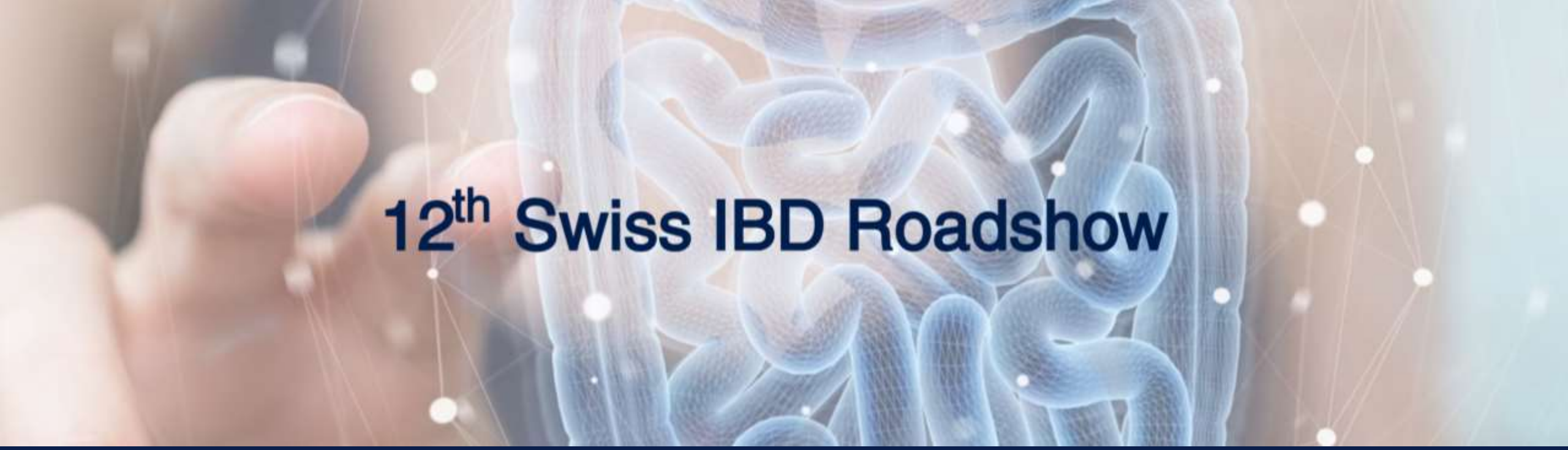


Acceleration in IBD Treatment:
How early and holistic care leads to better outcomes

Professor Bruce Sands, MD, MS

References in this presentation can be requested by health care professionals via Medinfo.ch@abbvie.com.

Supported by AbbVie AG, Alte Steinhauserstrasse 14, 6330 Cham

RISN-CH-00150-E 06/2025

Disclosures

Research Grants	Janssen
Consulting Fees	AbbVie, Alimentiv, Amgen, AstraZeneca, Boehringer-Ingelheim, Bristol Myers Squibb, Celltrion, Eli Lilly and Company, Galapagos, Genentech, Gilead Sciences, Glaxo SmithKline, J&J Innovative Medicine, Merck & Co. Pfizer, Sanofi, Takeda, Teva
Speaking Fees	Abivax, Alimentiv, Bristol Myers Squibb, Celltrion, Janssen, Eli Lilly and Company, Merck & Co. Pfizer, Sanofi, Takeda
Stock & Stock Options	Ventyx Biosciences

Dr. Sands is being supported by AbbVie for speaking and consulting during the Swiss Roadshow. Any opinions expressed are his own, and the content presented is under his direction.

Disclaimer

This presentation contains information on substances not authorized by Swissmedic and approved drugs that are being investigated (alone or in combination) for non-authorized indications. Safety and efficacy have not yet been established. AbbVie does not endorse the use of unapproved products or approved products outside of their label.

Agenda

- Meet Emma
- Bottom up or top down? – the window of opportunity
- Unveiling underlying inflammation through holistic monitoring
- How recent treatment innovations help us aim for higher targets
- Conclusions
- Questions?

Agenda

- **Meet Emma**
- Bottom up or top down? – the window of opportunity
- Unveiling underlying inflammation through holistic monitoring
- How recent treatment innovations help us aim for higher targets
- Conclusions
- Questions?

Emma

- 32 year old woman
- 4 months of fecal urgency and frequency
- Often awakens for diarrhea
- In the last 3 weeks, blood with bowel movements
- One episode of incontinence in the last week
- Has been trying aloe vera to ease the diarrhea

Past medical history

- G1P1, vaginal delivery with 2° tear

- **Social history**
  - Teaches 4th grade
  - Mother of a 4 year old, and planning to have a second child in the next year
  - “Stressed”, depressed mood
  - No tobacco, rare alcohol
- **Family history**
  - No GI problems
  - No GI cancers
  - Sister with diabetes mellitus type 1

This is a hypothetical patient case for discussion.
G, Gravida; P, Para; GI, gastrointestinal

Emma

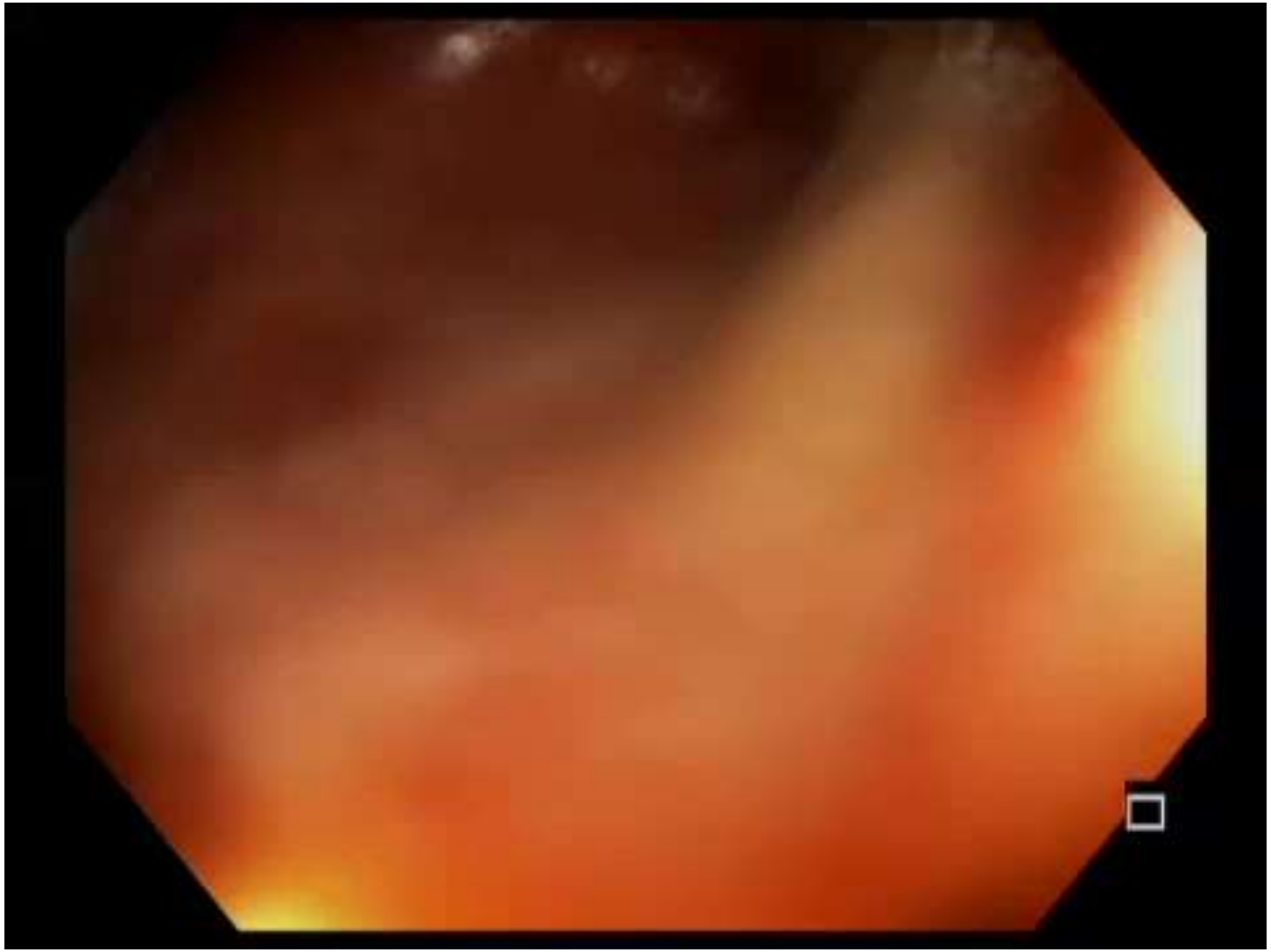
Physical examination

- Mildly anxious appearing
- BMI 21
- Normal vital signs
- Abdomen
  - Minimal tenderness in the left lower quadrant
- Perianal area: no skin tags, fissures or fistulas; slight decrease in resting tone

Labs

- Hemoglobin 11.1 g/dL
- CRP 3.0 mg/L (ULN 0.8)
- Stool studies: GI PCR negative, *C. difficile* negative
- Albumin 3.4 g/dL
- Fecal calprotectin: 1684 mcg/g

This is a hypothetical patient case for discussion.
ULN, upper limit of normal; GI, gastrointestinal; PCR, Polymerase Chain Reaction



Video provided by Dr. Bruce Sands.

Emma – diagnosed with ulcerative colitis

What treatment would you choose?*

A. 5-aminosalicylate (oral plus enema)
B. Prednisolone
C. Vedolizumab
D. Adalimumab
E. Infliximab
F. Ustekinumab
G. Anti-IL-23 antibody (guselkumab, mirikizumab, or risankizumab)
H. S1PR modulator (ozanimod or etrasimod)

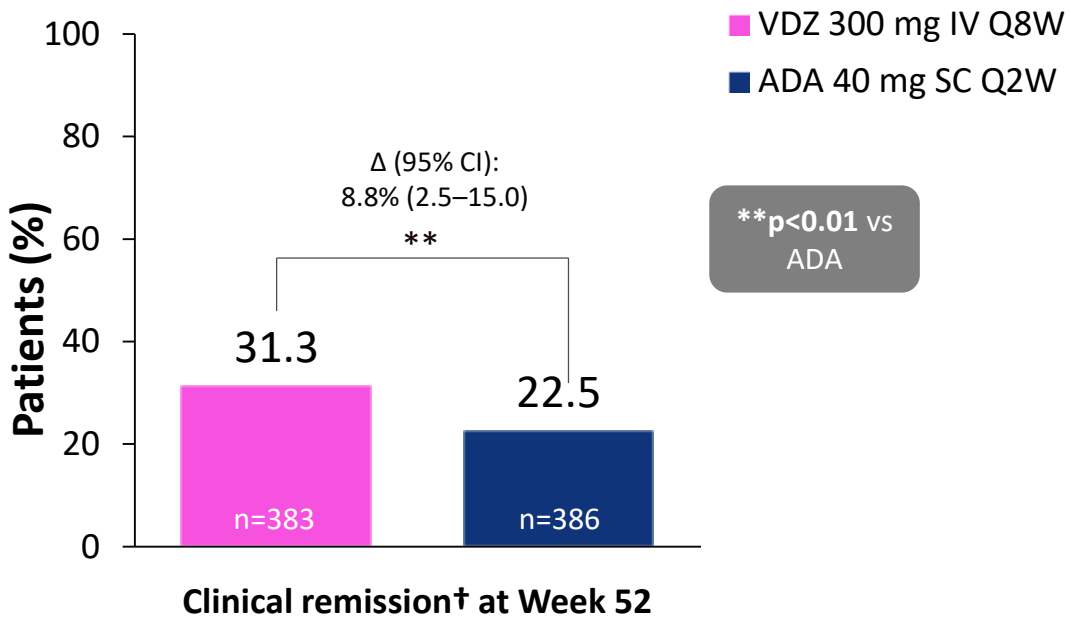
This is a hypothetical patient case for discussion. *Per Swissmedic label, all advanced therapies require at least a prior failure/intolerance/contraindication of a conventional therapy.
IL, interleukin; S1PR, sphingosine-1-phosphate receptor modulator.

VARSITY: Vedolizumab vs Adalimumab in UC

Clinical remission at Wk 52 and Durable Clinical Remission (Wks 14 & 52)

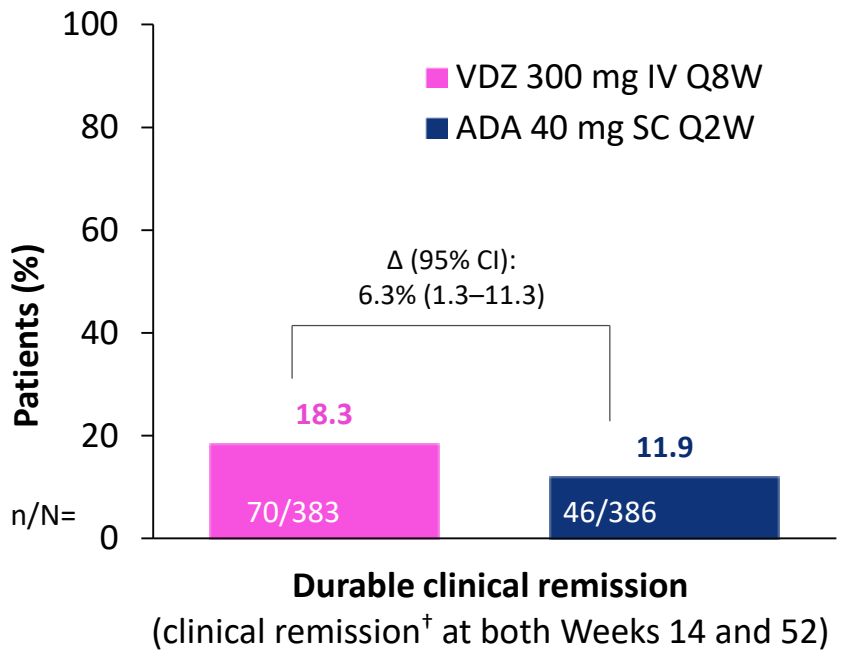
Primary endpoint

Clinical remission† at Week 52



Prespecified exploratory endpoint

Durable clinical remission



†Total Mayo score of ≤2 with no sub-score >1. N-numbers shown for the primary endpoint are for the treatment group, not the number of patients achieving remission within that group.
ADA, adalimumab; CI, confidence interval; Q2W, every 2 weeks; Q8W, every 8 weeks; VDZ, vedolizumab.
Adapted from Sands BE, et al. *N Engl J Med*. 2019;381:1215–26.

Agenda

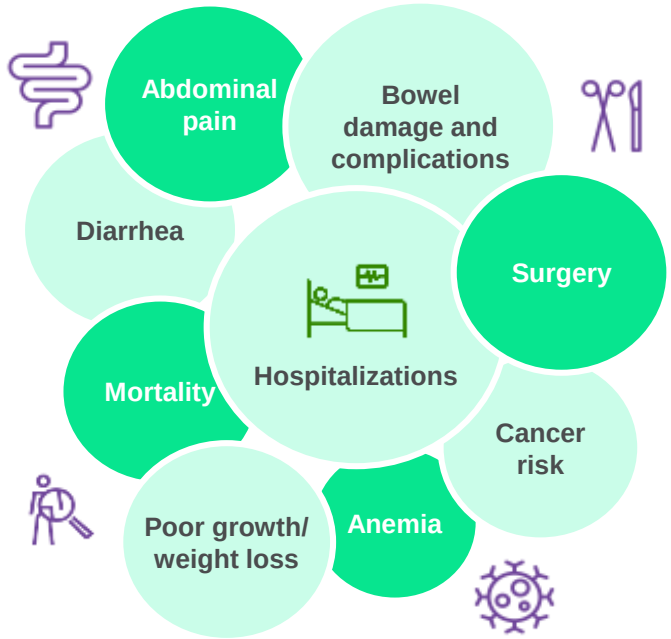
- Meet Emma
- **Bottom up or top down? – the window of opportunity**
- Unveiling underlying inflammation through holistic monitoring
- How recent treatment innovations help us aim for higher targets
- Conclusions
- Questions?

The Burden of IBD

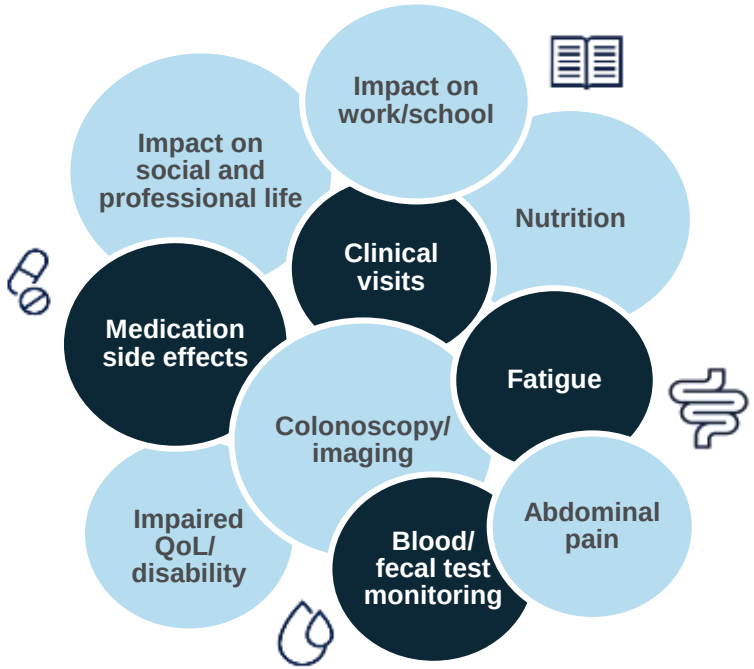
A **multifaceted** burden, compounded by distressing, debilitating symptoms that can[1]:

- Restrict patients' freedom
- Contribute to social isolation
- Reduce their psychological/physical well-being
- Curb productivity

Disease outcomes[2–10]



Patient-reported outcomes[2–10]



IBD, inflammatory bowel disease; QoL, quality of life.

1. Ghosh S, et al. *Inflamm Bowel Dis.* 2017;23(3):333–340. 2. Barreiro-de Acosta M, et al. *Adv Ther*. 2023;40(5):1975–2014. 3. Fiorino G, et al. *United European Gastroenterol J*. 2020;8(4):410–417. 4. Jaiswal V, et al. Med. 2023;102(6):e32775. 5. Knowles SR, et al. *Inflamm Bowel Dis*. 2018;24(4):742–751. 6. Ricciuto A, et al. *Crit Rev Clin Lab Sci*. 2019;56(5):307–320. 7. Seyedian S, et al. *J Med Life*. 2023;12(2):113. 8. Tannoury J, et al. *Aliment Pharmacol Ther*. 2021;53(10):1098–1107. 9. van Gennep S, et al. *Dig Dis Sci.* 2021;66:2916–2924. 10. Yzet C, et al. *Clin Gastroenterol Hepatol*. 2020;18(10):2256–2261.

How can we achieve the best IBD outcomes today?

- Early diagnosis and treatment[1-3]
- Treating to targets that make a difference[4-6]
- Holistic monitoring to maintain treatment targets[7-13]
- Use of effective therapies that can achieve targets[14-15]

1. Colombel JF, et al. Gastroenterology. 2017;152:351–361. 2. Fumery M, et al. Clin Gastroenterol Hepatol. 2018;16:343–56. 3. Noor N, et al. Lancet Gastroenterol Hepatol. 2024;9:415–27. 4. Turner D, et al. Gastroenterology. 2021;160:1570–83. 5. Colombel et al. Lancet. 2018;390:2779. 6. Shah C, et al. Clin Gastroenterol Hepatol. 2016;14:1245–55.e8. 7. Thomassen BJM, et al. J Crohns Colitis. 2024;18:371–2; 8. Sudhakar P, et al. Gut. 2023;72:192–204; 9. Bressler B, et al. Gastroenterology. 2015;148:1035–58.e3. 10. Gordon H, et al. J Crohns Colitis. 2024;18:1–37; 11. Farrell D, et al. J Crohns Colitis. 2015;10;315–22; 12. Gosh S and Mitchell R. J Crohns Colitis. 2007;1:10–20; 13. Marín-Jiménez I, et al. Inflamm Bowel Dis. 2017;23:1492–8. 14. Gordon H, et al. J Crohns Colitis. 2024;18,10:1531-1555. 15. Raine T, et al. J Crohn's Colitis. 2022.16,1: 2-17.

Diagnostic delay is longer in CD vs UC[1]

Data from the Swiss IBD cohort study

Diagnostic delay in CD patients is significantly longer compared to UC patients (median 9 versus 4 months, P < 0.001).

UC

Nonsteroidal anti-inflammatory drug intake and **male gender** are associated with long diagnostic delay in UC (>12 months).

CD

Age <40 years at diagnosis and **ileal disease** were identified as independent risk factors for long diagnostic delay in CD (>24 months).

