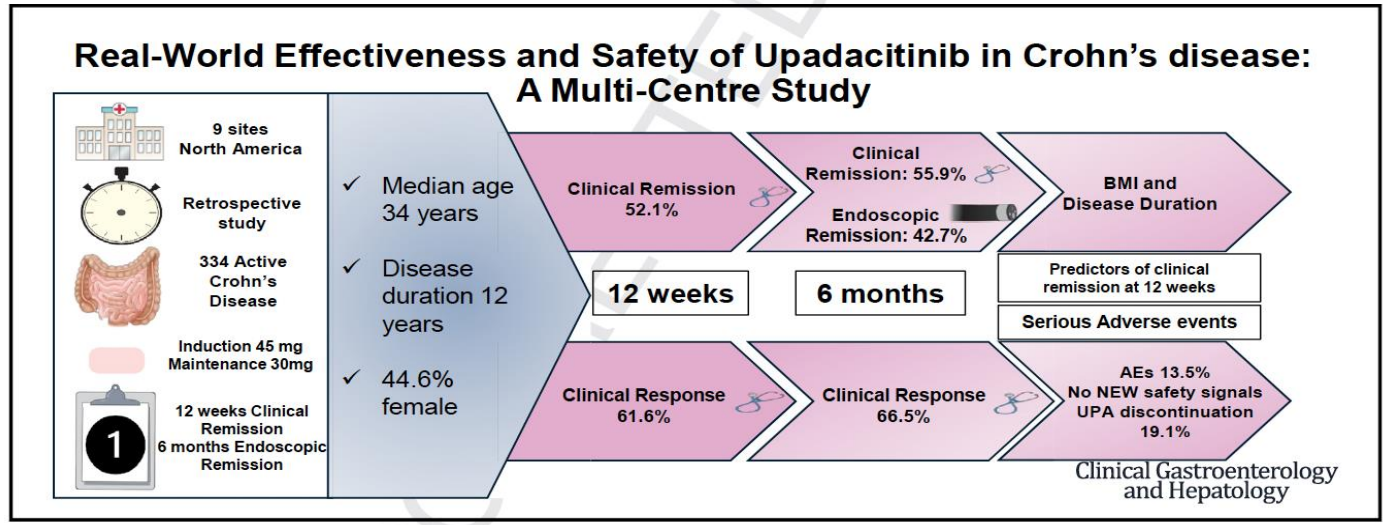


BACKGROUND & AIMS: We aimed to describe the real-world effectiveness and safety of upadacitinib (UPA), an oral Janus kinase 1 inhibitor, in patients with Crohn's disease (CD).