1. Vavricka, Stephan R et al. Inflam bowel dis vol. 18,3 (2012): 496-505.

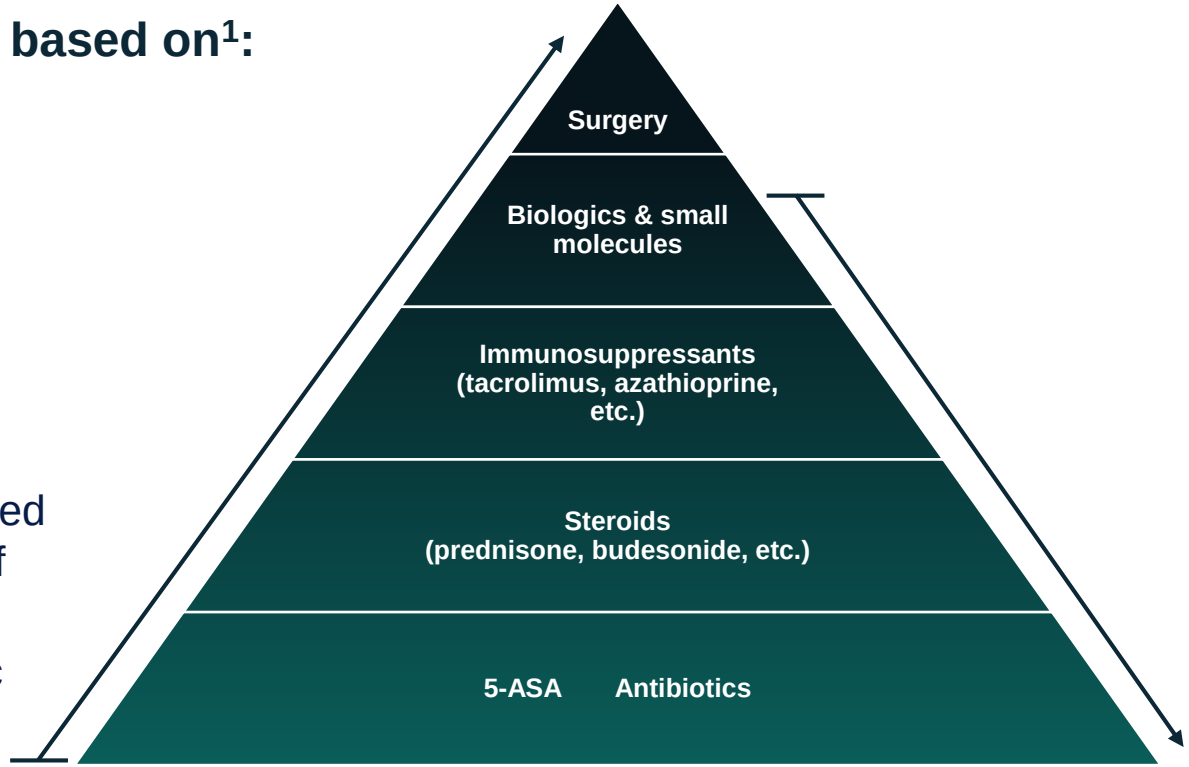
General Treatment Considerations for IBD

IBD treatment should be based on[1]:

- ✓Symptoms activity
- ✓Disease severity
- ✓Comorbidities
- ✓Goal of remission

Traditional Step-Up Approach[2,3]

- Delayed initiation of advanced therapies following failure of conventional therapies
- Potential to lose therapeutic window of opportunity and develop complications



IBD Treatment Approaches[1]

Top-Down Approach[2,3,*]

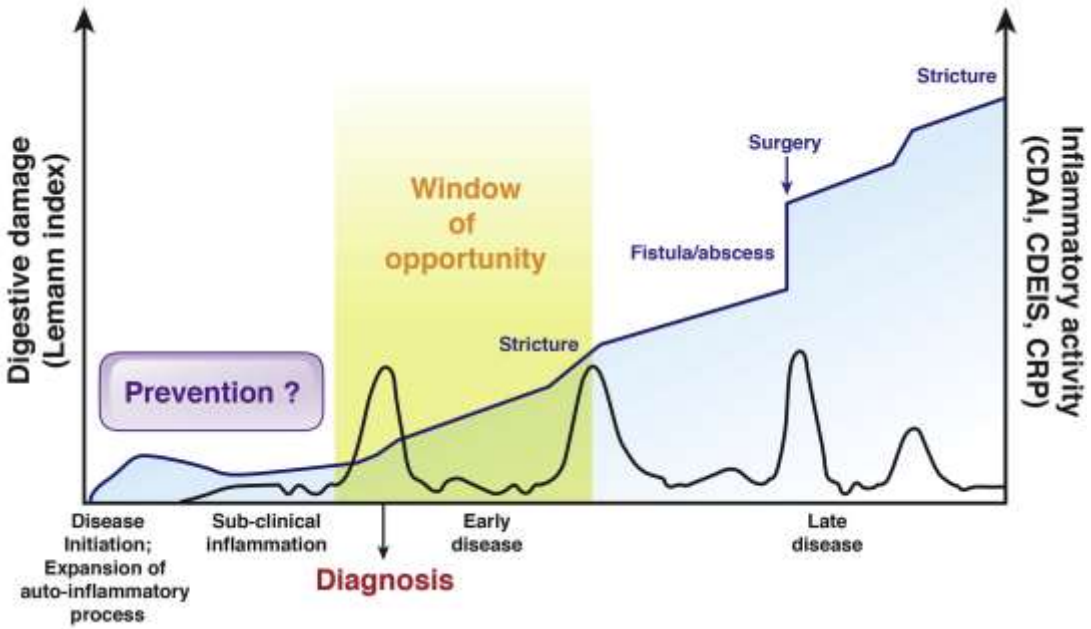
- Early initiation with advanced therapies to leverage window of opportunity
- Mitigate potential failure with conventional therapies, and prevent accumulation of damage with late disease

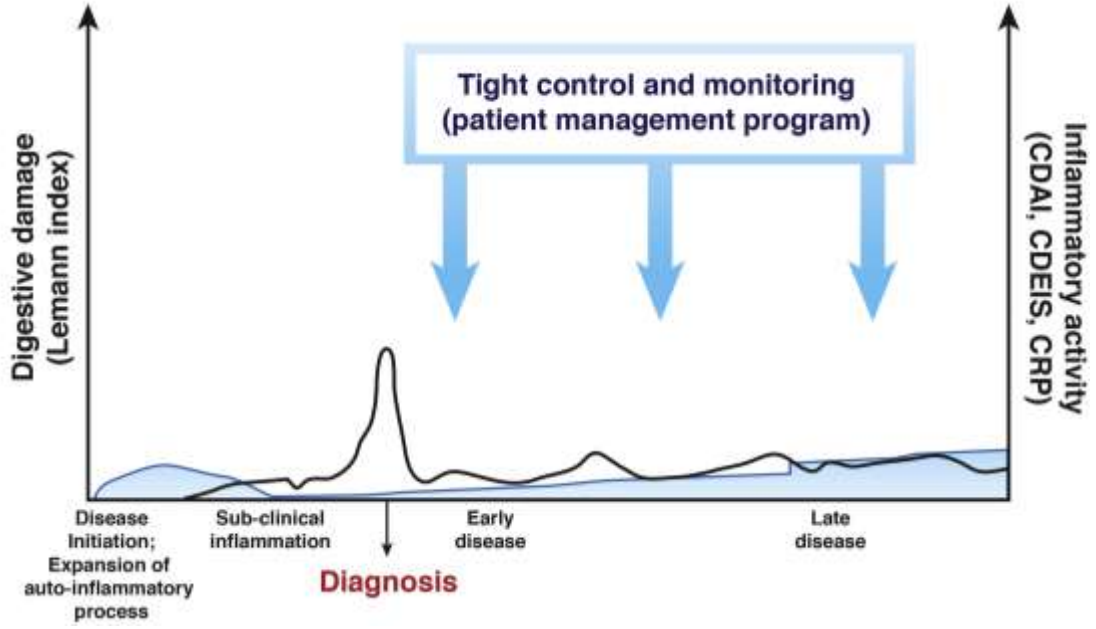
Guideline recommendations may vary with regards to initial therapy for patients with moderate disease[4]

AGA Guidelines | **ACG Guidelines** | **ECCO Guidelines**

*The top-down treatment approach in UC has limited data and further studies are needed to understand this concept in UC. 5-ASA, 5-aminosalicylic acid; ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; ECCO, European Crohn's and Colitis Organisation; IBD, inflammatory bowel disease; UC, ulcerative colitis. 1. Crohn's & Colitis Foundation. Inflammatory Bowel Diseases. Clinical Primer and Care Pathway Tool Kit: https://www.crohnscolitisfoundation.org/sites/default/files/2020-03/Inflammatory%20Bowel%20Disease%20Clinical%20Primer%20and%20Care%20Pathway%20Tool%20Kit.pdf, accessed June 10 2025. 2. Noor N, et al. *Lancet Gastroenterol Hepatol*. 2024;415–427. 3. Colombel JF, et al. *Lancet*. 2017;390(11014):2779–2789. 4. Okobi O et al. *Curues*. 2021;13:e16859.

Disease Modification in CD:
There Is a Clear Window of Opportunity for Intervention[1]



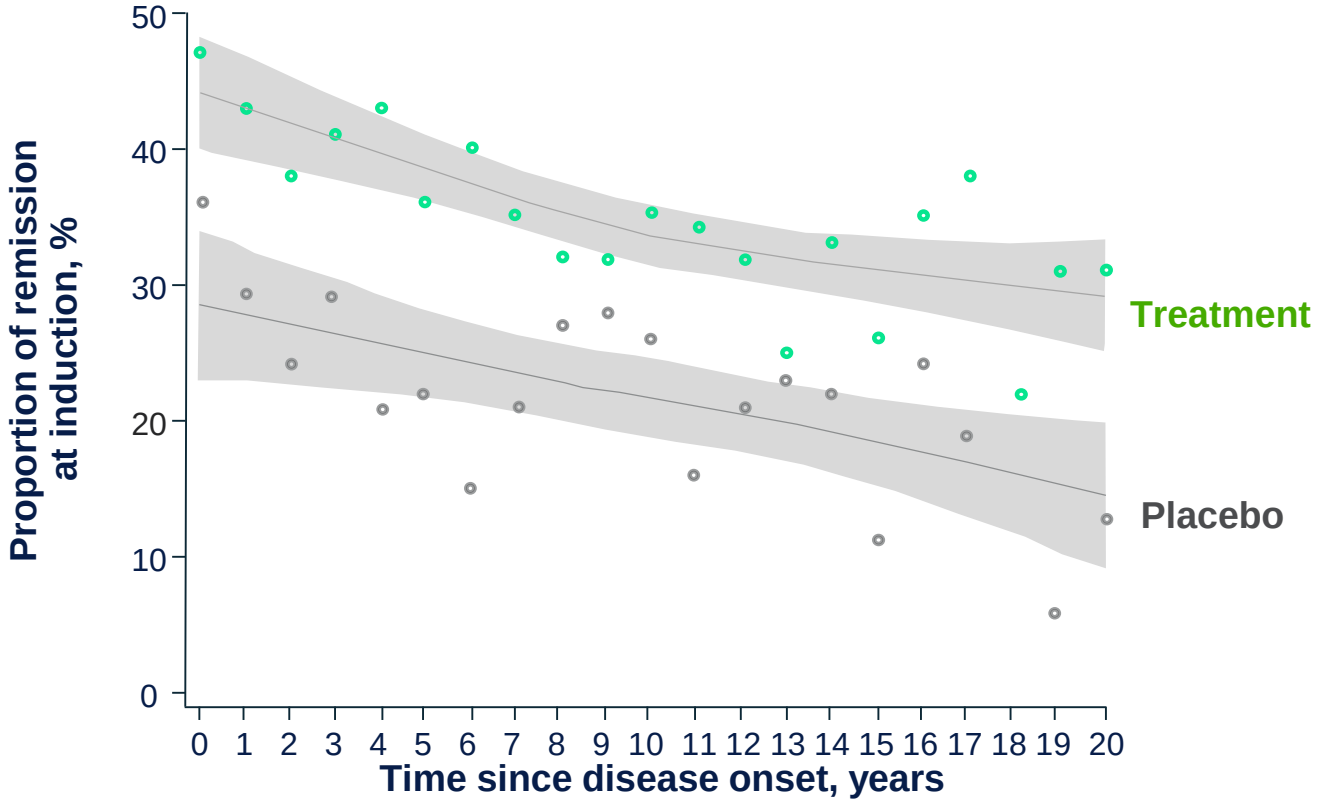


CDAI, Crohn's Disease Activity Index; CDEIS, Crohn`s Disease Endoscopic Index of Severity

1. Colombel JF, et al. *Gastroenterology*. 2017;152:351–361.

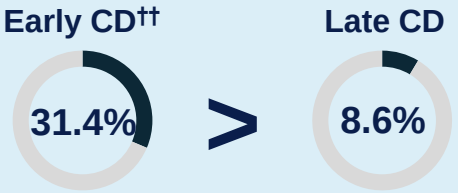
Earlier use of biologic therapies has the potential to improve clinical outcomes in CD[1,2]

Rate of induction remission†‡ by duration of disease at initiation of treatment for CD trials§[1]



In a *post-hoc* analysis LOVE-CD trial (prospective, multicenter, open-label trial):[2]

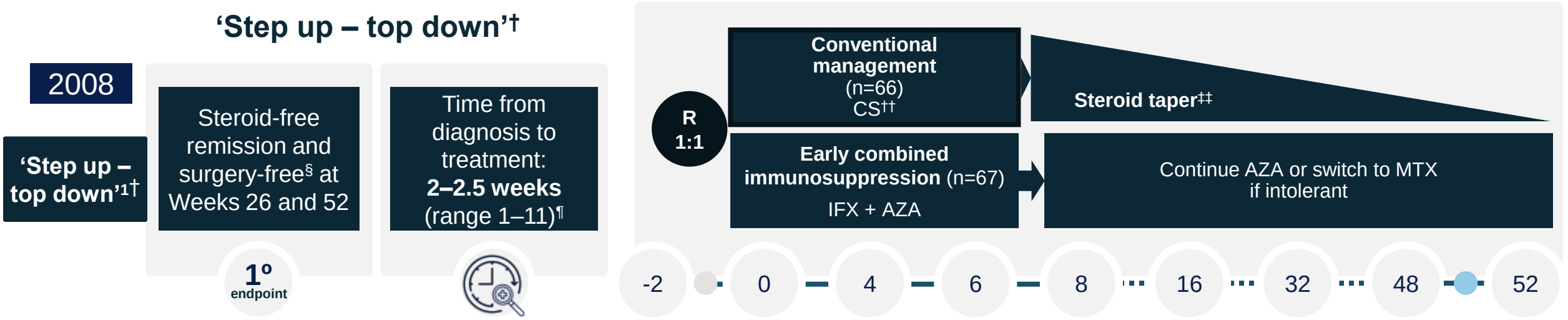
Primary composite endpoint
Clinical and endoscopic remission¶ at Week 26 and 52 respectively



ITT (p=0.001)

†Meta-analysis of 16 randomized placebo-controlled trials of approved biologics in CD; N=6,168. ‡Only clinical and CRP outcomes were examined, as endoscopic data were unavailable for most of the trials. §Dots denote proportion of an outcome averaged per respective year. ¶Defined as CDAI ≤150 and SES-CD <4. ††Early CD was defined as diagnosis <2 years and treatment-naïve OR only treated with corticosteroids and/or immunomodulators; late CD was defined as diagnosis >2 years and previously treated with corticosteroids, immunomodulators, and anti-TNFs.
CDAI, Crohn's Disease Activity Index; CRP, C-reactive protein; ITT, intent-to-treat; SES-CD, Simple Endoscopic Score for Crohn's Disease; TNF, tumour necrosis factor.
1. Figure adapted from: Ben-Horin S, et al. *Gastroenterology*. 2022;162:482–94; 2. D'Haens GR, et al. Presented at the United European Gastroenterology Week (UEGW), 12–15 October 2024, Vienna, Austria: OP147.

Building a history of evidence on early control of CD



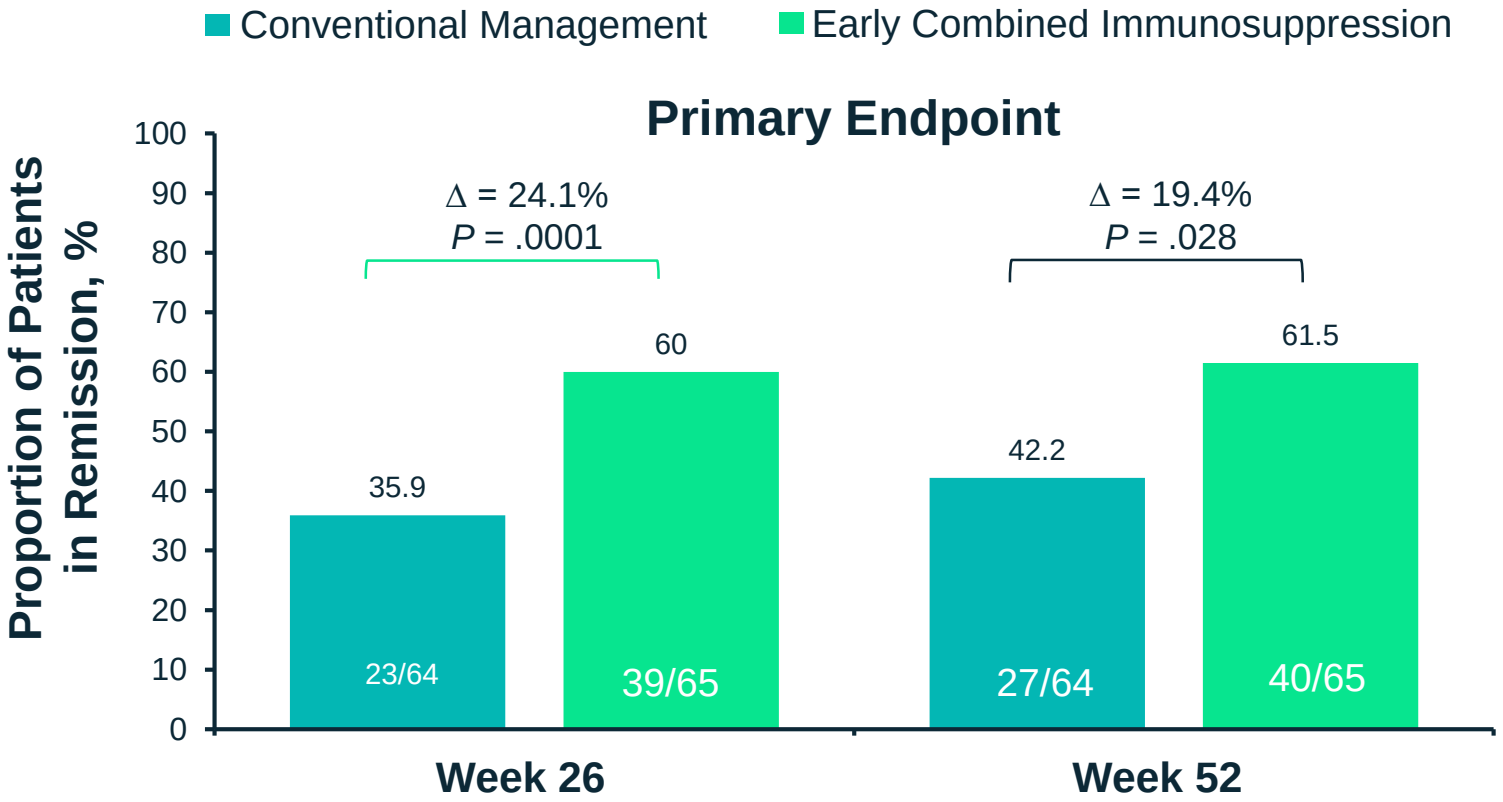
†‘Step up – top down’ was an investigator-initiated, randomized, open-label trial between May 2001 and Jan 2004. ‡PROFILE was a randomized, open-label, active-controlled, biomarker-stratified trial over a 4-year period between Dec 29, 2017 and Jan 5, 2022. Inclusion criteria: Patients had CD diagnosed within 6 months of study start using clinical, endoscopic, histological and radiological methods; active, symptomatic disease (HBI ≥7); biochemical evidence of active inflammation with CRP >ULN, FCP ≥200 µg/g or both; endoscopic evidence of active CD (SES-CD ≥4 for ileal-only disease or ≥6 for ileocolonic/colonic disease), and naïve to immunomodulator and biologic therapy. §‘Surgery’ refers to bowel resection. ¶Active disease was defined as a CDAI >200 for a minimum of 2 weeks before randomization. ††Methylprednisolone or budesonide. ‡‡If patient responded to treatment (after 3 to 8 weeks). §§Randomization stratified by: Biomarker subgroup (IBDhi or IBDlo), endoscopic inflammation (mild, moderate or severe) and extent (colonic or other).

AZA, azathioprine; CDAI, Crohn’s disease activity index; CRP, C-reactive protein; CS, corticosteroids; FCP, fecal calprotectin; HBI, Harvey-Bradshaw Index; IFX, infliximab; IMM, immunomodulator; MTX, methotrexate; PROFILE, predicting outcomes for Crohn's disease using a molecular biomarker; SES-CD, simple endoscopic score for Crohn’s disease; ULN, upper limit of normal.

1. D’Haens G, et al. *Lancet*. 2008;371:660–7; 2. Noor N, et al. *Lancet Gastroenterol Hepatol*. 2024;9:415–27.

Impact of Early Combined Immunosuppression vs Conventional Therapy in CD[1]

Primary endpoint:
Proportion of patients in remission at weeks 26 and 52
Remission = CDAI <150, absence of bowel resection, complete withdrawal of CS

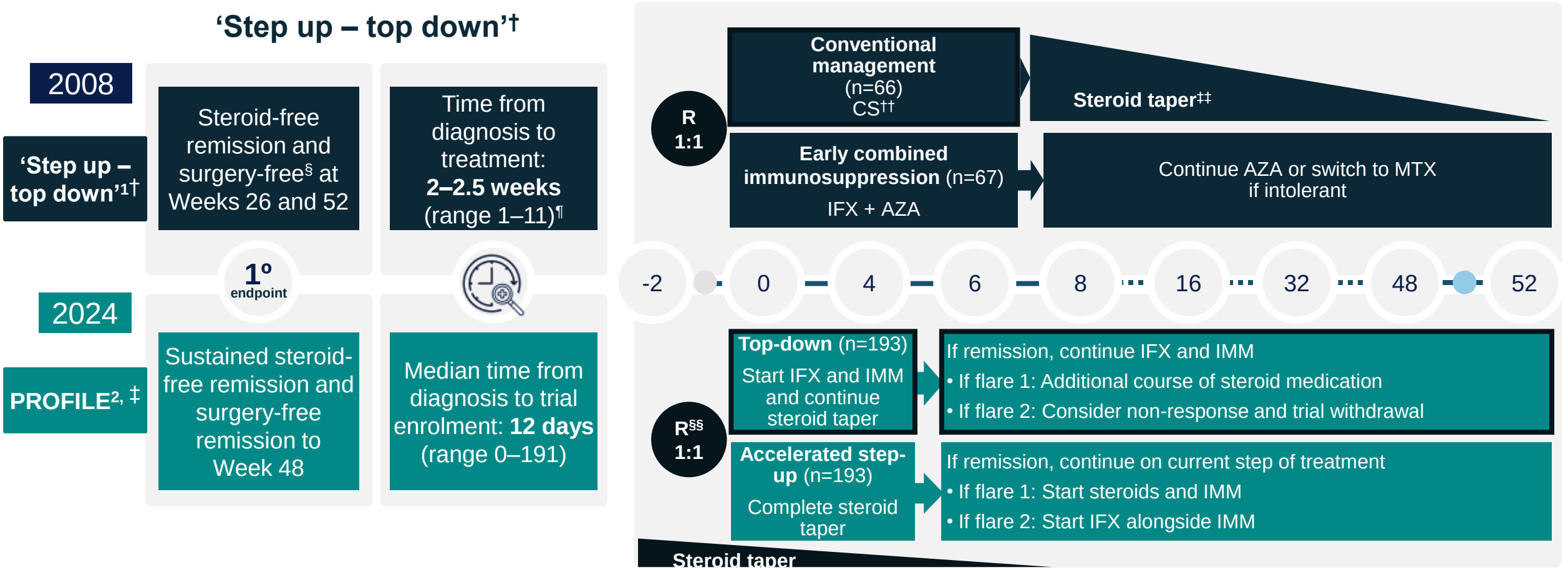


Early combined therapy was more effective than conventional management for inducing remission and reducing steroid use

Serious AEs occurred in 30.8% of early combination group vs 25.3% of conventional therapy group (*P* = 1.0)

1. D'Haens G et al. *Lancet*. 2008;371:660-667. CDAI, Crohn's Disease Activity Index; CS, corticosteroid; AE, adverse event.