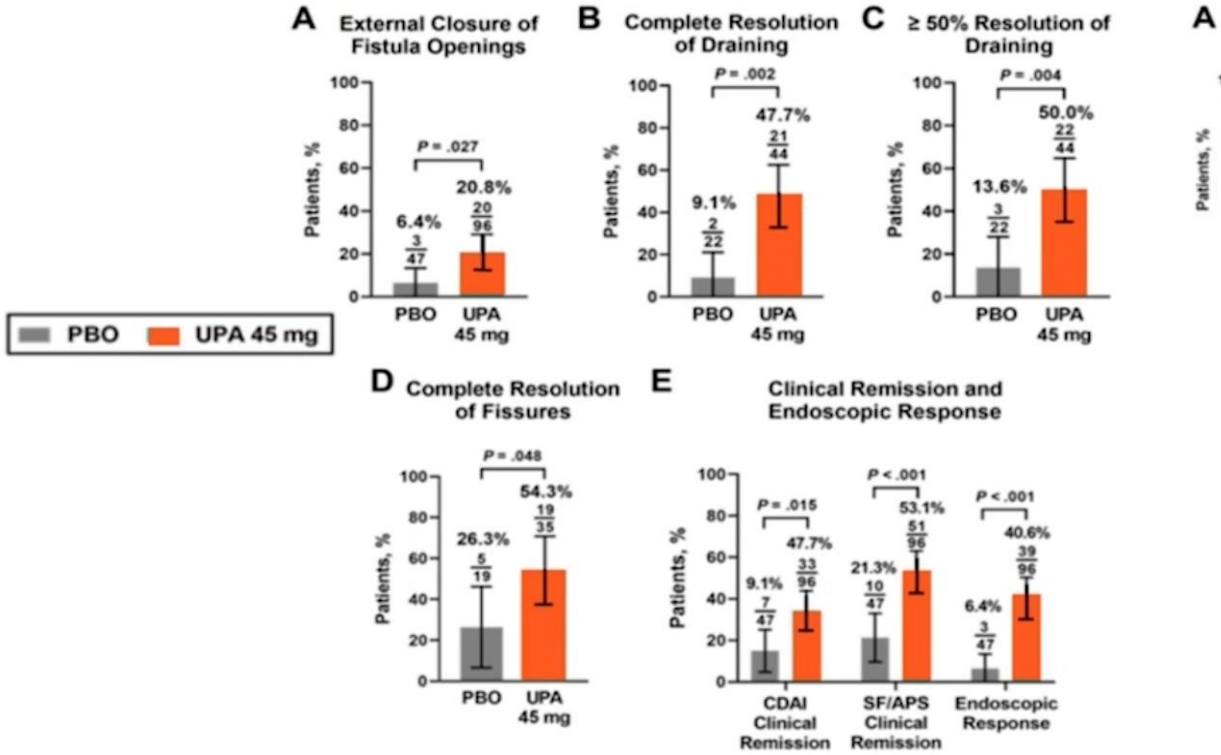
METHODS: A retrospective analysis was conducted across 9 centers in the United States, focusing on adults with CD treated with UPA 45 mg as induction therapy for active luminal disease. The copri-

UNCORRECTED PROOF

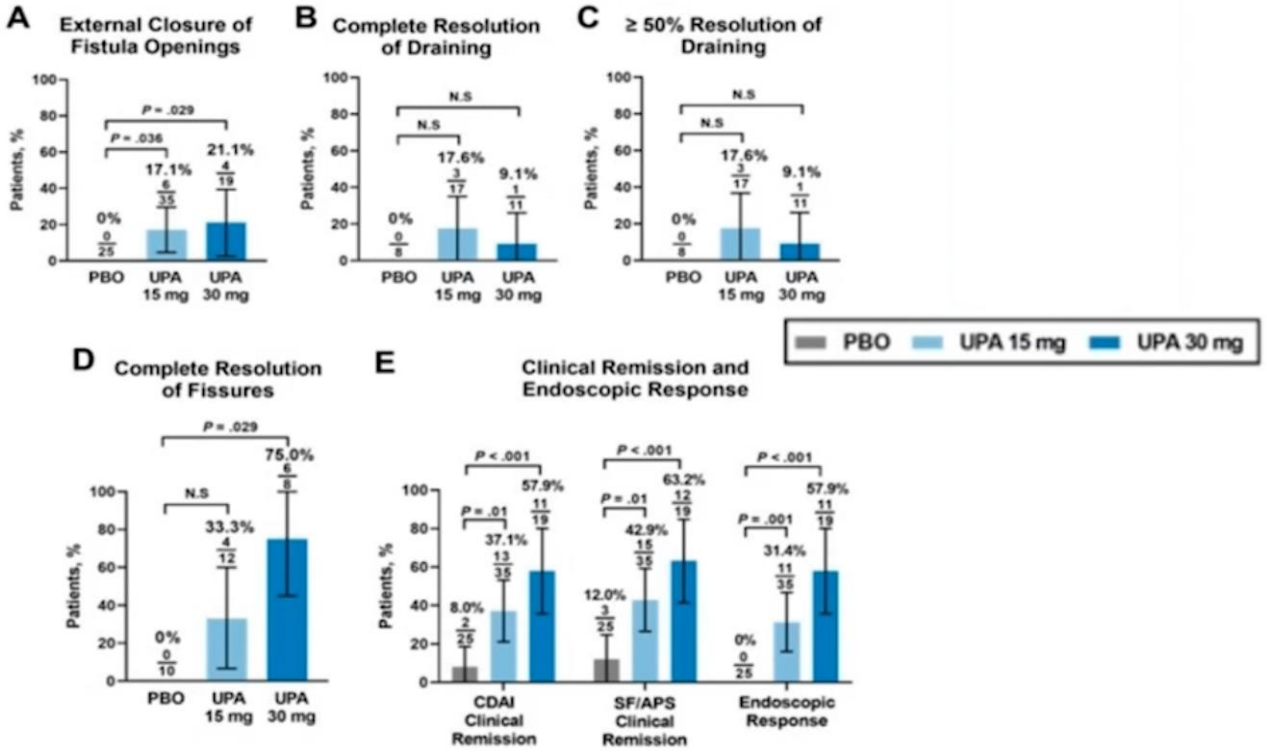
Upadacitinib is Effective for the Treatment of Fistulizing Crohn's Disease: Post-hoc Phase 3 Data