Building a history of evidence on early control of CD



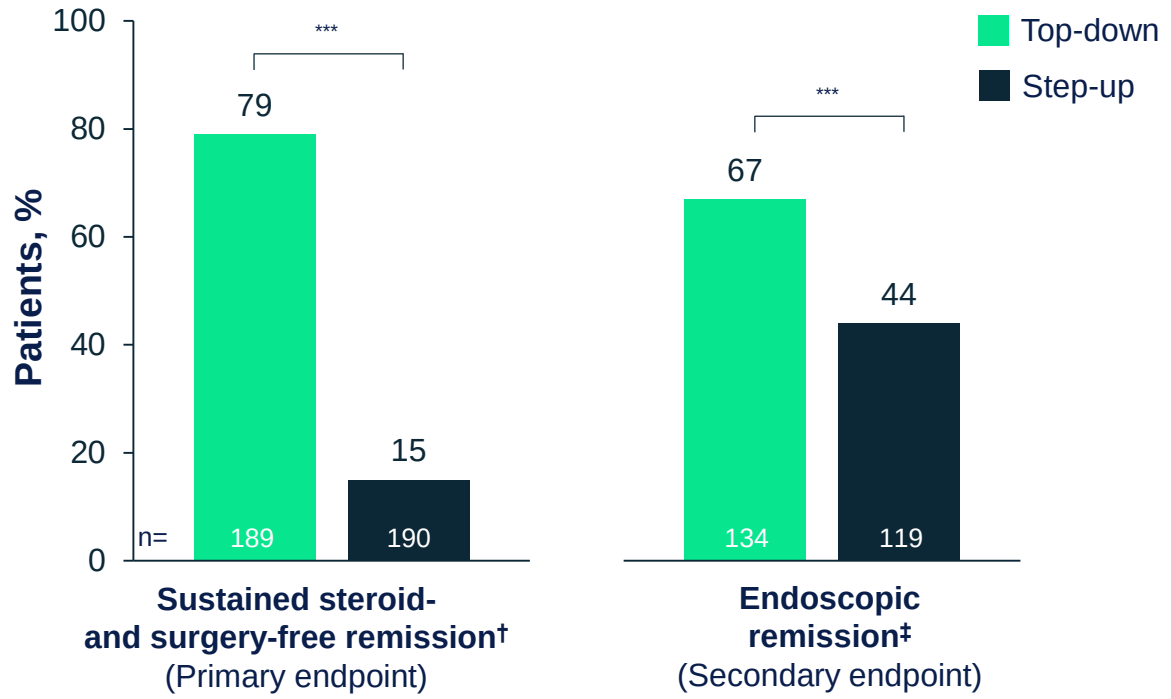
†‘Step up – top down’ was an investigator-initiated, randomized, open-label trial between May 2001 and Jan 2004. ‡PROFILE was a randomized, open-label, active-controlled, biomarker-stratified trial over a 4-year period between Dec 29, 2017 and Jan 5, 2022. Inclusion criteria: Patients had CD diagnosed within 6 months of study start using clinical, endoscopic, histological and radiological methods; active, symptomatic disease (HBI ≥7); biochemical evidence of active inflammation with CRP >ULN, FCP ≥200 µg/g or both; endoscopic evidence of active CD (SES-CD ≥4 for ileal-only disease or ≥6 for ileocolonic/colonic disease), and naïve to immunomodulator and biologic therapy. §‘Surgery’ refers to bowel resection. ¶Active disease was defined as a CDAI >200 for a minimum of 2 weeks before randomization. ††Methylprednisolone or budesonide. ‡‡If patient responded to treatment (after 3 to 8 weeks). §§Randomization stratified by: Biomarker subgroup (IBDhi or IBDlo), endoscopic inflammation (mild, moderate or severe) and extent (colonic or other).

AZA, azathioprine; CDAI, Crohn’s disease activity index; CRP, C-reactive protein; CS, corticosteroids; FCP, fecal calprotectin; HBI, Harvey-Bradshaw Index; IFX, infliximab; IMM, immunomodulator; MTX, methotrexate; PROFILE, predicting outcomes for Crohn's disease using a molecular biomarker; SES-CD, simple endoscopic score for Crohn’s disease; ULN, upper limit of normal.

1. D’Haens G, et al. *Lancet*. 2008;371:660–7; 2. Noor N, et al. *Lancet Gastroenterol Hepatol*. 2024;9:415–27.

For newly diagnosed CD in PROFILE, a top-down treatment approach led to improved outcomes at one year compared with an accelerated step-up approach[1]

Outcomes at Week 48



Significant improvement for all secondary outcomes
(all p<0.0001, except hospital admissions and surgeries, p=0.023)

Fewer disease flares, lower need for steroids and higher QoL
(all p<0.0001)

Fewer AEs and serious AEs, including fewer complications requiring abdominal surgery

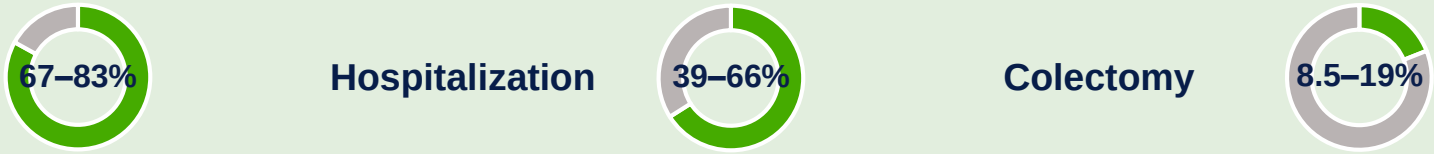
The prognostic biomarker in PROFILE showed no benefit

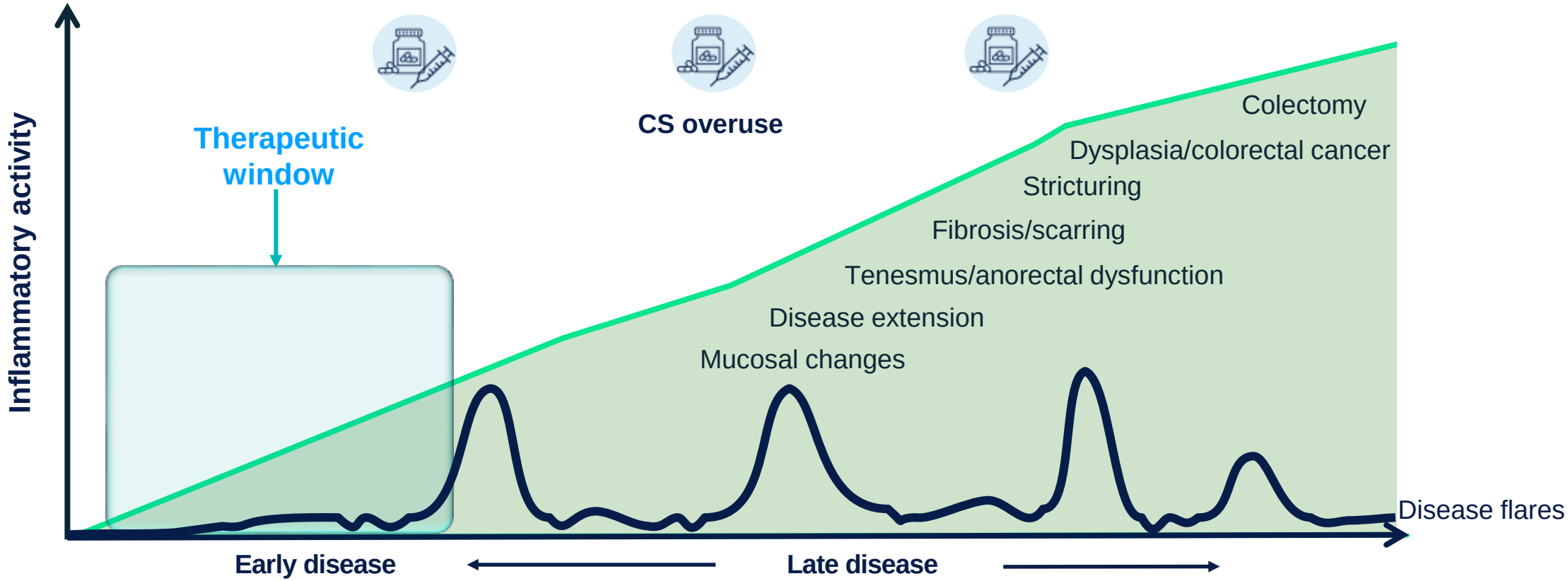
***"Top-down treatment** should be considered **standard of care** for patients with newly diagnosed active CD"*[1]

***p<0.001 vs step-up treatment regimen. Treatment strategies used in PROFILE: Top-down: Early combined immunosuppression with IFX and immunomodulator; accelerated step-up: Conventional. †Steroid- and surgery-free remission: From completion of the protocolized (maximum eight-week) steroid induction course. Remission defined as symptoms being resolved (HBI <5) or inflammatory markers being settled (both CRP ≤ULN and FCP <200 µg/g) or both at all trial visits after BL. ‡Endoscopic remission: SES-CD ulcer subscore of 0 based on centrally read endoscopic scores, or where ileo-colonoscopies had not been videorecorded, locally read SES-CD scores.
AE, adverse event; BL, baseline; CRP, C-reactive protein; FCP, fecal calprotectin; HBI, Harvey-Bradshaw Index; IFX, infliximab; PROFILE, predicting outcomes for Crohn's disease using a molecular biomarker; SES-CD, Simple Endoscopic Score for Crohn's Disease; QoL, quality of life; ULN, upper limit of normal.
1. Noor N, et al. *Lancet Gastroenterol Hepatol*. 2024;9:415–27.

There is a need for early intervention to avoid the long-term impact on uncontrolled inflammation in UC[1-2]

Estimated 10-year cumulative risks in multiple long-term cohort studies in UC[3]





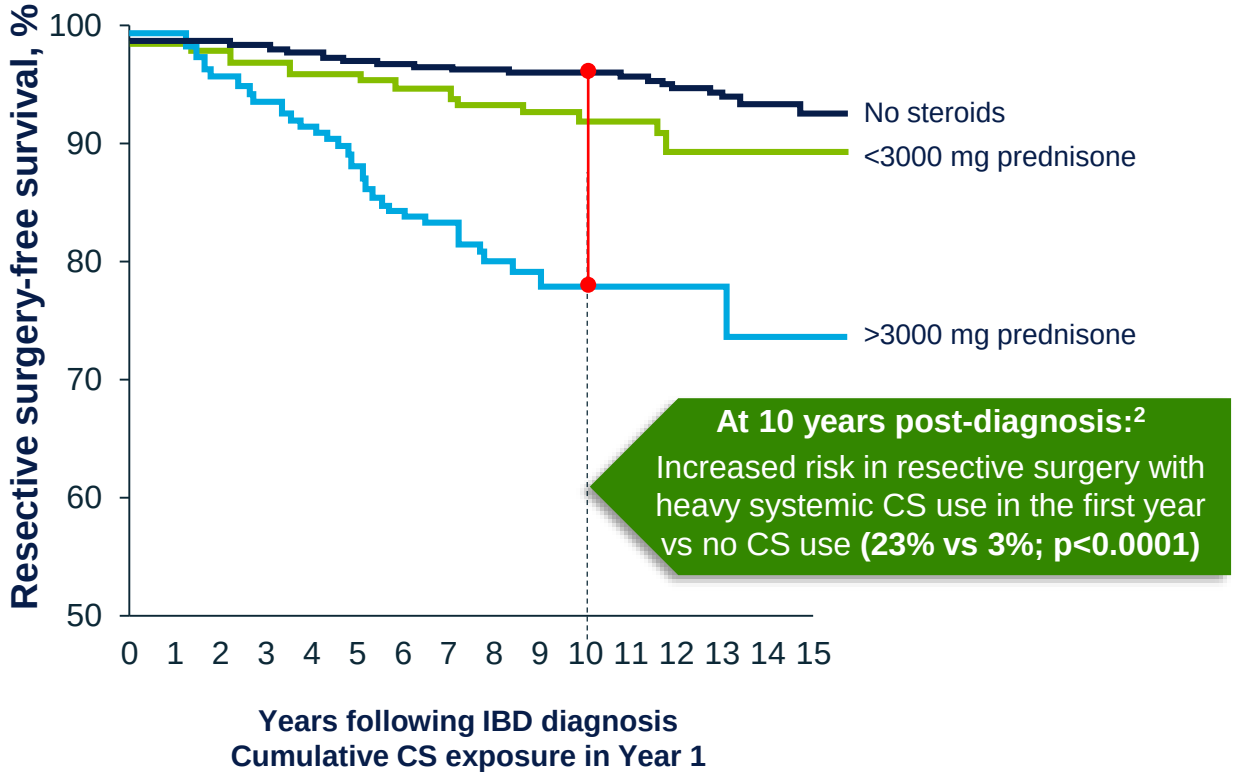
Adapted from 1. Solitano V, et al. *J Clin Med.* 2020;9:2646 and 2. Torres J, et al. *Inflamm Bowel Dis*. 2012;18:1356–63.
3. Fumery M, et al. *Clin Gastroenterol Hepatol*. 2018;16:343–56. CS, corticosteroid.

Delayed initiation of advanced treatment leads to CS overuse in UC

Factors associated with CS use and excess within the last 12 months[1]

- Moderat or severe disease activity vs. mild or inactive ($p<0.05$)
- Number of previous biological therapies ($p<0.05$)
- Ongoing therapy with 5-ASA ($p<0.05$)

Prolonged use of systemic CS in UC is associated with increased risk of resective surgery‡[2]



‡Based on a literature search in MEDLINE using PubMed to identify population-based studies (published in the period from 2010 to 2020) from Europe, which reported the epidemiology and disease course of IBD patients (N=5,300).[2]

1. Nancey S, et al. J clin med. 2024.13,9 2652. 2. Targownik LE, et al. *Inflamm Bowel Dis.* 2014;20:622–30.

CS, corticosteroid

Predictors of higher risk for disease complications in UC

Assessing prognosis at an early stage of inflammation is essential for the development of an appropriate management plan[1–3]

Step-up
Avoid intensive therapy, immunosuppression, and adverse events

Top-down
Assure early intensive therapy to avoid complications and delay disease progression and surgery

SPRINT is an ongoing open label study evaluating step-up vs top-down algorithms in UC[6]

National and international IBD treatment guidelines recommend steroid-sparing therapies for maintenance of clinical remission[7–9]

Immunomodulators

Advanced treatment

Risk factors for poor UC prognosis[4,5]

- Young age at diagnosis†
- Extensive bowel involvement
- Severe endoscopic disease‡
- Prior hospitalization
- High CRP
- Low serum albumin
- *Clostridioides difficile*[10]
- Steroid resistance[11,12]

†Aged <40 years. ‡Spontaneous bleeding and/or ulcerations.

CRP, C-reactive protein. 1. Torres J, et al. *J Crohns Colitis.* 2016;10:1385–94; 2. Burisch J, et al. *J Crohn's Colitis*. 2023;17:2002–11; 3. Solitano V, et al. *J Clin Med*. 2020;9:2646; 4. Rubin DT, et al. *Am J Gastroenterol*. 2019;114:384–413; 5. Magro F, et al. *J Crohns Colitis*. 2017;11:649–70; 6. EU Clinical Trials Register. SPRINT. Available at: https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-003420-16/ES. Accessed: February 2025; 7. Lichtenstein GR, et al. *Am J Gastroenterol.* 2018;113:481–517; 8. Rubin DT, et al. *Am J Gastroenterol*. 2019;114:384–413; 9. Raine T, et al. *J Crohns Colitis*. 2022;16:2–17; 10. Balram B, et al. *J Crohn's Colitis.* 2019;13:27–38; 11. Dubois-Camacho K, et al. *World J Gastroenterol.* 2017;23:6628–38; 12. Jemmali C, et al. *J Crohn's Colitis*. 2020;14:S494–5.

Agenda

- Meet Emma
- Bottom up or top down? – the window of opportunity
- **Unveiling underlying inflammation through holistic monitoring**
- How recent treatment innovations help us aim for higher targets
- Conclusions
- Questions?

STRIDE-II is a strategic framework that can help facilitate the therapeutic management of IBD through tight-monitoring

STRIDE-II suggested algorithm

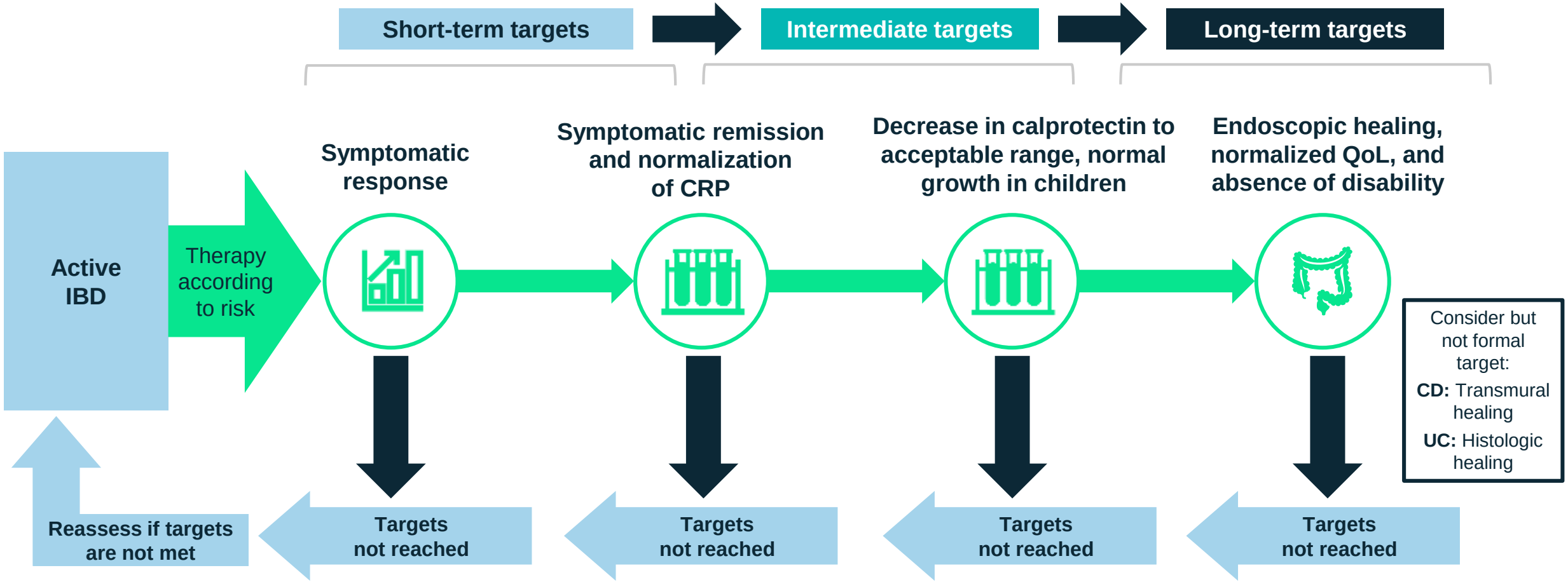


Figure adapted from Turner D, et al. *Gastroenterology.* 2021;160:1570–83.
CRP, C-reactive protein; QoL, quality of lif; STRIDE, Selecting Therapeutic Targets in Inflammatory Bowel Disease.

STRIDE-II defines thresholds for achieving each target

Throughout: Consider changing treatment if target has not been achieved†

Immediate target

Clinical response:
- Decrease of ≥50% in PRO2
  - **CD:** AP and SF
  - **UC:** RB and SF
- Insufficient as long-term target

Intermediate target

Patient outcomes improved when combining targets

Clinical remission:
- CD: PRO2 AP score ≤1 and SF score ≤3 or HBI <5
- UC: PRO2 RB score = 0 and SF = 0, or partial Mayo <3 and no score >1
- Insufficient as long-term target

Normalization of FC and CRP:
- CRP <ULN
- FC 100–250 µg/g‡

Endoscopic healing is commonly defined as MES ≤1, but **MES = 0** (complete endoscopic healing) is associated with **superior disease outcomes**

Long-term target

Endoscopic healing:
- **CD:** SES-CD <3 points or absence of ulcerations§
- **UC:** MES = 0, ≤1; or UCEIS ≤1§

Normalized QoL and absence of disability

Disease duration

†Time to achieving the target varies based on therapy and mechanism. ‡The cut-off value of FC is dependent on the desired outcome. Lower thresholds (e.g. <100 µg/g) have been proposed for reflecting deep healing (both endoscopic and transmural healing) or histologic healing, whereas higher values (e.g. <250 µg/g) reflect less stringent outcomes (e.g. MES of 0 or 1 in UC). §Assessment of EH can be achieved by sigmoidoscopy or colonoscopy. When not feasible, alternatives in CD can be capsule endoscopy or balloon enteroscopy.

AP, abdominal pain; CRP, C-reactive protein; EH, endoscopic healing; FC, fecal calprotectin; HBI, Harvey-Bradshaw Index; MES, Mayo Endoscopic Subscore; PRO2, patient-reported outcome – two items; QoL, quality of life; RB, rectal bleeding; SES-CD, Simple Endoscopic Score for Crohn's Disease; SF, stool frequency; STRIDE, Selecting Therapeutic Targets in Inflammatory Bowel Disease; UCEIS, Ulcerative Colitis Endoscopic Index of Severity; ULN, upper limit of normal.

Turner D, et al. *Gastroenterology*. 2021;160:1570–83.

Are we achieving disease control based on STRIDE-II? (IBD-PODCAST[a])

A non-interventional, cross-sectional, multicenter, multicountry study aiming to estimate the proportion of patients with either CD or UC with **suboptimal disease control** based on STRIDE-II criteria in a real-world setting **across 10 countries**

Suboptimal disease control was reported in:

44%

Of patients with **UC**
(477/1077)

- **Short-term: 21.1%** (26/123)
- **Intermediate-term: 41.2%** (14/34)
- **Long-term: 47.5%** (437/920)

52%

Of patients with **CD**
(578/1108)

- **Short-term: 20.2%** (17/84)
- **Intermediate-term: 20.0%** (15/75)
- **Long-term: 57.5%** (546/949)

[a]A retrospective and cross-sectional study conducted in 10 European countries.

STRIDE, Selecting Therapeutic Targets in Inflammatory Bowel Disease. D'Amico F, et al. *United European Gastroenterol J*. 2024;12(6):705-716.

CS overuse and impaired QoL were identified as key reasons for suboptimal disease control (IBD-PODCAST)

IBD-PODCAST is a non-interventional, cross-sectional, multicenter, multicountry study aiming to estimate the proportion of patients with either CD or UC with **suboptimal disease control** based on STRIDE-II criteria in a real-world setting **across 10 countries**

44% of patients with UC and **52%** of patients with CD were **not adequately controlled** on current therapy due to:†‡

CS overuse

In intermediate-term treatment phase:¶
CD (93.3%) and UC (78.6%)††

In long-term treatment phase:¶
CD (12.3%) and UC (28.4%)††

Impaired QoL§

In long-term treatment phase:¶
CD (64.8%) and UC (66.8%)††

Clinically-significant EIMs

Signs of active inflammation

Fistulas in CD

†77.3% patients with CD and 65.3% patients with UC were on targeted immunomodulators (advanced therapies). ‡At index point. §Impaired QoL: SIBDQ <50 points.
¶The duration of current IBD treatment was calculated during the pre-index period to determine the STRIDE-II-based treatment phase (i.e., short-term phase, intermediate-term phase, or long-term phase).
††Analysis for UC and CD were conducted separately.
CS, corticosteroids; EIM, extraintestinal manifestation; QoL, quality of life; SIBDQ; short inflammatory bowel disease questionnaire; STRIDE, Selecting Therapeutic Targets in Inflammatory Bowel Disease.
D'Amico F, et al. *United European Gastroenterol J*. 2024;12:705–16.

Monitoring includes assessing inappropriate or excess corticosteroid use

ECCO guidelines (CD)

The presence of CS dependency or excess should all warrant a CS-sparing strategy:[1]

- ✓ >1 course of CSs in a year
- ✓ Unable to taper CSs within 3 months of initiation†
- ✓ Relapse within 3 months of stopping CSs

ECCO guidelines (UC)

CS-sparing agents should be initiated for patients showing:[2]

- ✓ CS-refractory disease
- ✓ Intolerance of, or contraindication to, CSs
- ✓ >1 course of CSs in a year
- ✓ A flare upon tapering

CS courses should be limited to a maximum of 3 months

Identify CS excess

Routine follow-up and asking the patient about their CS use[3–5]

Patient information sheet on CSs to all patients[3]

†In CD, an inability to wean CSs below the equivalent of prednisolone 10 mg/day or budesonide 3 mg/day.
CS, corticosteroid; ECCO, European Crohn's and Colitis Organisation.
1. Torres J, et al. *J Crohns Colitis*. 2020;14:4–22; 2. Raine T, et al. *J Crohns Colitis*. 2022;16:2–17; 3. Selinger CP, et al. *Aliment Pharmacol Ther.* 2019;50:1009–18; 4. Ghosh S, et al. *Dig Dis Sci*. 2019;64:1142–9; 5. Selinger CP, et al. *Aliment Pharmacol Ther*. 2017;46:964–73.

Impaired QoL and CS overuse were identified as key reasons for suboptimal disease control (IBD-PODCAST)

44% of patients with UC and **52%** of patients with CD were **not adequately controlled** on current therapy due to:†‡

CS overuse

In intermediate-term treatment phase:¶
CD (93.3%) and UC (78.6%)††

In long-term treatment phase:¶
CD (12.3%) and UC (28.4%)††

Impaired QoL§

In long-term treatment phase:¶
CD (64.8%) and UC (66.8%)††

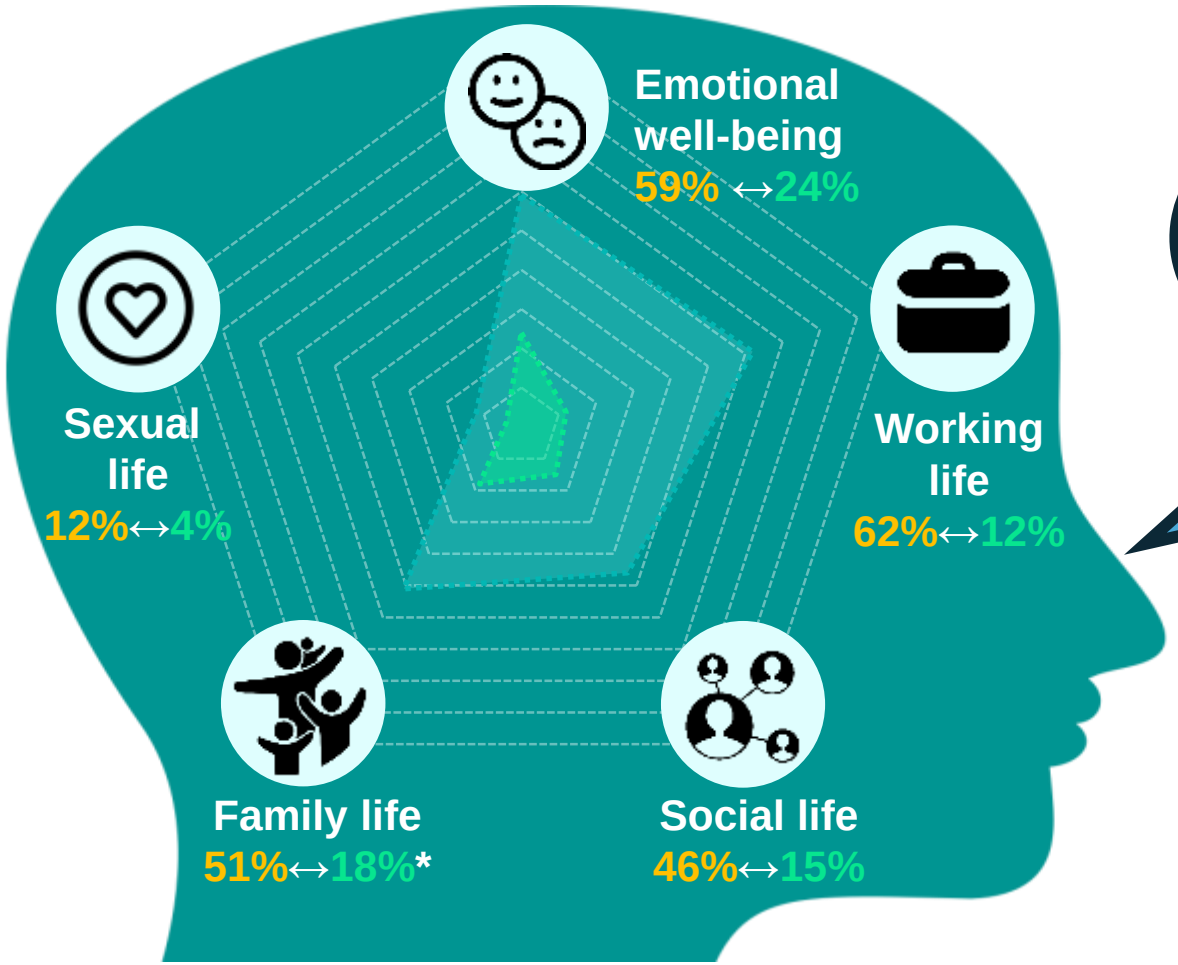
Clinically-significant EIMs

Signs of active inflammation

Fistulas in CD

†77.3% patients with CD and 65.3% patients with UC were on targeted immunomodulators (advanced therapies). ‡At index point. §Impaired QoL: SIBDQ <50 points.
¶The duration of current IBD treatment was calculated during the pre-index period to determine the STRIDE-II-based treatment phase (i.e., short-term phase, intermediate-term phase, or long-term phase).
††Analysis for UC and CD were conducted separately.
CS, corticosteroids; EIM, extraintestinal manifestation; QoL, quality of life; SIBDQ; short inflammatory bowel disease questionnaire; STRIDE, Selecting Therapeutic Targets in Inflammatory Bowel Disease.
D'Amico F, et al. *United European Gastroenterol J*. 2024;12:705–16.

Holistic monitoring is important for capturing the substantial and wide range of intestinal and extraintestinal symptoms affecting patients with IBD[1–7]



…But do we ask our patients questions beyond physical symptoms?

What do patients and physicians think?

How often patients feel they are asked about psychosocial aspects (n=903)[7]

How often HCPs ask their patients about these aspects (n=170)[7]

*All p<0.05; chi-squared test for proportions.

1. Thomassen BJM, et al. *J Crohns Colitis*. 2024;18:371–2; 2. Sudhakar P, et al. *Gut*. 2023;72:192–204; 3. Bressler B, et al. *Gastroenterology*. 2015;148:1035–58.e3;
4. Gordon H, et al. *J Crohns Colitis*. 2024;18:1–37; 5. Farrell D, et al. *J Crohns Colitis*. 2015;10;315–22; 6. Gosh S and Mitchell R. *J Crohns Colitis*. 2007;1:10–20; 7. Marín-Jiménez I, et al. *Inflamm Bowel Dis.* 2017;23:1492–8.

IBD Disk can be used to assess QoL

Patients assess the **impact** of IBD on their **daily lives** using a **10-item questionnaire** with **VAS scores** (“Absolutely disagree” = 0 to “Absolutely agree” = 10) marked on a **colored disk**

1. **Abdominal pain**
2. **Regulating defecation**
3. **Interpersonal interactions**
4. **Education and work**
5. **Sleep**
6. **Energy**
7. **Emotions**
8. **Body image**
9. **Sexual functions**
10. **Joint pain**

- ✓ Monitor IBD-associated disability
- ✓ Set short- and long-term goals
- ✓ Monitor treatment efficacy
- ✓ Encourage adherence
- ✓ Focus on specific issues of disability

Initial assessment
High scores/high disease burden

Therapeutic goal
Low scores/low disease burden

Figure taken from Ghosh S, et al. Inflamm Bowel Dis. 2017;23:333–40.
QoL, quality of life; VAS, visual analog scale.
Ghosh S, et al. Inflamm Bowel Dis. 2017;23:333–40.

STRIDE-II recommends normalization of biomarkers as an intermediate treatment target

FCP and **CRP** are easy, low-cost and **non-invasive** biomarkers that can be used post-induction and **regularly throughout a patient's disease** course

FCP, CRP and ESR can **predict** endoscopic activity

Recommended thresholds:

FCP to 100–250 µg/g	CRP values under ULN

FCP cutoff value is dependent on desired outcome:

Lower FCP thresholds (<100 µg/g) may reflect **endoscopic** and transmural healing (deep healing), or **histological healing**

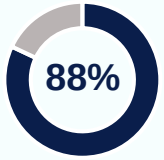
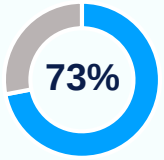
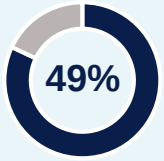
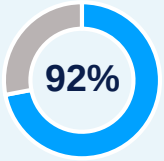
Higher FCP values (<250 µg/g) may reflect **less stringent outcomes** (e.g. MES of 0 or 1 in UC)

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FCP, fecal calprotectin; MES, Mayo endoscopic subscore; STRIDE, Selecting Therapeutic Targets in Inflammatory Bowel Disease; ULN, upper limit of normal.

Turner D, et al. *Gastroenterology*. 2021;160:1570–83.

Biomarkers (FCP and CRP) correlate with disease activity

FCP is a highly sensitive diagnostic tool in estimating endoscopic IBD activity; while CRP has higher specificity, it has lower sensitivity vs FCP[1,2]

	Sensitivity†	Specificity†	AUC†
FCP[3]	 95% CI (84–90%)‡	 95% CI (66–79%)‡	**0.89** (0.86–0.91%)‡
CRP[3]	 (34–64%)‡	 (72–98%)‡	**0.72** (0.68–0.76)‡

Two measurements of **FCP**, 1 month apart, may best predict flares before clinical symptoms[2]

A **combination** of **FCP** with **clinical activity indices or CRP** may be better to assess endoscopic activity and healing vs FCP alone[4]

†Meta-analysis of 19 studies (N=2,499) in patients with previously diagnosed UC or CD presenting with symptoms suggestive of endoscopically active disease.[3] ‡95% CI.
AUC, area under the curve; CI, confidence interval; CRP, C-reactive protein; FCP, fecal calprotectin.

1. Rokkas T, *J Gastrointestin Liver Dis.* 2018;27:299–306; 2. Turner D, et al. *Gastroenterology.* 2021;160:1570–83; 3. Mosli MH, et al. *Am J Gastroenterol. 2015*;110:802–19; 4. Bodelier A, et al. *Dig Dis Sci.* 2017;62:465–72.

CALM Trial: Impact of Timely Therapy Escalation in CD[1,2]

Clinical Management

Prednisone burst and taper followed by

No adalimumab (wk 0-11)

Adalimumab 160 → 80 → 40 Q2W (wk 12-23)

Adalimumab 40 QW (wk 24-35)

- Adalimumab 40 Q2W de-escalation

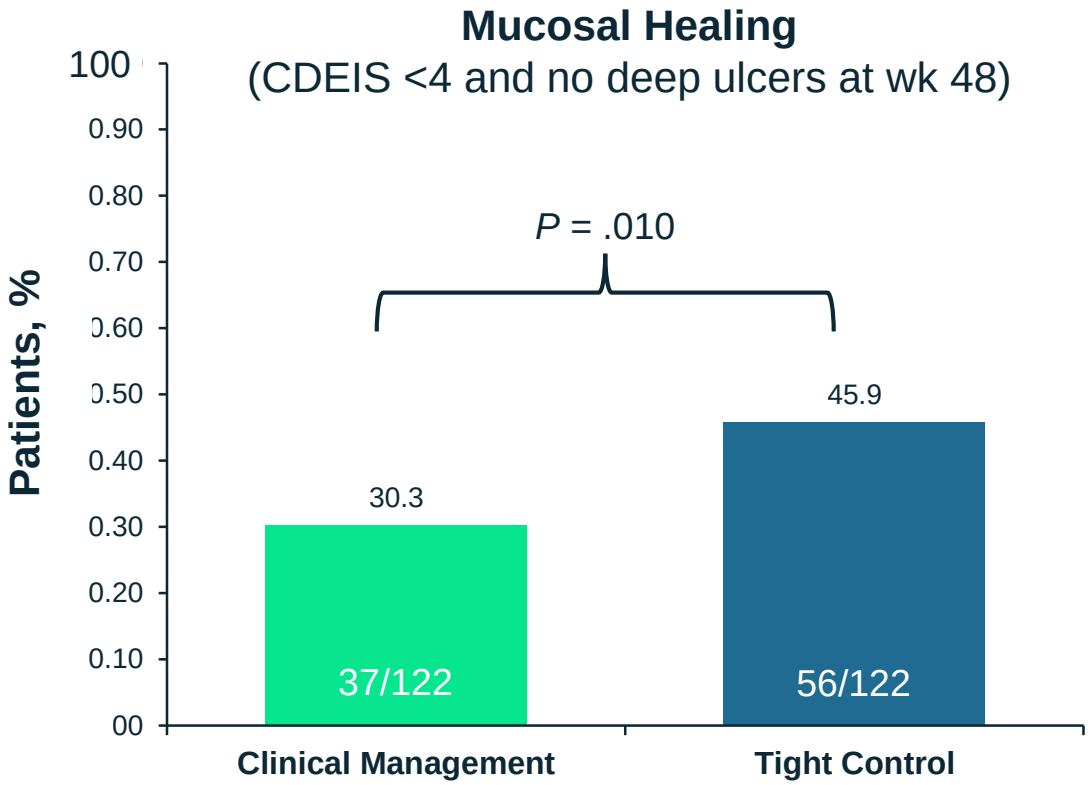
Adalimumab QW + AZA (wk 36-48)

- Adalimumab 40 Q2W + azathioprine de-escalation

Tight Control

Prednisone burst and taper followed by

- Escalation of therapy driven by CDAI, fecal calprotectin, CRP, and prednisone use

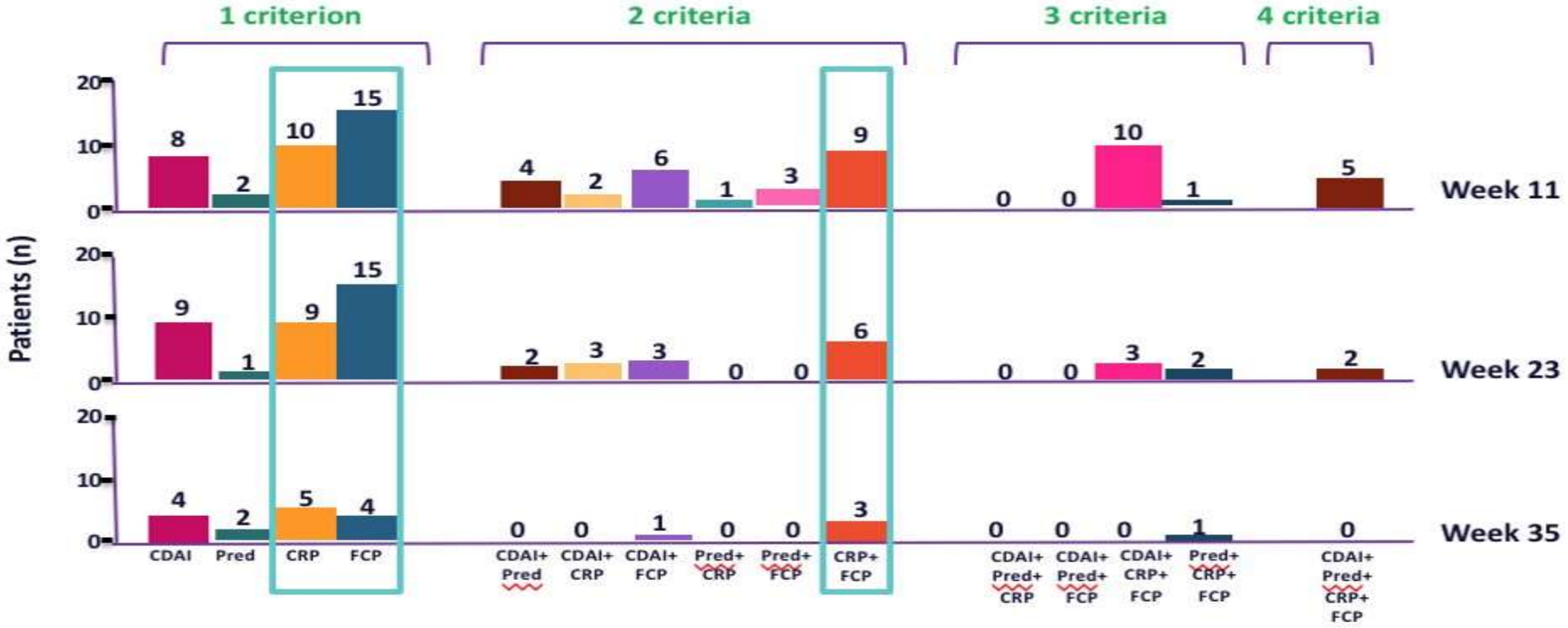


Proportion of patients reaching CDEIS <4 and no deep ulcers was greater in those with FC <250 mcg/g (74%, *P* < .001) FC <250 mcg/g, CRP <5 mg/L, and CDAI <150 → sensitivity/specificity of 72%/63% CDEIS <4 with no deep ulcers 48 wk after randomization → positive/negative predictive values of 86%/42%

1. Colombel et al. *Lancet*. 2018;390:2779. 2. Reinisch W et al. *Inflamm Bowel Dis*. 2020;26:1562-1571.

Wk, week; Q2W, every 2 weeks; QW, every week; CDAI, Crohn's disease activity index; CDEIS, Crohn's Disease Endoscopic Index of Severity; FC, fecal calprotectin.