Subgroup analysis of U-EXCEL, U-EXCEED and U-ENDURE (n=143; 126 perianal, 19 enterocutaneous)

Induction Outcomes

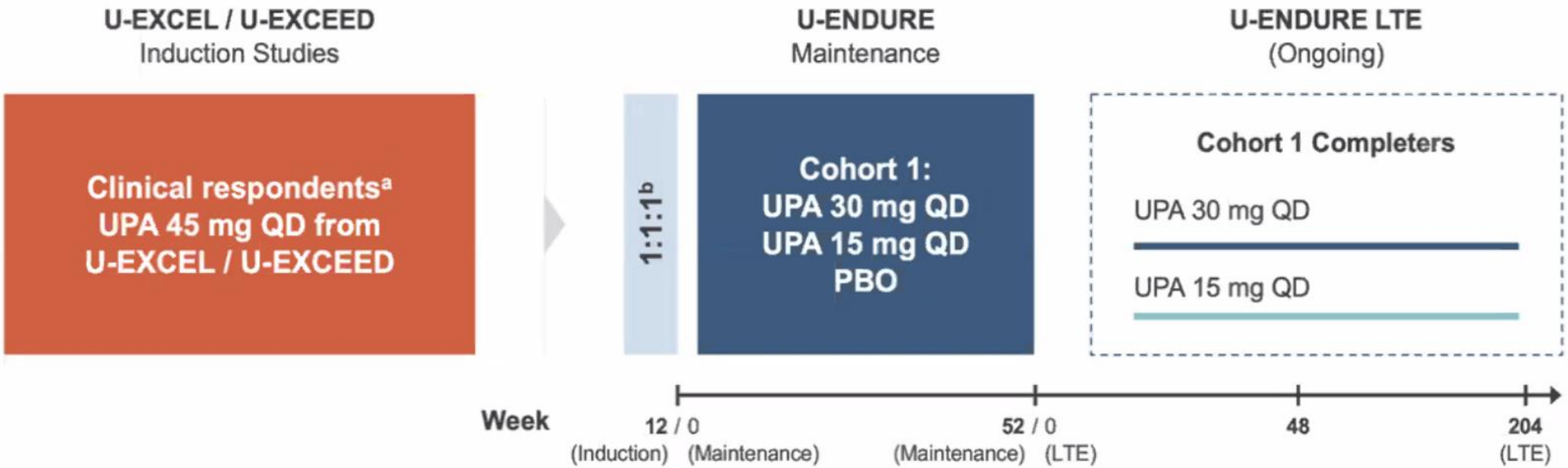


Maintenance Outcomes



Colombel JF, *et al*. Presented at DDW. May 2023. 947.