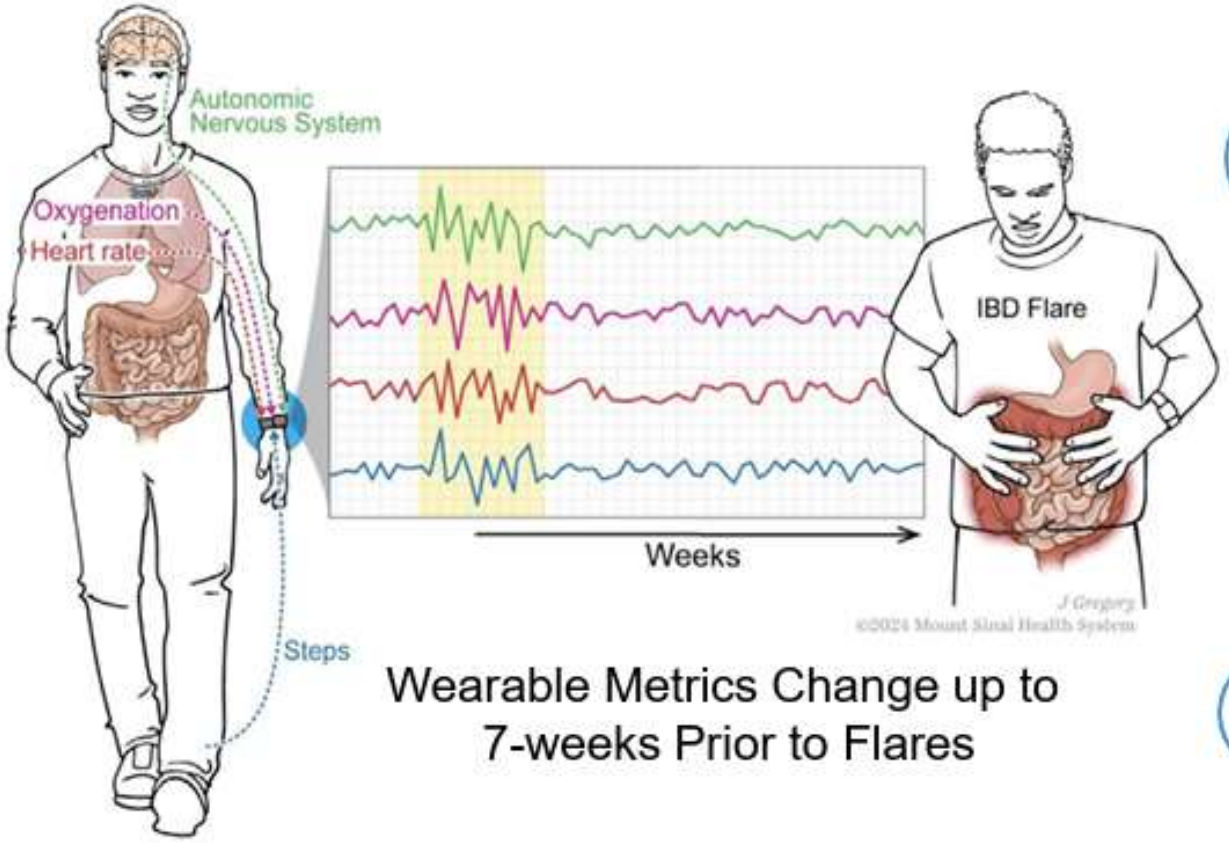
Biomarkers were important for driving treatment escalation in the CALM trial[1]



- The most common reason for escalation was biomarkers (FC/CRP) rather than symptoms (CDAI)
- Managing patients with CD by clinical symptoms alone may not adequately control underlying inflammation
- Biomarker levels (CRP and FC) can guide treatment dose increases that lead to superior endoscopic and clinical outcomes

1. Reinisch W et al. Inflamm Bowel Dis. 2020;18;26:1562-1571. CDAI, Crohn's disease activity index; FC, fecal calprotectin; Pred; Prednison.

Physiologic data collected from wearable devices may identify and predict IBD flares[1]



- 309 participants across 36 states
- Circadian patterns of heart rate variability identify inflammatory and symptom flares
- Heart rate and resting heart rate are higher during inflammatory and symptom flares
- Lower daily steps during inflammatory flares
- Wearable metrics identify subclinical inflammation and whether inflammation is present during symptom flares

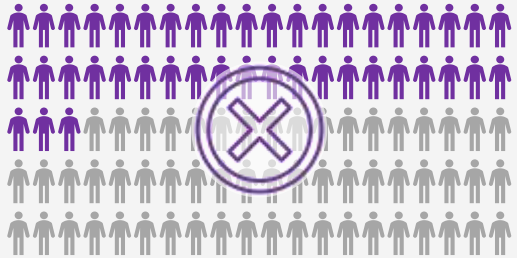
1. Hirten RP et al. Gastroenterology 2025;168:939–951

Mucosal healing is associated with improved long-term outcomes and less complications for patients with CD

In a meta-analysis of 673 patients with CD from 12 studies, achieving mucosal healing was associated with durable outcomes†[1]

Long-term clinical remission (≥50 weeks) was achieved by:

69% of patients WITH mucosal healing at first assessment‡
(n/N=193/280)



43% of patients WITHOUT mucosal healing at first assessment‡
(n/N=131/308)

Evidence from other studies indicates that mucosal healing is also associated with:§

Lower risk of:

- Disease progression[2]
- Future CS treatment[3]
- Inflammation after 5 years[3]
- Hospitalization[4]
- Treatment failure[4]
- Surgery[1,3,4]

Increased rates of CS-free remission and CS-free remission without flares[5]

To modify the natural course of CD and gain long-term control, treatment must go beyond symptomatic remission[6]

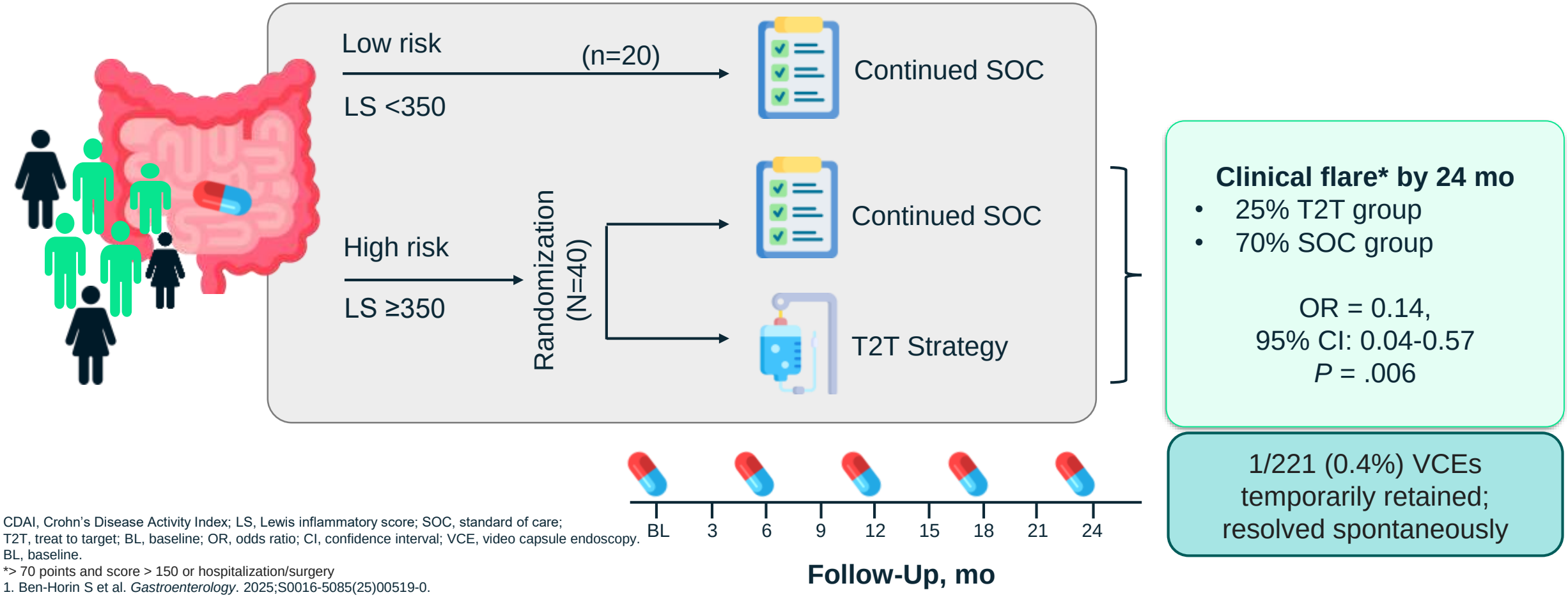
†Study design: The impact of mucosal healing attained after medical therapy for CD was assessed in a meta-analysis of 673 patients from 12 studies, which included eight non-randomized, prospective, observational cohort studies; three *post-hoc* analyses of randomized clinical trials; and one randomized clinical trial. Definitions of mucosal healing: Eight studies defined mucosal healing as an SES-CD of 0 or a complete absence of ulcerations; the remaining studies defined mucosal healing as SES-CD 0–2 and no ulcerations observed, Lewis Score <135, SES-CD 0–3, or an endoscopic score of 0 or 1 on a scale of up to 2. ‡At least one endoscopic assessment of mucosal healing either by upper endoscopy, enteroscopy, colonoscopy, and/or video capsule endoscopy performed between one month from study outset and six months prior to the last follow-up. §Definitions of mucosal healing vary. Please refer to the specific definitions of endpoints within the individual publications.

CS, corticosteroid; SES-CD, Simple Endoscopic Score for Crohn's Disease.

1. Shah SC, et al. *Aliment Pharmacol Ther*. 2016:43:317–33; 2. Ungaro RC, et al. *Gastroenterology*. 2020;159:139–47; 3. Frøslie KF, et al. *Gastroenterology*. 2007;133:412–22; 4. Yzet C, et al. *Clin Gastroenterol Hepatol*. 2020;18:2256–61; 5. Baert F, et al. *Gastroenterology*. 2010;138:463–8; 6. Atreya R and Neurath MF. *Visc Med*. 2017;33:82–8.

Video Capsule Endoscopy as a T2T Measurement Strategy[1]

Patients with small bowel-involved (L1/L3) CD in corticosteroid free clinical remission (CDAI < 150)



Clinical flare* by 24 mo

- 25% T2T group
- 70% SOC group

OR = 0.14,
95% CI: 0.04-0.57
P = .006

1/221 (0.4%) VCEs temporarily retained; resolved spontaneously

CDAI, Crohn's Disease Activity Index; LS, Lewis inflammatory score; SOC, standard of care; T2T, treat to target; BL, baseline; OR, odds ratio; CI, confidence interval; VCE, video capsule endoscopy.
BL, baseline.
*> 70 points and score > 150 or hospitalization/surgery

1. Ben-Horin S et al. *Gastroenterology*. 2025;S0016-5085(25)00519-0.

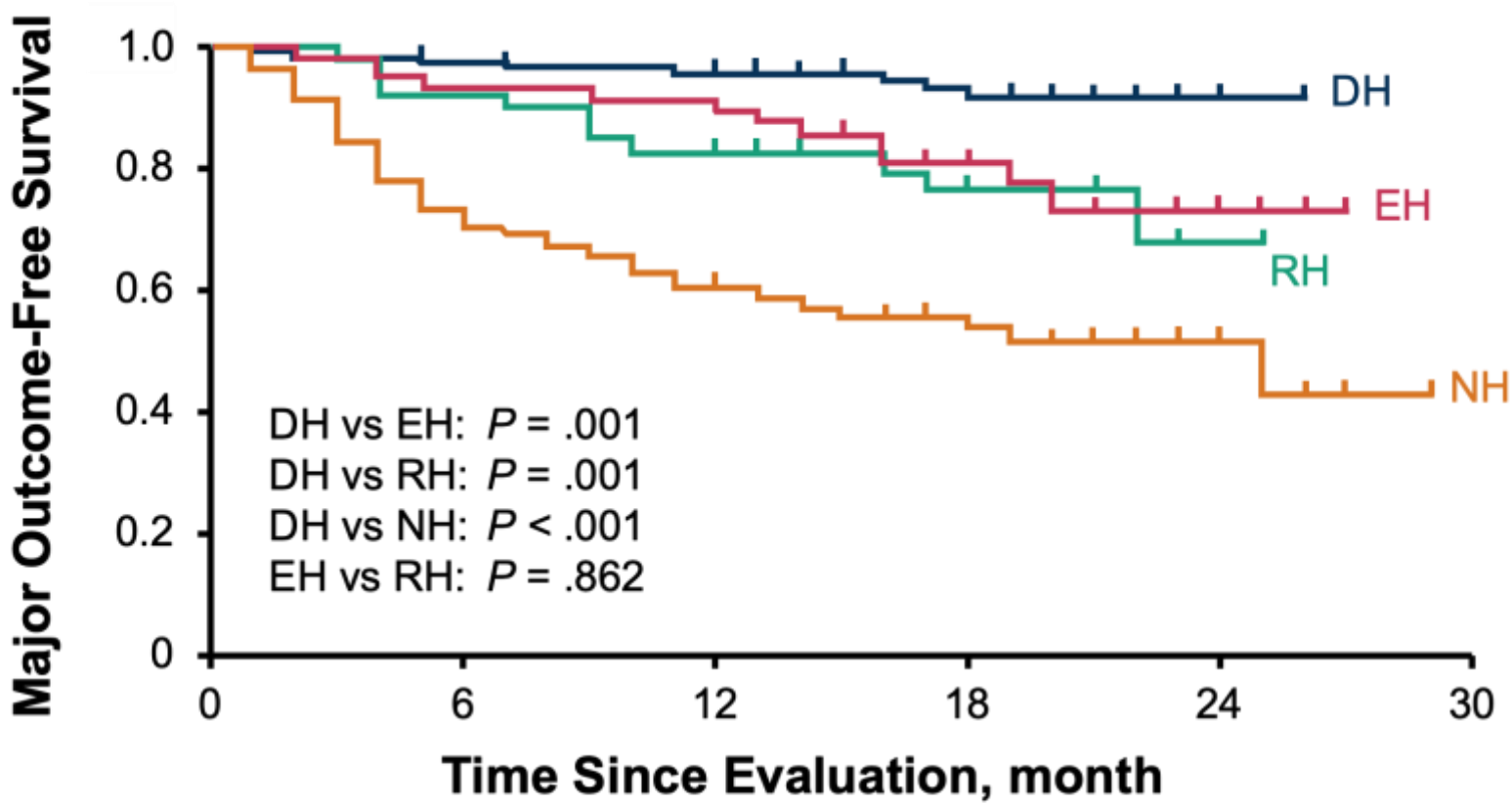
Deep Healing Is Associated With Long-Term Outcomes in CD[1]

Deep Healing (DH)

Presence of both endoscopic healing (EH) and radiologic healing (RH)

Non-Healing (NH)

Absence of both EH and RH

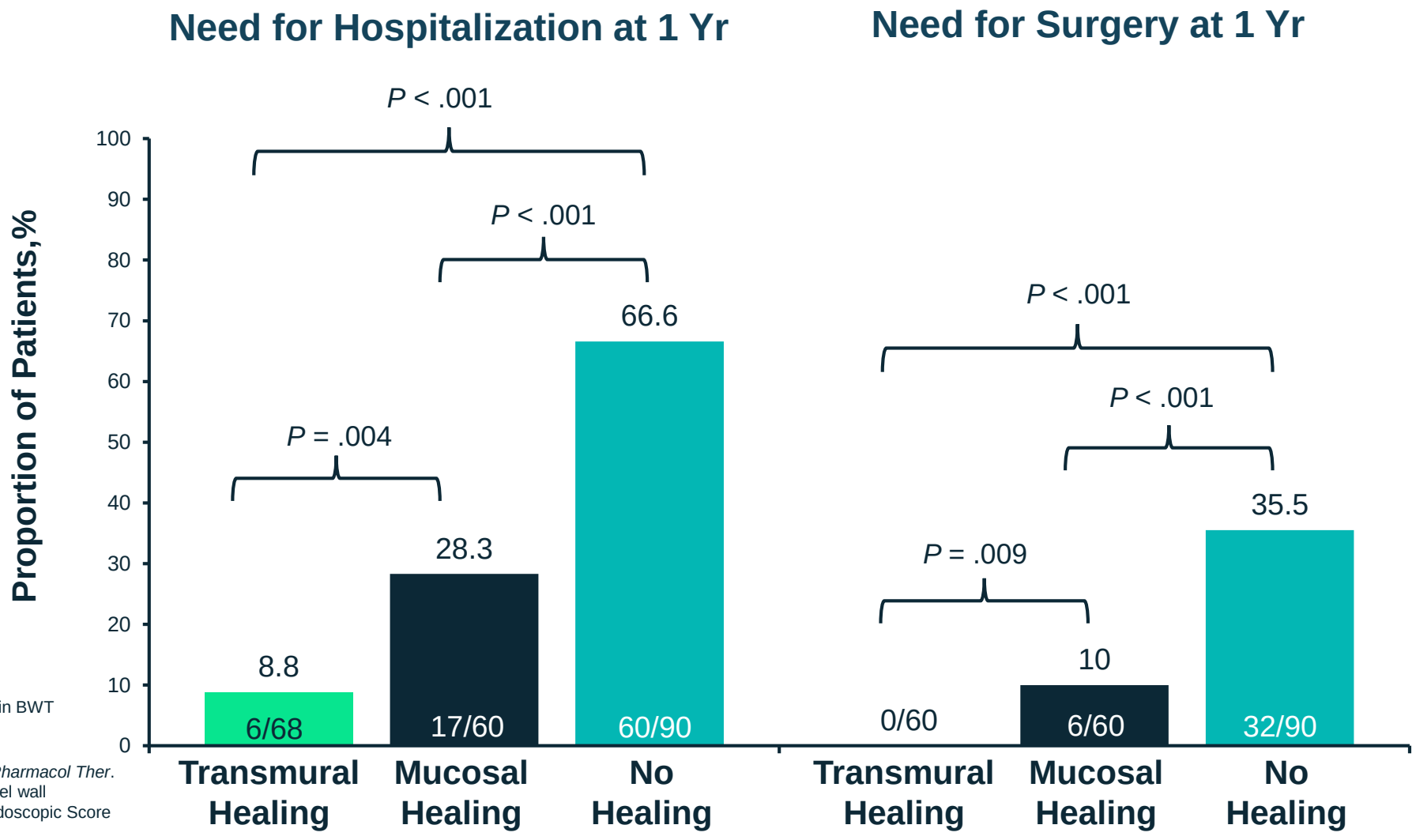


No. at Risk					
DH	114	11	99	53	3
EH	59	53	48	23	2
RH	41	37	29	20	1
NH	178	114	88	38	5

Major outcomes were defined as: anti-TNF dose intensification, switch to other biologics, CD-related bowel resection, and hospitalization.

1. Oh K et al. *Clin Transl Gastroenterol*. 2022;13:e00442.

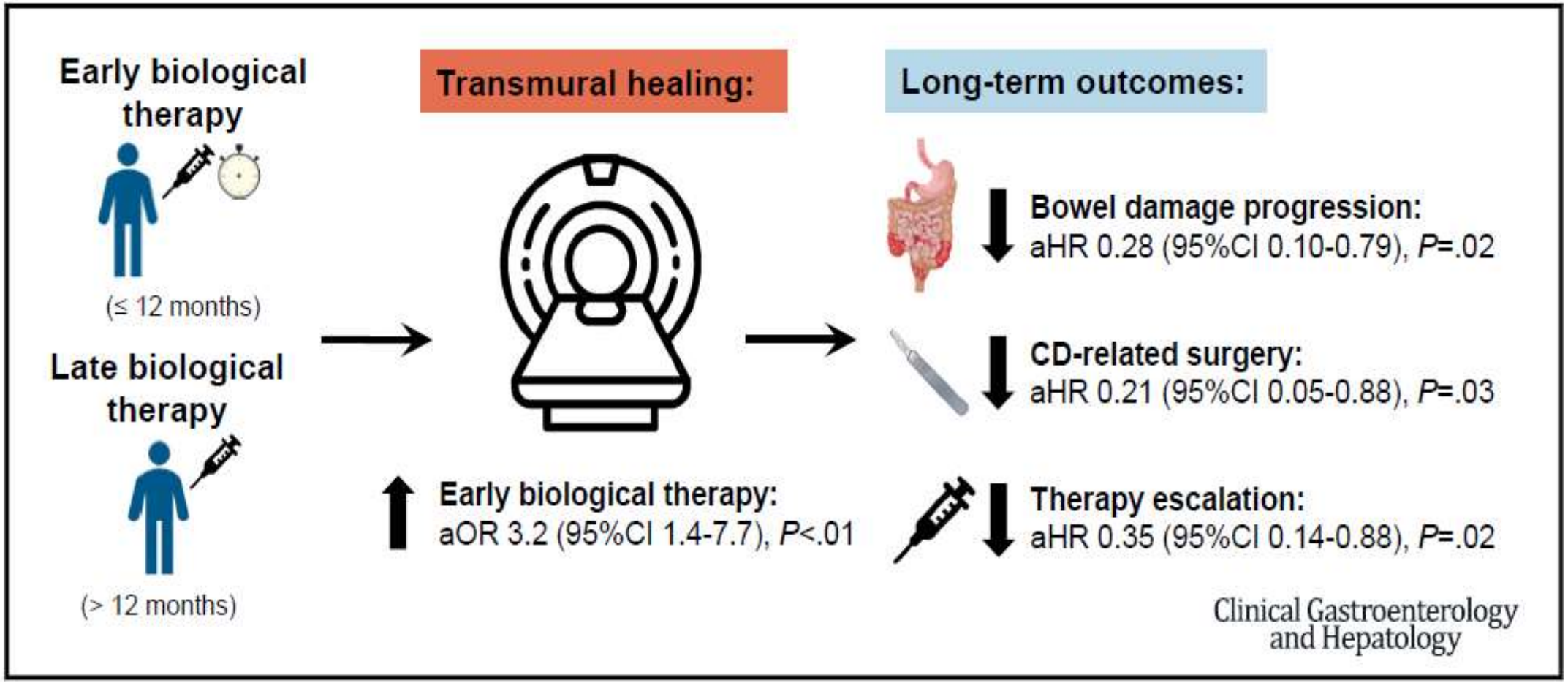
Transmural Healing Is Better Than Mucosal Healing[1]



Transmural Healing: decrease in BWT to values ≤3 mm
Mucosal Healing: SES-CD ≤2

1. Castiglione F et al. *Aliment Pharmacol Ther*. 2019:49;1026-1039. BWT, bowel wall thickness; SES-CD, Simple Endoscopic Score for Crohn Disease

Early biological therapy within 12 months of diagnosis leads to higher transmural healing rates in Crohn's disease



aOR, adjusted odds ratio; CI, confidence interval; aHR, adjusted hazard ratio. Transmural healing was defined as complete normalization of all MRE parameters.

Revés J, et al. Clin gastro hep. 2025.23,7: 1194-1203.e2.

MRE and IUS are Both Sensitive for Detecting Ileal Inflammation in CD[1]

Sensitivity and Specify of MRE and Ultrasound for the Extent and Presence of Small Bowel and Colonic Disease Against the Consensus Reference

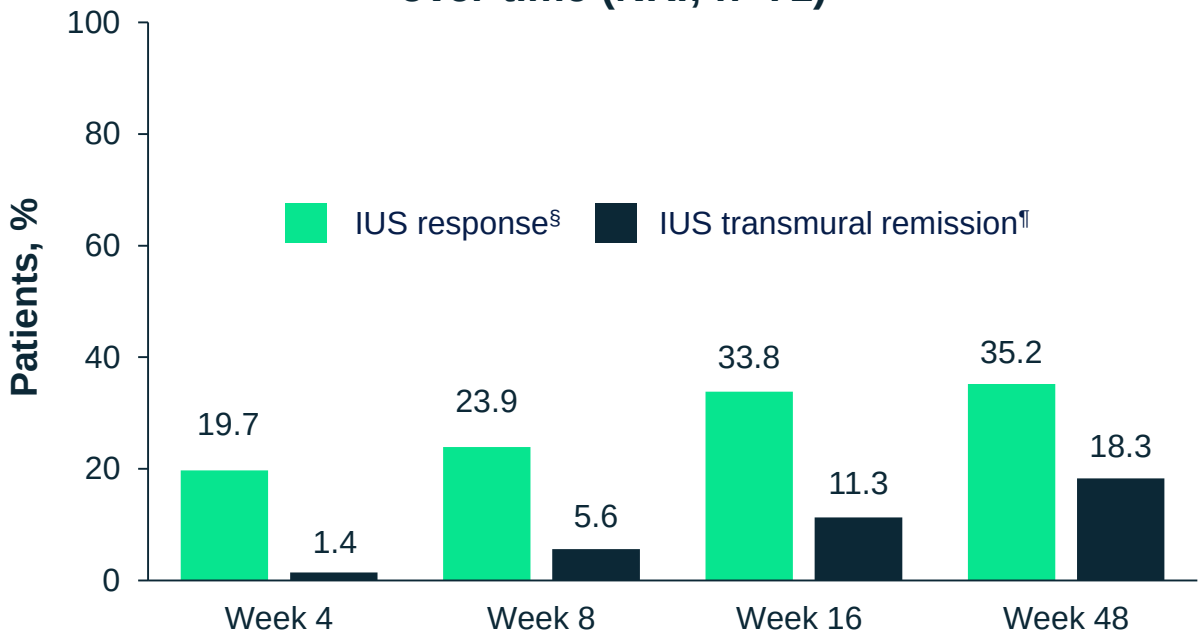
Test	TP	FN	FP	TN	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Small bowel disease extent						
MRE	171	62	5	46	80 (72-86)	95 (85-98)
Ultrasound	152	81	13	38	70 (62-78)	81 (64-91)
Small bowel disease presence						
MRE	210	23	5	46	97 (91-99)	96 (86-99)
Ultrasound	193	40	13	38	92 (84-96)	84 (65-94)
Colonic disease extent						
MRE	35	94	17	138	22 (14-32)	93 (87-97)
Ultrasound	29	100	17	138	17 (10-27)	93 (87-97)
Colonic disease presence						
MRE	76	53	17	138	64 (50-75)	96 (90-98)
Ultrasound	84	45	17	138	73 (59-83)	96 (90-98)

CI, confidence interval; FN, false negative; FP, false positive; MRE, magnetic resonance enterography; TN, true negative; TP, true positive

1. Taylor SA et al. *Lancet Gastroenterol Hepatol*. 2018;3:548-558

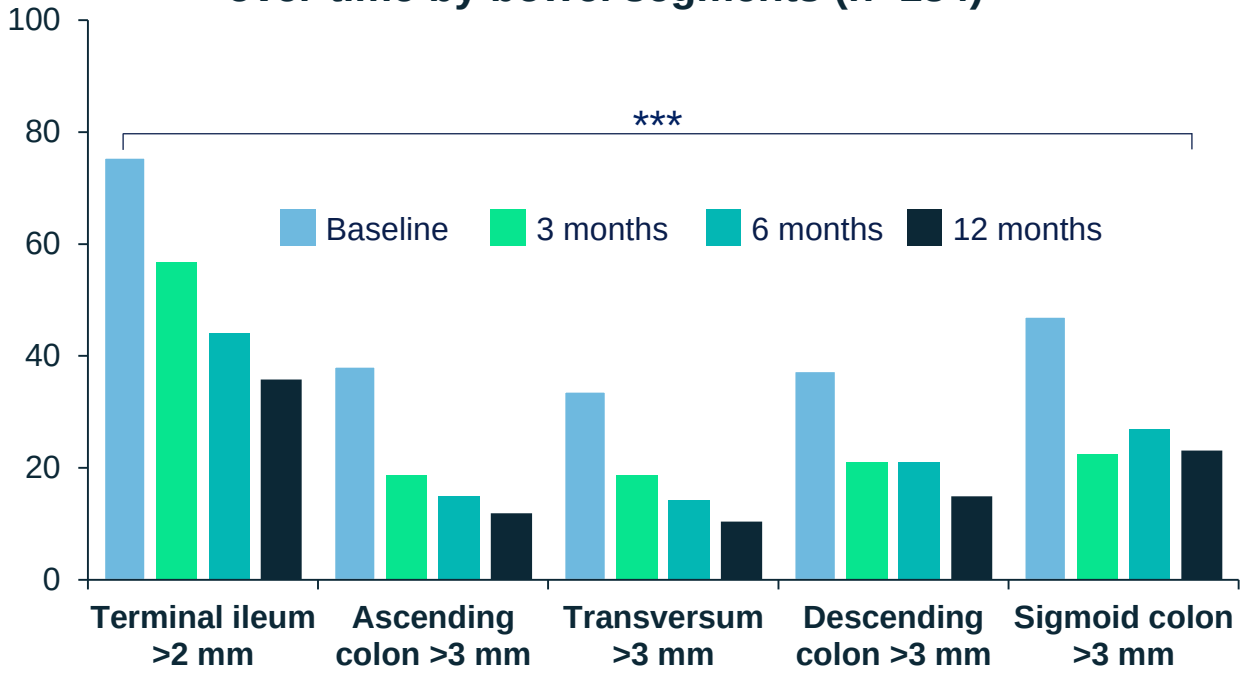
IUS can be used to monitor early response to treatment in CD

STARDUST: IUS response and transmural remission over time (NRI; n=71)†[1]



IUS response and transmural remission **progressively increased** through Week 48 with biologic therapy and was observed **as early as Week 4**[1]

TRUST: Proportion of patients with change in BWT over time by bowel segments (n=134)‡[2]



BWT significantly improved in **all bowel segments**, and normalization was detectable via IUS **3 months** after treatment intensification[2]

***p<0.001 for all visits vs BL per segment.
†Most affected bowel segment at BL by IUS used for all analyses. ‡12-month multicenter, prospective, non-interventional study of 234 patients with CD experiencing a flare (HBI ≥7) who received treatment intensification, mostly with an anti-TNF. §IUS response: ≥25% BWT reduction from BL. ¶Transmural remission: Normalization of BWT, blood flow (color Doppler signal), bowel wall stratification and inflammatory mesenteric fat.
BL, baseline; BWT, bowel wall thickness; CRP, C-reactive protein; HBI, Harvey-Bradshaw Index; IUS, intestinal ultrasound; NRI, non-responder imputation; SoC, standard of care; STARDUST; Study of Treat to Target Versus Routine Care Maintenance Strategies in CD Patients treated with Ustekinumab; TNF, tumor necrosis factor; TRUST, transabdominal ultrasonography of the bowel in subjects with Crohn's disease to monitor disease activity; T2T, treat-to-target. 1. Kucharzik T, et al. *Clin Gastroenterol Hepatol*. 2023;21:153–63 and supplementary data; 2. Kucharzik T, et al. *Clin Gastroenterol Hepatol*. 2017;15:535–42.

Benefits and limitations of IUS in IBD

Benefits

- **Inexpensive** and **widely available**[1–3]
- Good correlation with **MH** and **endoscopy**[2,3]
- **Accurate**[1,2]
- Used at **POC**[1]
- **Sensitive**[4]
- **Non-invasive**[1]

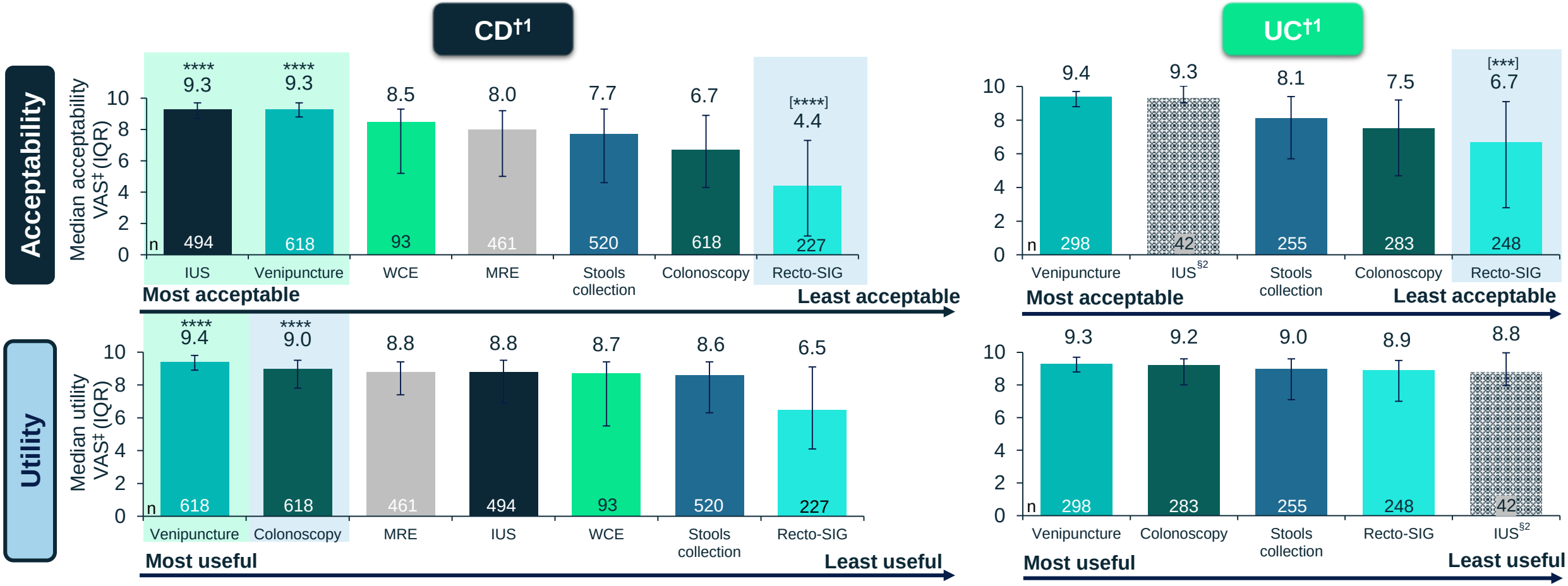
Limitations

- Require **experienced practitioners**[5]
- Exam may be **limited by** the patient's **physique** and **body build**[5]
- **Limited visualization**[6]
- Precise measurement of disease extent is difficult in **extensive small bowel CD**[6]
- Limited visualization of **rectum in UC**[7]
- Overlying bowel gas may obscure **proximal (duodenal) disease**[6]
- Challenges in **standardizing IUS results** in **clinical practice**[6]

CT, computerized tomography; IUS, intestinal ultrasound; MH, mucosal healing; MRI, magnetic resonance imaging; POC, point-of-care.

1. Maaser C, et al. *J Crohns Colitis.* 2019;13:144–64; 2. Nardone OM, et al. *Front Med*. 2022;9:898092; 3. Kucharzik T, et al. Clin Gastroenterol Hepatol. 2023;21:153–63; 4. Cleveland NK. et al. *Curr Gastroenterol Rep*. 2024;26:31–40; 5. Wilkens R, et al. Gastroenterology. 2022;162:1476–1492; 6. Chavannes M, Clin Gastroenterol Hepatol. 2024;22:1790–95. 7. de Voogd, Floris et al. Gastroenterology, 2022;163:1569 - 1581

IUS, biomarkers, WCE and MRE are more acceptable forms of monitoring tools than endoscopic procedures for patients with IBD



Data for IUS acceptability and utility in UC have been sourced from an alternate reference. No conclusions or comparisons should be made based on these data.

Figures adapted from 1. Buisson A, et al. *Inflamm Bowel Dis*. 2017;23:1425–33; 2. Rajagopalan A, et al. *JGH Open*. 2019;4:267–72.

****Most acceptable/useful; p<0.0001 vs other monitoring tools. [***]Least acceptable; p<0.0001 vs other monitoring tools. [****]Least acceptable; p<0.001 vs other monitoring tools.

†Nationwide survey of patients with IBD: Of 923 collected questionnaires, 916 were suitable for analysis (CD patients, n=618; UC patients, n=298).[1] ‡VAS ranged from 0 (absolutely unacceptable or useless) to 10 (totally acceptable or useful).[1]

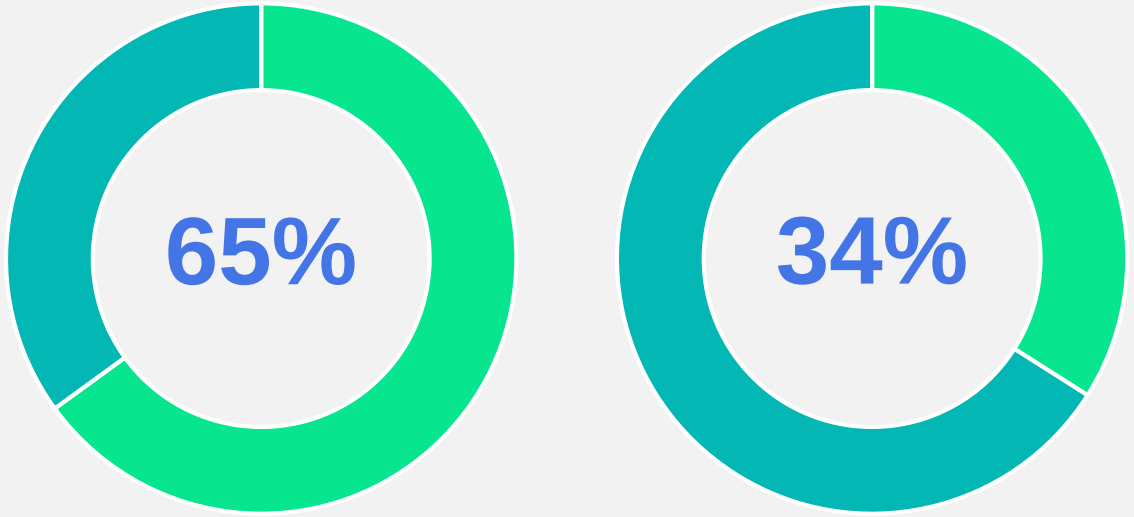
§Study of 121 consecutive patients who underwent IUS and completed questionnaire within study period (patients with CD; n=79, patients with UC; n=42).[2]

IQR, interquartile range; IUS, intestinal ultrasound; MRE, magnetic resonance enterocolonography; Recto-SIG, rectosigmoidoscopy; VAS, visual analog scale; WCE, wireless capsule endoscopy.

Mastering inflammation to achieve mucosal healing should be the aim of treatment in UC to improve long-term clinical outcomes[1]

In a meta-analysis of 2,073 patients from 13 studies, achieving mucosal healing† led to sustained outcomes[1]

Long-term clinical remission (≥52 weeks and at least 6 months after MH1)‡ achieved by:[1]



of patients WITH MH1
(n/N=461/712)

of patients WITHOUT MH1
(n/N=226/669)

Evidence from other studies indicates that mucosal healing is also associated with:

- Lower rates of relapse[2,3]
- Increased corticosteroid-free remission[1,4,5]
- Lower rates of hospitalization[5,6]
- Decreased need for surgery, e.g. colectomy[1,5]
- Decreased impact on work and leisure activities[7]

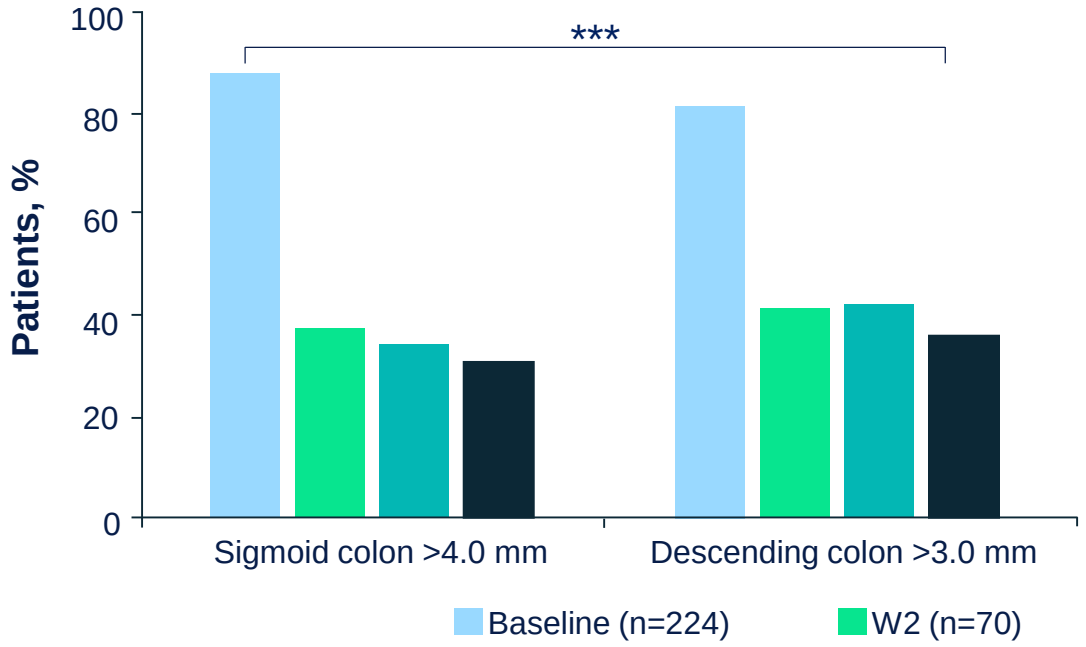
In patients in clinical remission, those with worsening bowel symptoms are **more likely to relapse if they have not achieved mucosal healing**[8]

†**Mucosal healing** MES = 0/1, although two studies defined mucosal healing as ESS = 0.[1]
‡At least one endoscopic assessment after initiation of UC therapy performed between 1 and 6 months from study outset to assess for mucosal healing.[1]
ESS, endoscopic subscore; MES, Mayo Endoscopic Subscore; MH1, mucosal healing at first assessment.

1. Shah C, et al. *Clin Gastroenterol Hepatol.* 2016;14:1245–55.e8; 2. Yoon H, et al. *Gastroenterology.* 2020;159:1262–75.e7; 3. Barreiro-de Acosta M, et al. *J Crohns Colitis.* 2016;10:13–9; 4. Colombel JF, et al. *Gastroenterology*. 2011;141:1194–201; 5. Rubin T, et al. *Am J Gastroenterol*. 2019;114:384–413; 6. Ardizzone S, et al. *Clin Gastroenterol Hepatol*. 2011;9:483–9; 7. Armuzzi A, et al. *BMC Gastroenterol*. 2020;20:18; 8. Horio R, et al. *JGH Open*. 2024;8:e70011.