Efficacy & Safety of Upadacitinib Maintenance Treatment in Patients With Moderate to Severe CD: U-ENDURE Long-Term Extension Study, Year 2 Results



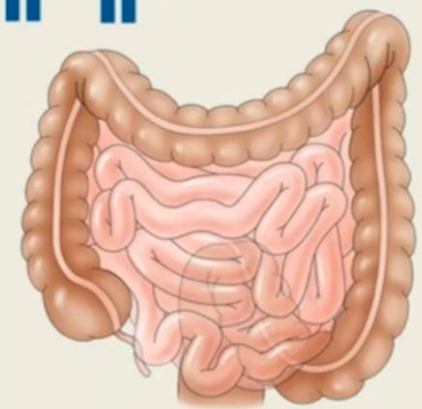
- Patients who completed the U-ENDURE 52-week maintenance SS1 were eligible for enrollment in the subsequent LTE substudy
- Efficacy was assessed in cohort 1 SS1 completers from LTE week 0 to week 48 in UPA-treated patients using NRI and AO analyses
- Safety was assessed from maintenance week 0, with up to 260 cumulative weeks of maintenance and LTE treatment exposure (cutoff date: 19 Dec 2023)
- Inadequate responders[e] to PBO or UPA 15 mg QD in the LTE could receive rescue therapy; if patients received rescue therapy, efficacy after rescue was analyzed separately (not presented here)

EXPLORER: VDZ, ADA, MTX Combo

Phase 4, open-label study of vedolizumab, adalimumab, and methotrexate combination therapy in Crohn's disease

Patients

N = 55



Biologic naïve patients with newly diagnosed, moderate to high risk CD

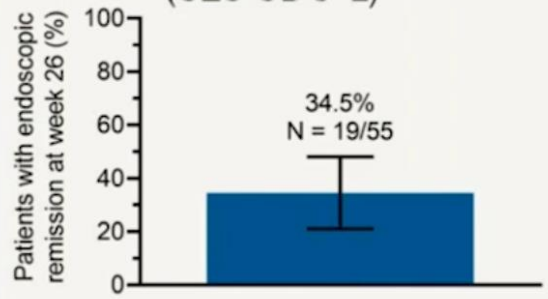
Treatment

Triple combination therapy

- IV vedolizumab 300 mg at weeks 0, 2, and 6 and every 8 weeks until week 102
- SC adalimumab 160 mg at week 0, 80 mg at week 2, and 40 mg every 2 weeks until week 26
- Oral methotrexate 15 mg weekly until week 34

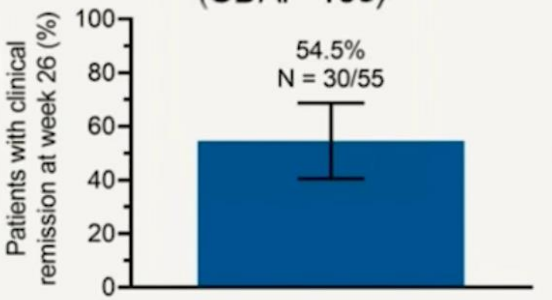
Primary end point

Endoscopic remission at week 26 (SES-CD 0–2)



Secondary end point

Clinical remission at week 26 (CDAI <150)



Post hoc Bayesian analysis[a]

Probability that triple combination therapy produces higher endoscopic remission than benchmark rates for…	…placebo ≥99.9%
	…vedolizumab monotherapy = 86.3%
	…adalimumab monotherapy = 71.4%

[a]*Beta*(1.667, 5) prior. Posterior mean endoscopic remission rate = 33.5% (95% credible interval: 22.4, 45.7).
CD, Crohn's disease; CDAI, Crohn's Disease Activity Index; IV, intravenous; SC, subcutaneous; SES-CD, Simple Endoscopic Score for Crohn's Disease

Clinical Gastroenterology and Hepatology

Colombel JF et al, *Clin Gastroenterol Hepatol* 2023 (online early).