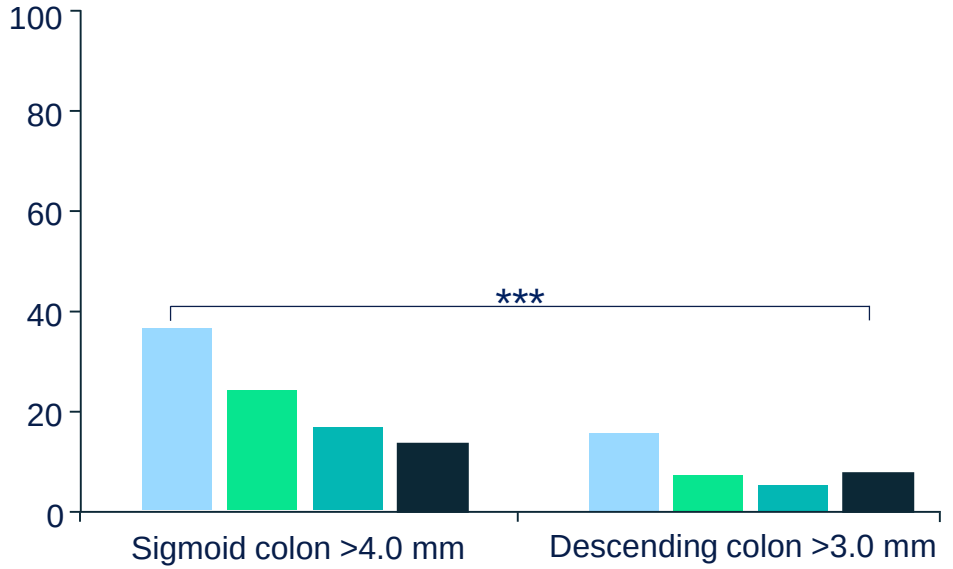
IUS can also be used to assess short-term treatment response in UC (TRUST&UC)

Increased bowel wall thickness over time†



BWT correlated with endoscopic disease activity (p=0.001)†‡, indicating that monitoring BWT alone has the potential to inform treatment decisions

Increased bowel vascularization over time†



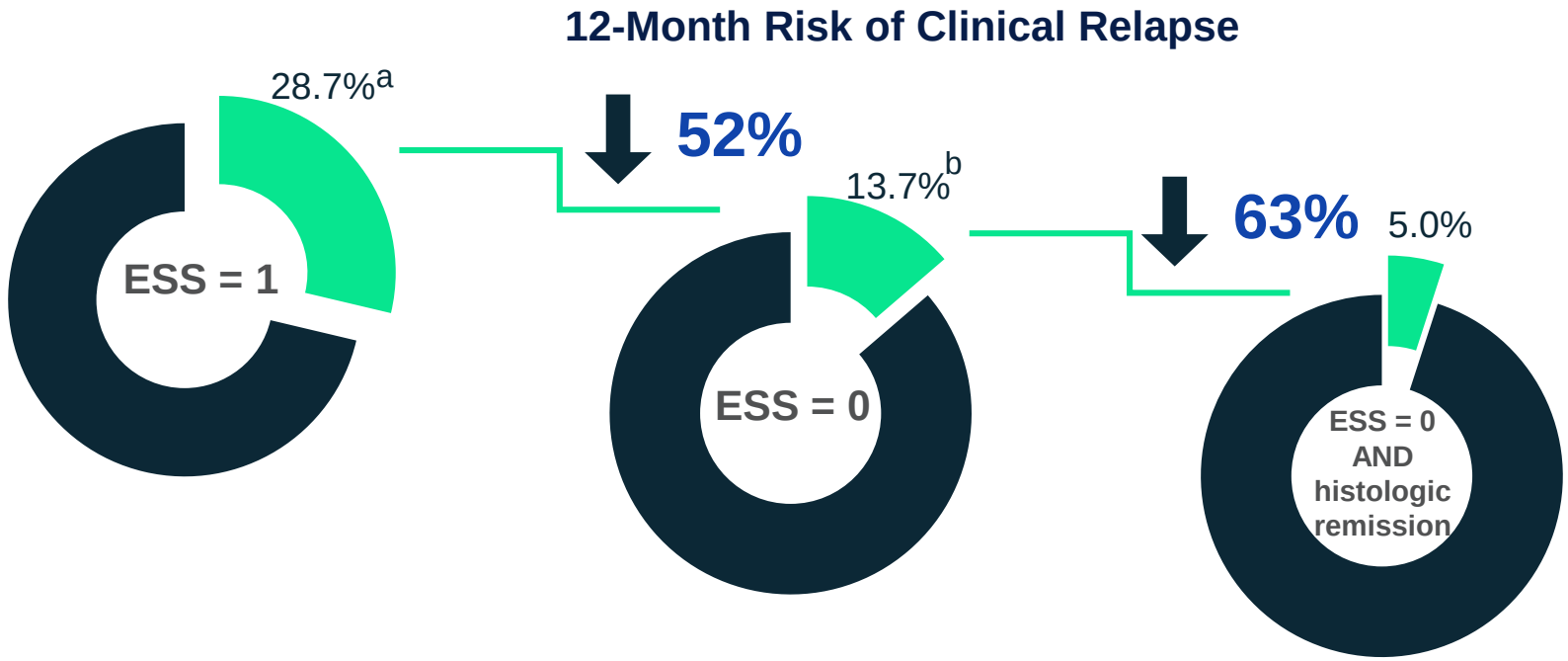
IUS can be used to visualize the large bowel and quantify inflammation and disease-related complications

***p<0.001 vs BL.
†A prospective, observational study, performed between November 2015 to March 2018 at 42 German IBD-specialized centers representing different care levels including outpatient and inpatient care sites (45.2% IBD-specialized general practices, 38.1% general hospitals, and 16.7% university hospitals). ‡In a subset of patients (n=63, endoscopy date ±7 days from the date of the study visit)
BWT, bowel wall thickness; IUS, intestinal ultrasound; TRUST&UC, TRansabdominal Ultrasonography of the bowel in Subjects with IBD To monitor disease activity with UC; W, week.
Maaser C, et al. *Gut*. 2020;69:1629–36 and supplementary data.

The Benefit of Long-Term Outcomes in Achieving Stringent Endoscopic and Histologic Remission in UC

A systematic review and meta-analysis of patients with UC in clinical remission showed that:

Patients achieving more rigorous treatment endpoints (endoscopic and histologic remission) had a **substantially lower risk of clinical relapse** compared with patients achieving clinical remission



ESS, endoscopic subscore.
[a]Median 12-month risk of clinical relapse; [b]Estimated annual clinical relapse based on median 12-month risk of clinical relapse.

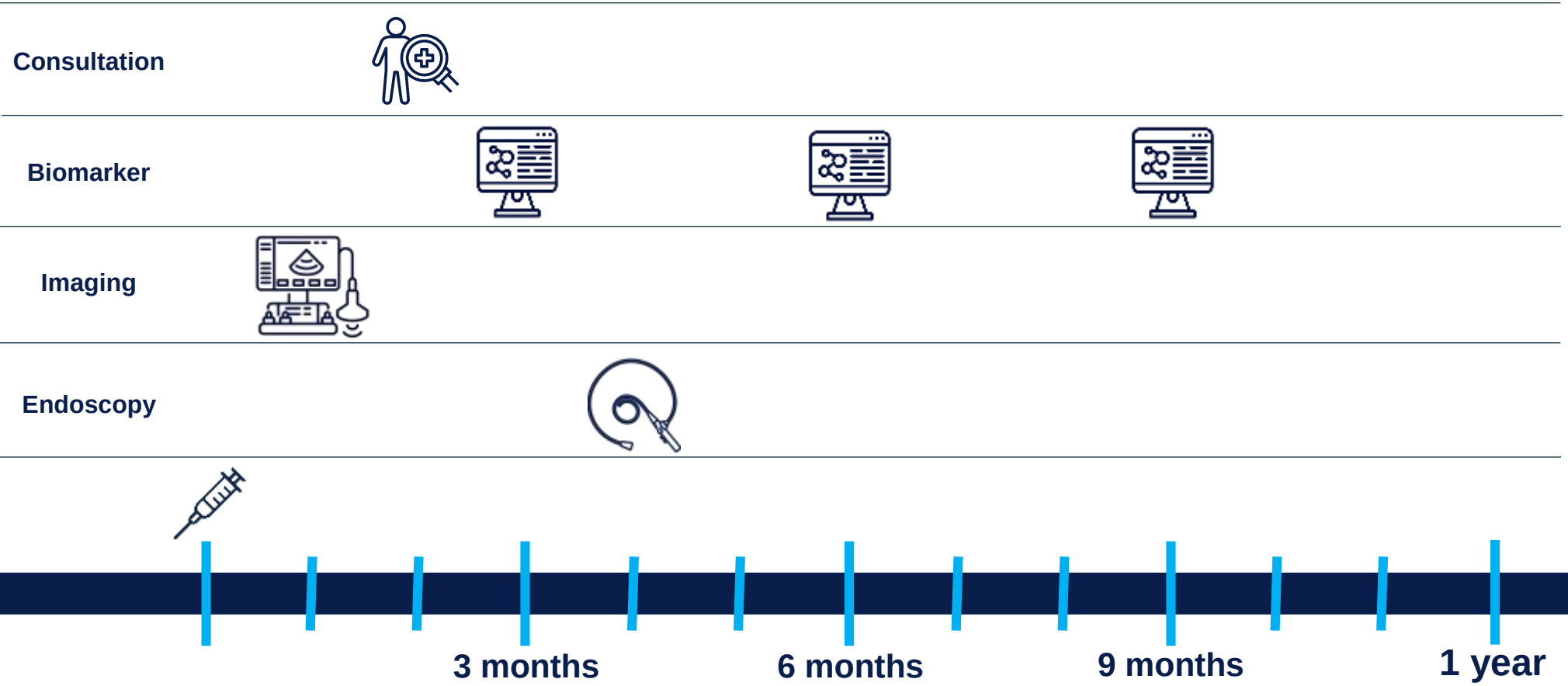
Yoon H, et al. Gastroenterology. 2020;159:1262-1275.

Emma

- Responded well to vedolizumab: IUS improvement at week 4, symptomatic remission at week 8, normalized CRP and fecal calprotectin at week 12 and endoscopic remission at week 16
- Mood has improved
- CRP and fecal calprotectin followed every 3 months
- At month 15, her CRP is normal but fecal calprotectin is 355, despite lack of symptoms
- Two weeks later she comes to the office and IUS shows increased bowel wall thickness and increase in color Doppler signal
- Colonoscopy: proximal extension to cecum, Mayo endoscopic subscore 2

This is a hypothetical patient case for discussion.
IUS, intestinal ultrasound.

Monitoring in clinical practice *(UC)*[1]



1. Opinion of Dr. Sands

Emma

What treatment next?

A. Prednisolone
B. Adalimumab
C. Infliximab
D. Ustekinumab
E. Anti-IL-23 antibody (guselkumab, mirikizumab, or risankizumab)
F. S1PR modulator (ozanimod or etrasimod)
G. JAK inhibitor (tofacitinib or upadacitinib)

This is a hypothetical patient case for discussion.
IL, interleukin; S1PR, sphingosine-1-phosphate receptor modulator; JAK, janus kinase.

Agenda

- Meet Emma
- Bottom up or top down? – the window of opportunity
- Unveiling underlying inflammation through holistic monitoring
- **How recent treatment innovations help us aim for higher targets**
  1. **CD**
  2. UC
- Conclusions
- Questions?

Pieces in the biologic choice puzzle[1]

DRUG

EFFICACY

INDICATION

RAPIDITYOFONSET

PHARMACOKINETICS/TDM

COMBINATIONVS.

POSITIONINGANDSEQUENCE

DURABILITY

SAFETY

INFECTION

CANCER

SPECIFICCONCERNSBYAGENT

ORMECHANISM

PATIENT

INDIVIDUALCHARACTERISTICS

AGES.STAGES.

COMORBIDITIESAND

PREFERENCES

DISEASECHARACTERISTICS

CDVSUC

DISEASE

BEHAVIOR/COMPLICATION

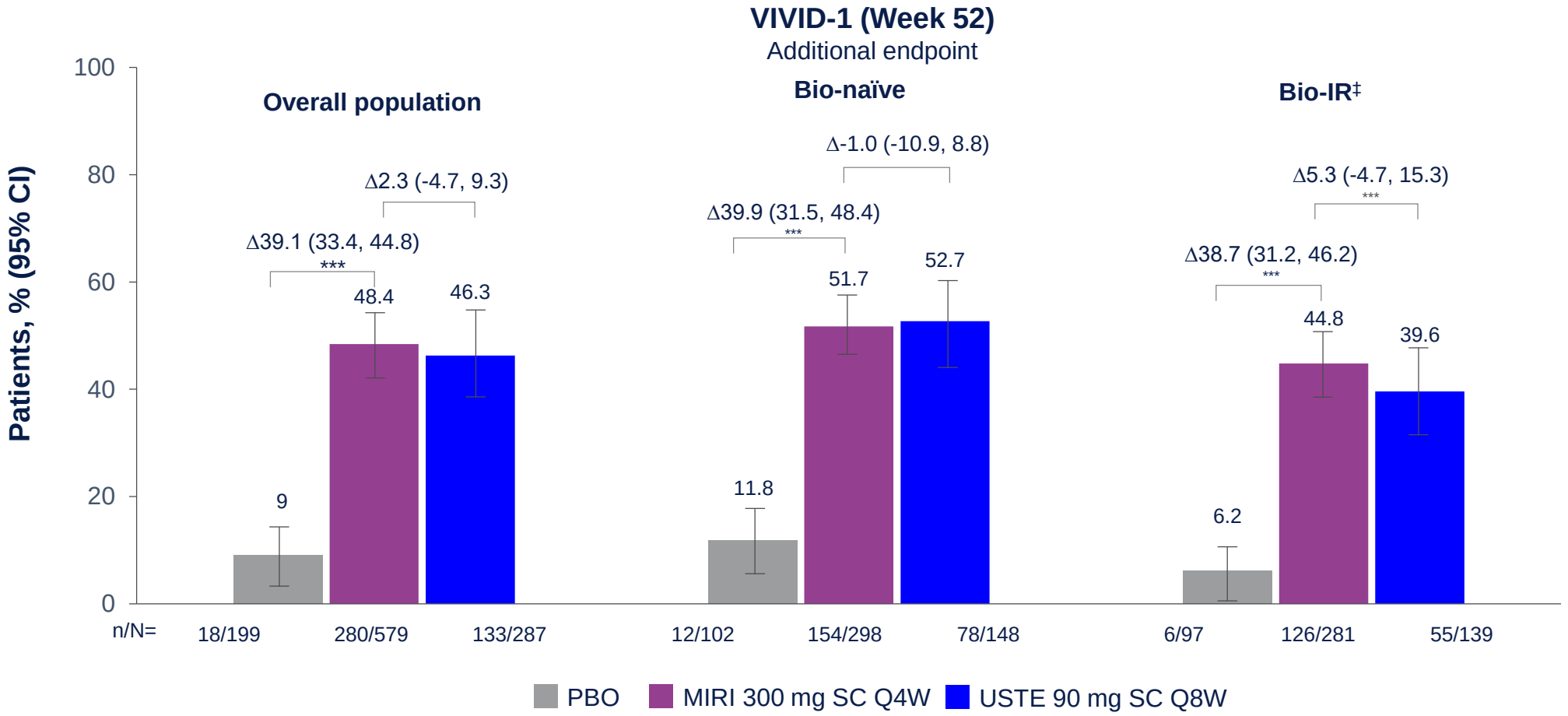
DISEASESEVERITY

EARLYVS.LATE

PRIORTREATMENTSUCCESSORFAILURE

1. Opinion of Dr. Sands. TDM, therapeutic drug monitoring; EIM, extraintestinal manifestation.

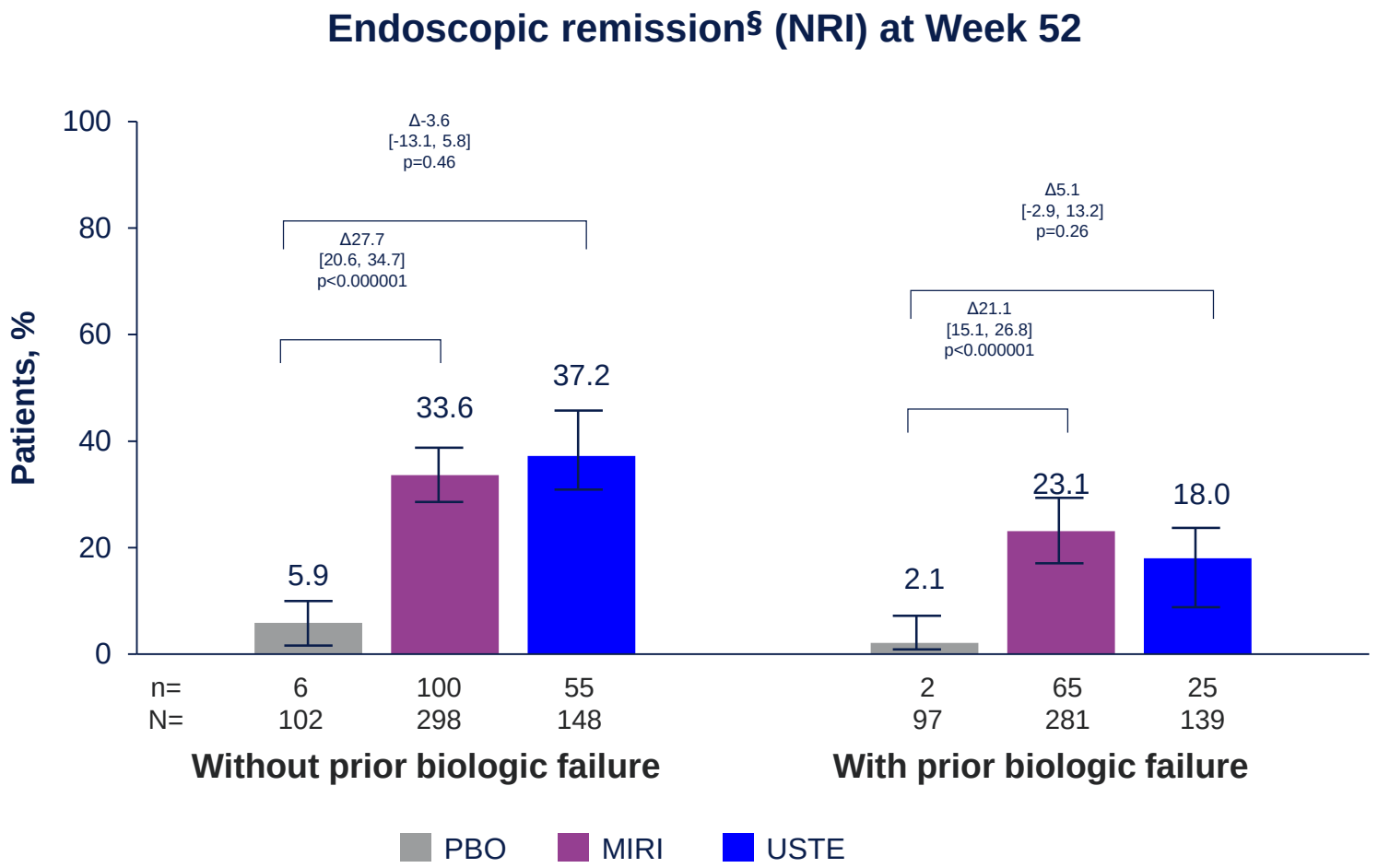
MIRI and USTE in CD: Endoscopic response† at Week 52



Mirikizumab is not approved by Swissmedic for patients with Crohn's disease.
Endoscopic response (NRI) at week 52.
†**Endoscopic response**: 50% or more reduction from baseline in SES-CD total score.
MIRI, mirikizumab; NRI, non-responder imputation; SES-CD, simple endoscopic score for CD; USTE, ustekinumab; W, Week.
Ferrante M, et al. *Lancet*. 2024;404:2423–36.

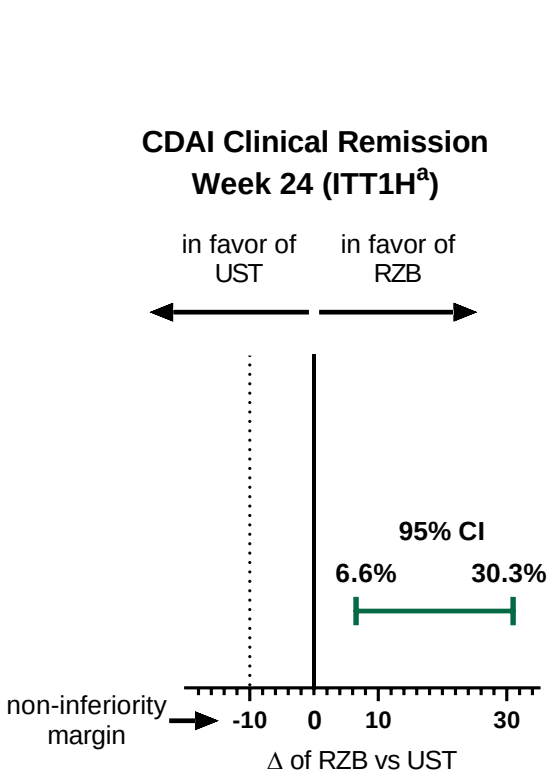
MIRI and USTE in CD: Endoscopic remission at Week 52

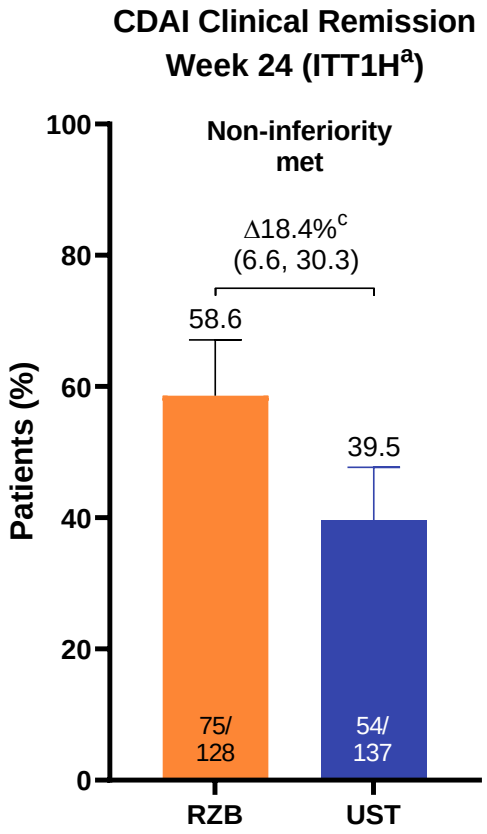
Prior Biologic Failure vs No Prior Biologic Failure

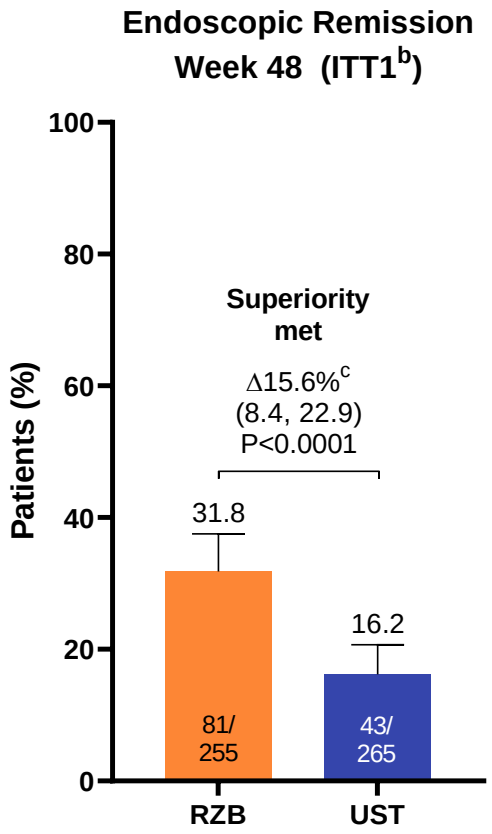


Mirikizumab is not approved by Swissmedic for patients with Crohn's disease.
MIRI, mirikizumab; NRI, non-responder imputation; USTE, ustekinumab; W, Week.
Jairath V, et al. *J Crohns Colitis.* 2024;18(Suppl 1):i62–4;.