And what is personalized treatment?

What we have learnt – one size does not fit all



Pediatric
Adult
Pregnancy
High risk patients
Refractory IBD
Associated EIMs

How Do We Put Together the Puzzle of Therapy Selection?

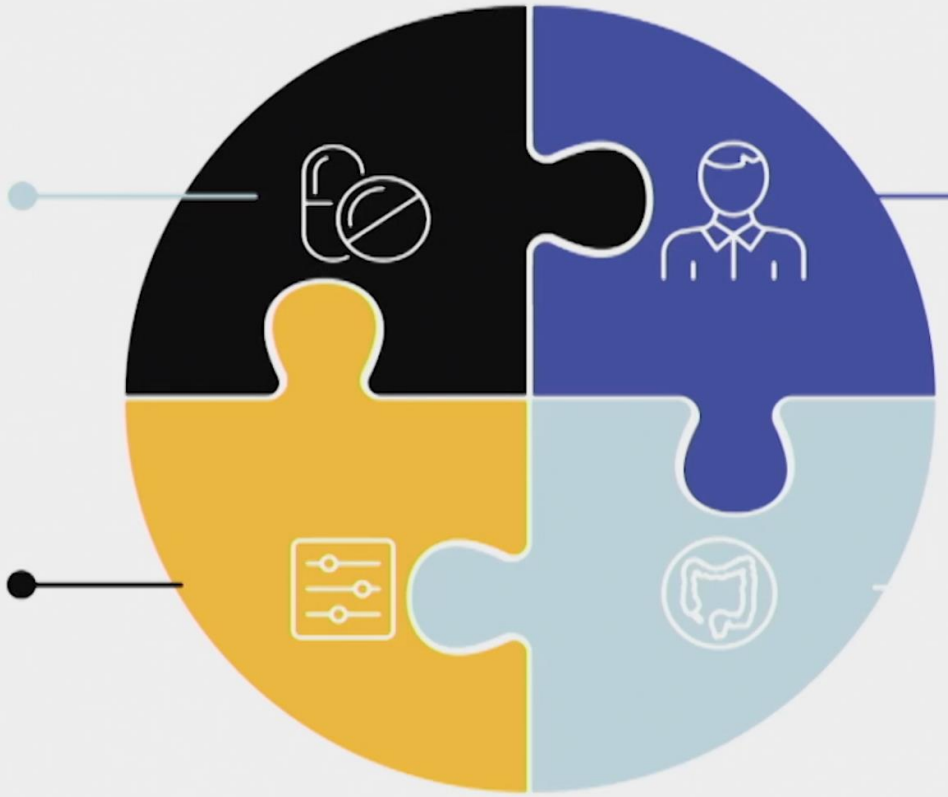
DRUG

Efficacy

Indication
Rapidity of onset
Durability
Pharmacokinetics/TDM
Combination vs. monotherapy
Positioning and sequence

Safety

Infection
Cancer
Specific concerns by agent or mechanism



PATIENT

Individual Characteristics

Age
Medical comorbidities
Preferences (IV/SQ/PO)
Insurance
Costs
Access to care

Disease Characteristics

CD vs. UC
Disease behavior/complication
Disease severity
Early vs. late
EIMs
Prior treatment success or failure
Anti-TNF naïve vs exposed

EIMs = extraintestinal manifestations; TDM = therapeutic drug monitoring

Advanced Therapy Choices in IBD

Individual Patient Characteristics



Pregnancy

Young woman with steroid-dependent UC planning to start a family

Any Biologic (Anti-TNF w/robust data)



Failed Anti-TNF

Young man with pan-UC who is a primary non-responder to anti -TNF

Uste, Tofa, Upa, Surgery



Newly Diagnosed

Newly diagnosed man with moderate CD with a personal history of lymphoma

Vedo, Uste, Risa







Shared Decision-making





Lifestyle Considerations

Businesswoman who travels often for work, with Crohn's ileitis

Ada, Risa, Uste



Unfavorable Pharmacokinetics

Older woman with pan-UC in whom you want to avoid immunomodulator, who has HLA-DQA1*05 genotype

Vedo, Uste, Miri, Ozanimod, Etrasimod



Perianal Disease

Woman admitted with severe rectal Crohn's with perirectal abscess s/p drainage and seton placement

Anti-TNF (+Azathioprine)



HLA = human leukocyte antigen; s/p = status post.

Positioning of Therapies by Subpopulations

Factor to Consider	Preferred Treatment
Age >65 yr (malignancy, infection, comorbidities)	▪ Risankizumab or Ustekinumab or Vedolizumab
Significant cancer history, lymphoma	▪ Risankizumab or Ustekinumab or Vedolizumab
Pregnancy	▪ TNF inhibitor, Azathioprine, Ustekinumab, or Vedolizumab, or Risankizumab
Perianal (complex) fistulizing disease	▪ TNF inhibitor (+ IMM)
Psoriasis (PsA)	▪ Risankizumab or Ustekinumab
Multiple sclerosis	▪ S1P modulator: Ozanimod
Extraintestinal manifestation: arthritis	▪ TNF inhibitor or JAKs
Previous TNF inhibitor failure	▪ CD: Risankizumab or Ustekinumab, then Vedolizumab ▪ UC: JAKs-Upa/Tofa, then Vedolizumab or Ustekinumab
Adherence concerns (immunogenicity)	▪ Oral vs SQ ▪ JAKs; Risankizumab or Ustekinumab; Vedolizumab
Unfavorable pharmacokinetics (HLA-DQA105)	▪ Risankizumab or Ustekinumab or Vedolizumab

Additional Considerations for Choice of Treatment in IBD

Clinical Scenario/ Co-existing Condition	Therapy Consideration
Perianal Crohn's Disease	Anti-TNF Upadacitinib
Enteropathic Arthropathy	Sulfasalazine Methotrexate Anti-TNF JAKinib
Plaque Psoriasis	Anti-TNF IL-23 Therapies MTX
Psoriatic Arthritis	Anti-TNF JAKinib IL-23 Therapies MTX
Rheumatoid Arthritis	Anti-TNF JAKinib MTX
Spondyloarthritis (AnkSpon and Sacroileitis)	Anti-TNF JAKinib
Alopecia	JAKinib
Multiple Sclerosis	Natalizumab (CD) Ozanimod (UC) (maybe Etrasimod (UC))

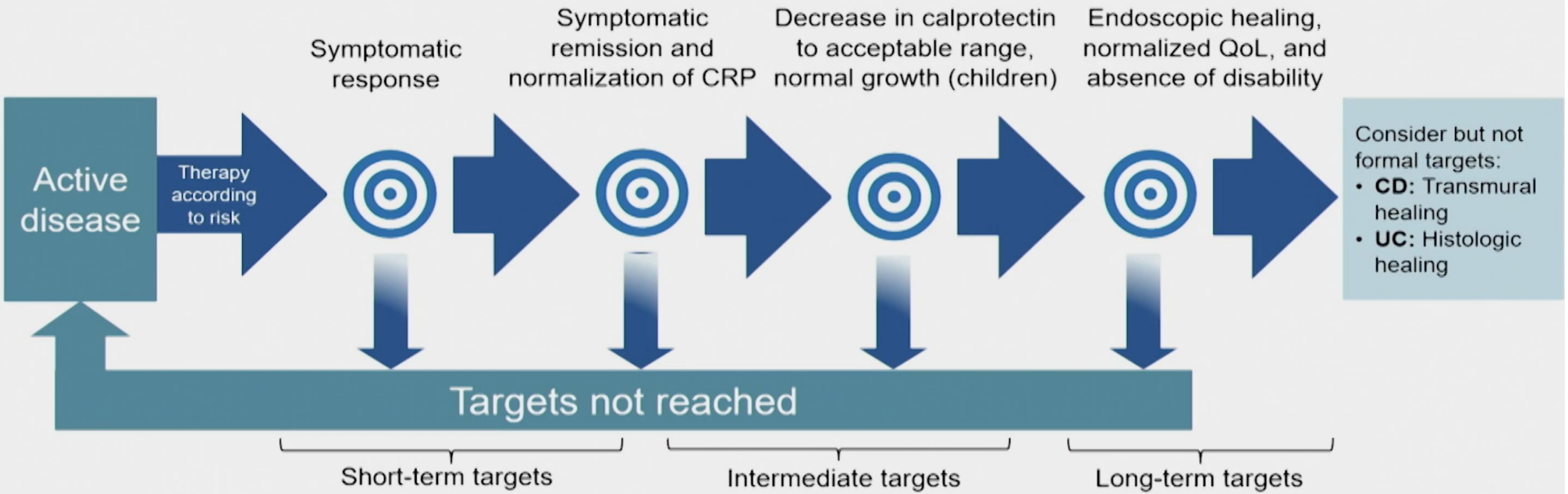
Situation	Absolutely or Relatively Contraindicated
Latent TB	Anti-TNF
Chronic hepatitis B	Anti-TNF Anti-IL23
Uveitis Macular Edema	S1P
Type 2/3 heart block	S1P
Lymphoma	Anti-TNF (?) Thiopurines
Melanoma	Anti-TNF
Cytotoxic chemotherapy	Immunosuppressive Treatments
Anti-drug antibodies to first anti-TNF	Consider non-anti-TNF options Protect against antibodies with next anti-TNF

Patient Specific Considerations

- ✓ Heavy disease burden – fixed dose SQ biologic may not be ideal
- ✓ Previous medication failures – TNF failure predicts poor response to all future therapies regardless of MOA
- ✓ Medical interactions (i.e. liver/kidney) – possible with small molecules, but few concerns with biologics
- ✓ Comorbid conditions –
  - If RA - TNF or JAK to potentially treat 2 diseases with 1 MOA
  - Psoriasis - consider UST or RISA
  - MS or CHF - avoid TNF
  - MS - consider S1P
  - Significant Cardiac disease - might avoid JAK and possibly S1P
  - Significant smoking – avoid JAK

What is the goal of therapy in IBD patient?

STRIDE-II: Treatment Targets in CD and UC

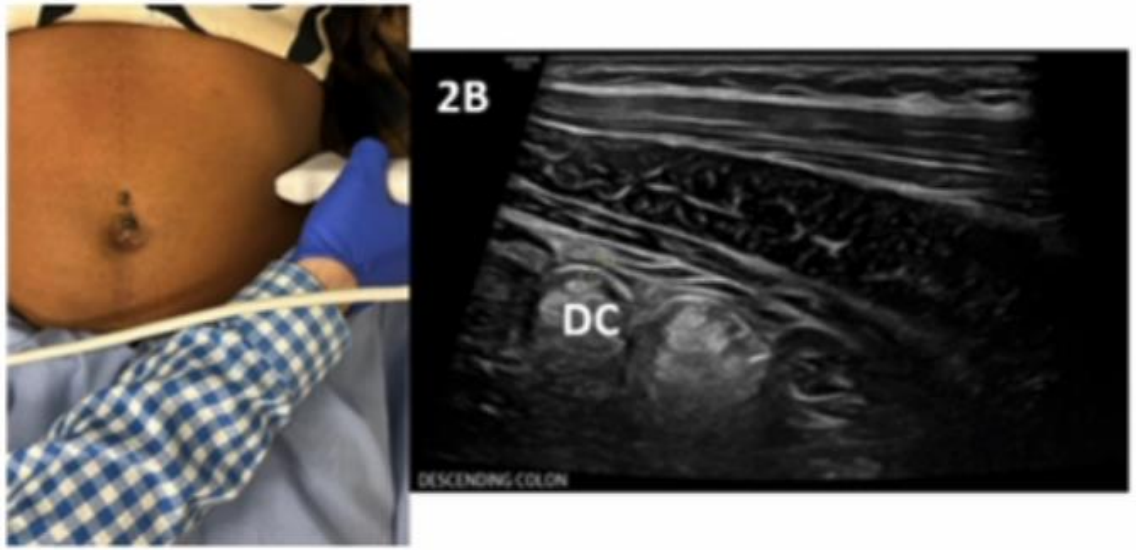


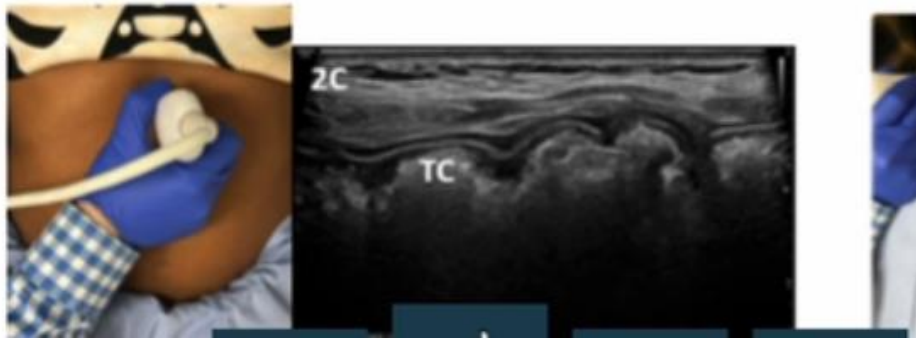
Turner D et al. *Gastroenterology*. 2021;160(5):1570-1583.

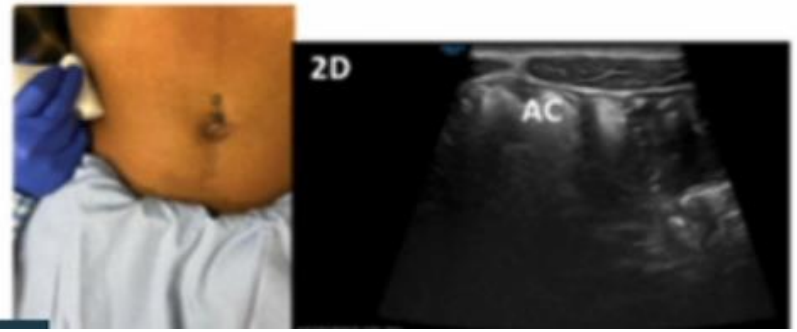
IUS Quickly Visualizes the Colon and Terminal Ileum

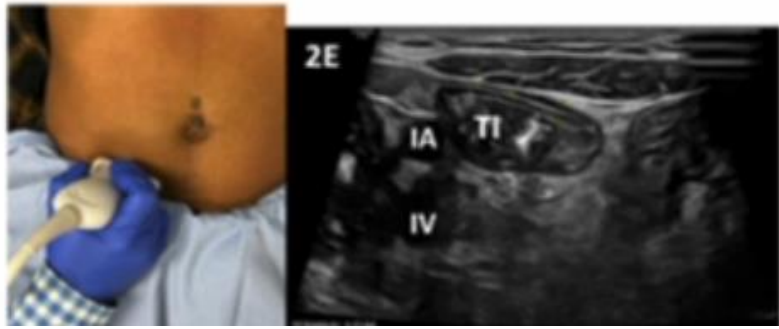













Thank you!!