Primary Endpoints: RZB demonstrated non-inferiority to UST for achieving clinical remission at week 24 and superiority to UST for achieving endoscopic remission at week 48







Ranked 2° endpoints for superiority also met:

- CDAI clinical remission at Wk 48
- Endoscopic response at Wk 48
- Endoscopic response at Wk 24
- Steroid-free endoscopic remission at Wk 48
- Steroid-free CDAI clinical remission at Wk 48

CDAI clinical remission: CDAI < 150
Endoscopic remission: SES-CD ≤ 4 and at least a 2-point reduction versus BL and no subscore > 1 in any individual variable, as scored by a central reviewer

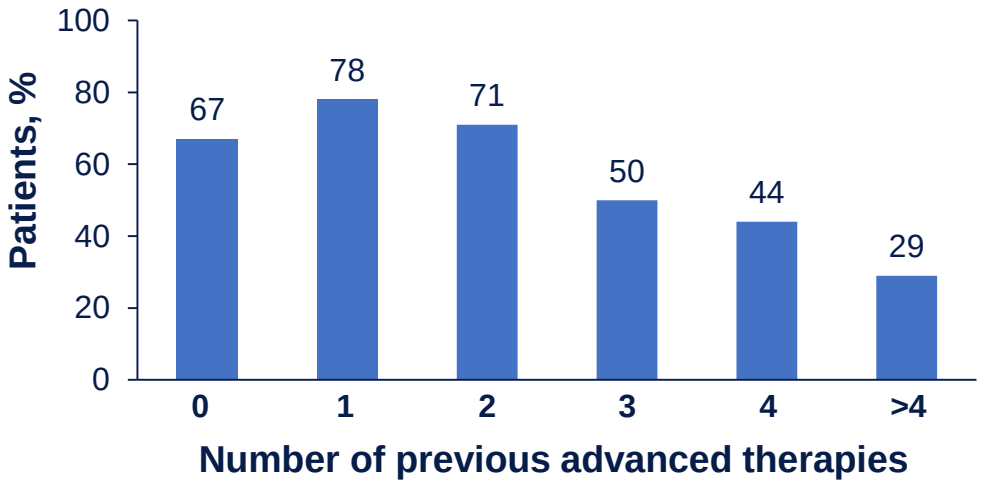
Nominal *P* <0.01 from a post hoc analysis testing for superiority

[a]ITT1H population: a subset of ITT1 population which includes the first ~50% of ITT1 patients
[b]ITT1 population includes patients who were randomized to UST or RZB (600 mg IV, 360 mg SC) and received at least one dose of study drug
[c]Differences adjusted by the stratification factors (number of times the subject failed prior anti-TNF therapy [≤ 1, > 1] and steroid use at baseline [yes, no])
% (n) represents the synthesized results from non-responder imputation incorporating multiple imputation to handle missing data
Non-inferiority for CDAI clinical remission at wk 24 was met if the lower bound of the 95% CI of adjusted risk difference was above -10%; if met, superiority for endoscopic remission at wk 48 was assessed

Peyrin-Biroulet L, et al. N Engl J Med. 2024 Jul 18;391(3):213-223.
CDAI, Crohn's disease activity index; RZB, Risankizumab; Ust, Ustekinumab; SES-CD, Simple Endoscopic Score for Crohn's Disease; BL, Baseline.

Risankizumab in CD: CS-free remission rates per line of prior therapy in Spanish real-world clinical practice[1,2]

CS-free remission† based on number of previous advanced therapies[2]



In a multivariate analysis, **a lower number of prior advanced therapies** was associated with **higher CS-free remission rates** ($p<0.01$)[1]

Safety

- 68 patients (7.9%) experienced AEs, 18 (2%) patients discontinued treatment
- Safety was consistent with the known profile of RZB in previous trials[1,2]

RZB demonstrates CS-free remission across all lines of therapy, with higher rates in patients with fewer lines of previous advanced therapy[1,2]

†HBI score <5 and no CS.[1,2]

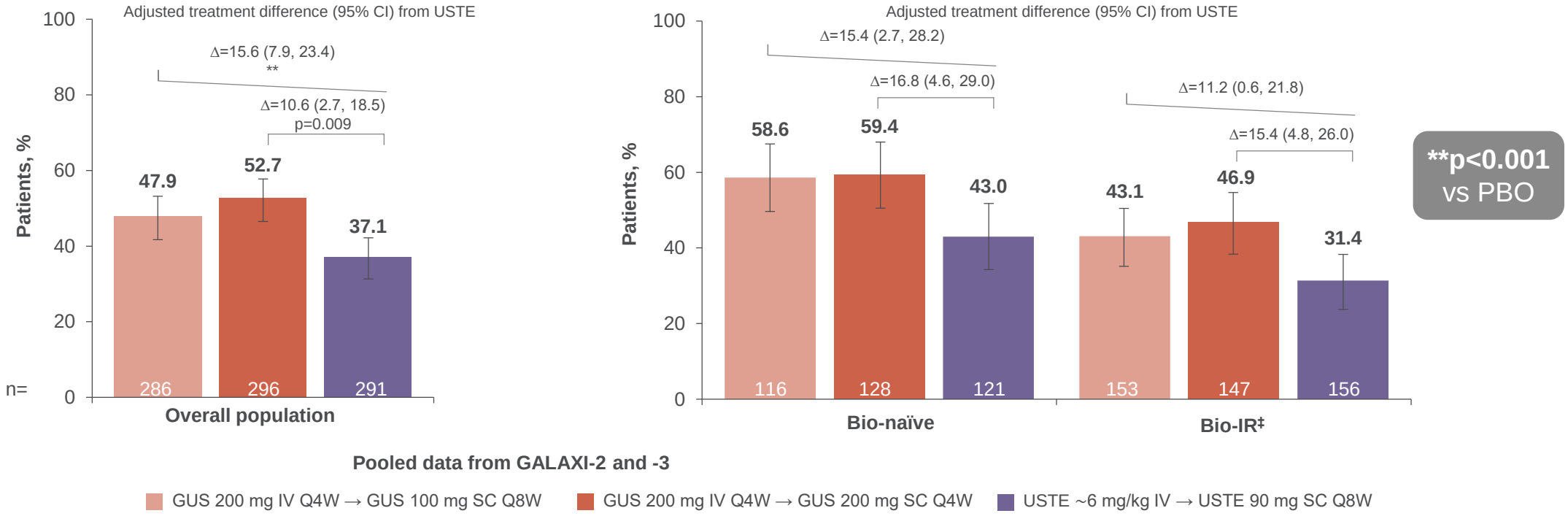
AE, adverse event; CS, corticosteroid; HBI, Harvey-Bradshaw Index; RZB, risankizumab.

1. Barreiro-de Acosta M, et al. Presented at the European Crohn's and Colitis Organisation (ECCO), 19–22 February 2025, Berlin, Germany: P0609;
2. Barreiro-de Acosta M, et al. Presented at the United Gastroenterology Week (UEGW), 12–15 October 2024; Vienna, Austria: A3.

Guselkumab in CD: Endoscopic response at week 48

Secondary endpoints (pooled analyses)

Endoscopic response† at Week 48



Note: Major secondary endpoints were multiplicity controlled. Sub-population analyses were not multiplicity controlled (p-values not shown). Treatment differences (Δ), CIs and p-values were based on the common risk difference by use of Mantel–Haenszel stratum weights and the Sato variance estimator. For the p-values, stratification was applied as follows: By baseline CDAI score (≤300 or >300), baseline SES-CD score (≤12 or >12), bio-IR status ('yes'/'no') and baseline corticosteroid use ('yes'/'no'). USTE group includes participants randomly assigned to USTE at Week 0, PBO participants who switched to USTE at Week 12 are not included. †Endoscopic response defined as ≥50% improvement from baseline in SES-CD or SES-CD ≤2. ‡Bio-IR, history of inadequate response or intolerance to previous biologic therapy.

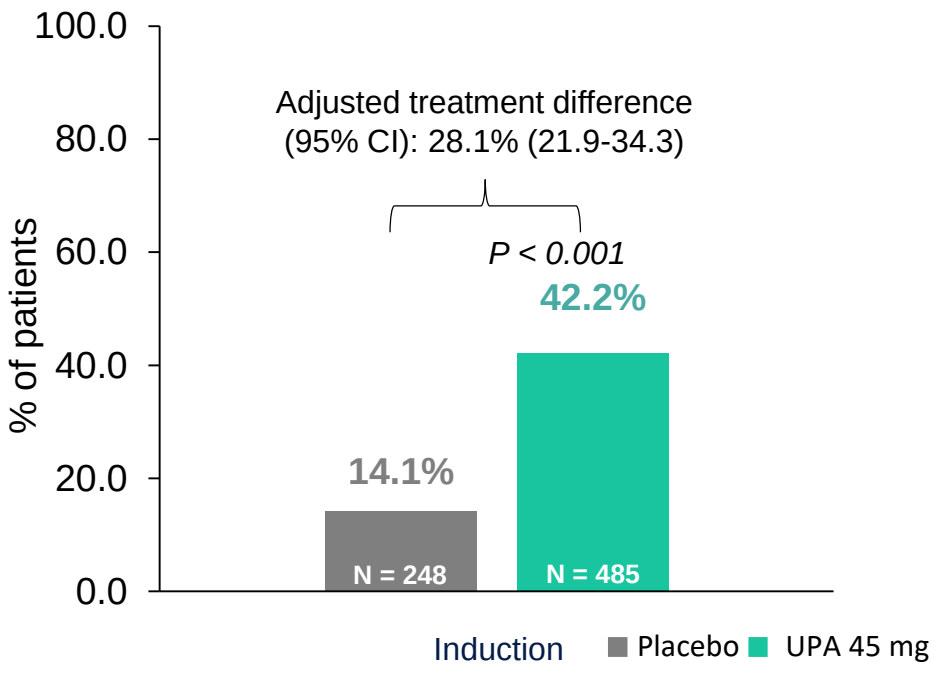
Bio-IR, biologic inadequate response; CDAI, Crohn's Disease Activity Index; CI, confidence interval; GUS, guselkumab; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; SES-CD, Simple Endoscopic Score for Crohn's Disease; USTE, ustekinumab.

Danese S, et al. Presented at United European Gastroenterology Week, 12–15 October 2024, Vienna, Austria: OP73.

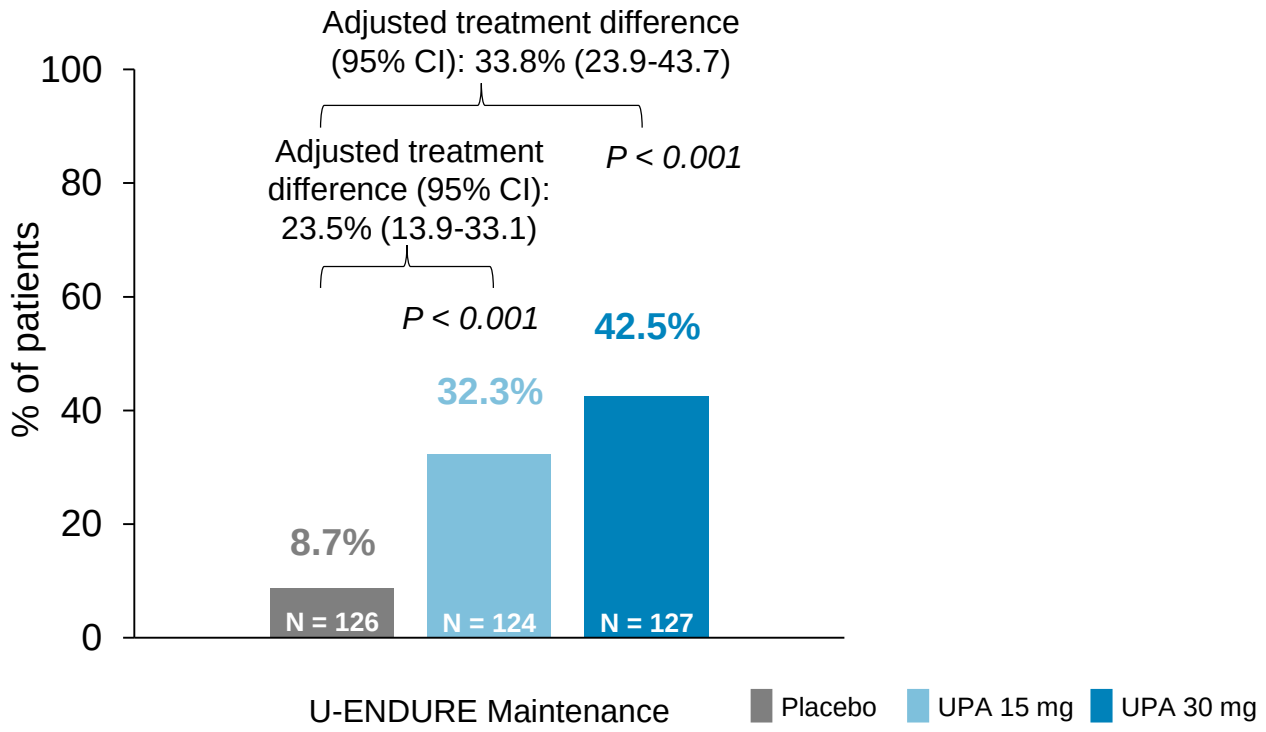
Upadacitinib in CD: Clinical remission at week 12 and 52[1]

Bio-IR Population

Clinical Remission per SF/APS (NRI-C) at week 12[1]



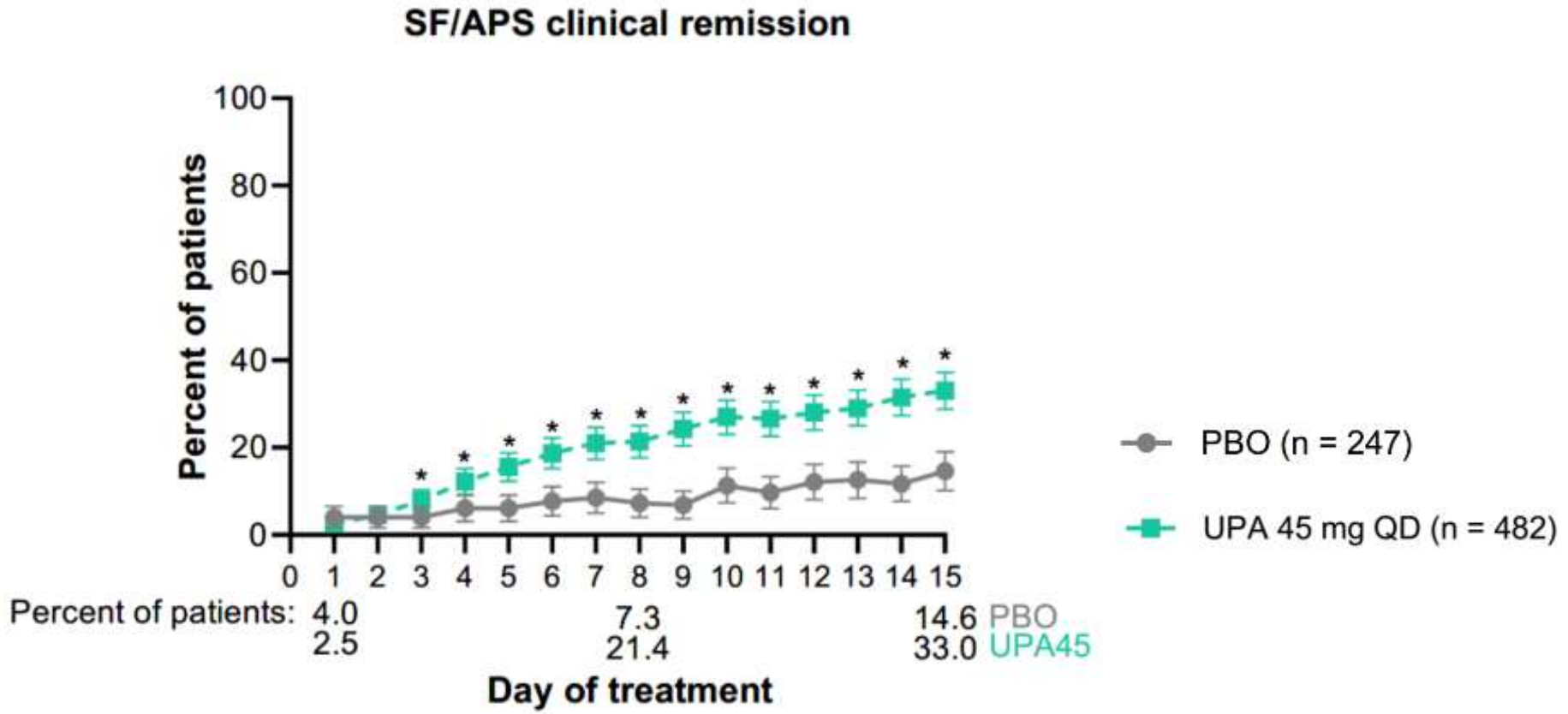
Clinical Remission per SF/APS (NRI-C) at week 52[1]



Adapted from 1. Peyrin-Biroulet et al. Clinical gastroenterology and hepatology. 2024. Incl. Suppl. All p-values are nominal.
Clinical remission (SF/APS): average daily SF ≤ 2.8 and not worse than BL AND average daily APS ≤ 1 and not worse than BL (co-primary Endpoint)
APS, abdominal pain score; Bio-IR, Biologics inadequate responders; BL, baseline; CI, confidence interval; COVID-19, coronavirus disease 2019; NRI-C, nonresponder imputation–COVID-19; SF, Stool frequency; UPA, Upadacitinib; CD, Crohn's disease.
1. Peyrin-Biroulet, Laurent et al. Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association vol. 22,10 (2024): 2096-2106.

Upadacitinib in CD: Rates of clinical remission in the first 15 days[1]

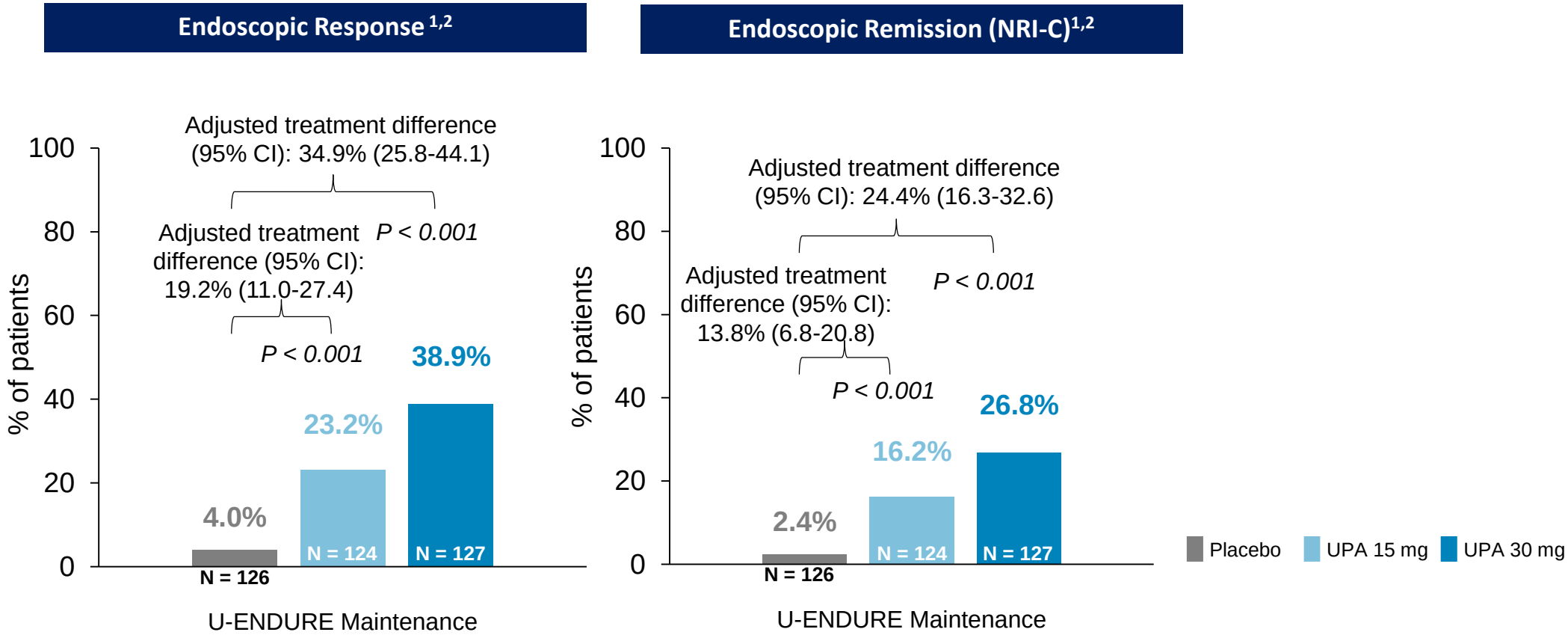
Bio-IR Population (U-Exceed and U-Excel)



Graph adapted from Colombel JF et al. Clin Gastroenterol Hepatol. Published online March 15, 2024.
Clinical remission (SF/APS): average daily SF ≤ 2.8 and not worse than BL AND average daily APS ≤ 1 and not worse than BL
Post-hoc analysis, Error bars represent 95% confidence intervals, based on Wald limits without continuity correction. *P < 0.05 vs PBO. All p-values are nominal.
APS, abdominal pain score; Bio-IR, Biologics inadequate responders; PBO, placebo; QD, once daily; SF, stool frequency; UPA, upadacitinib; UPA45, UPA 45 mg once daily; CD, Crohn's disease.
1. Colombel JF et al. Upadacitinib Reduces Crohn's Disease Symptoms Within the First Week of Induction Therapy. Clin Gastroenterol Hepatol. Published online March 15, 2024.

Upadacitinib in CD: Endoscopic response and remission at week 52[1]

Bio-IR Population

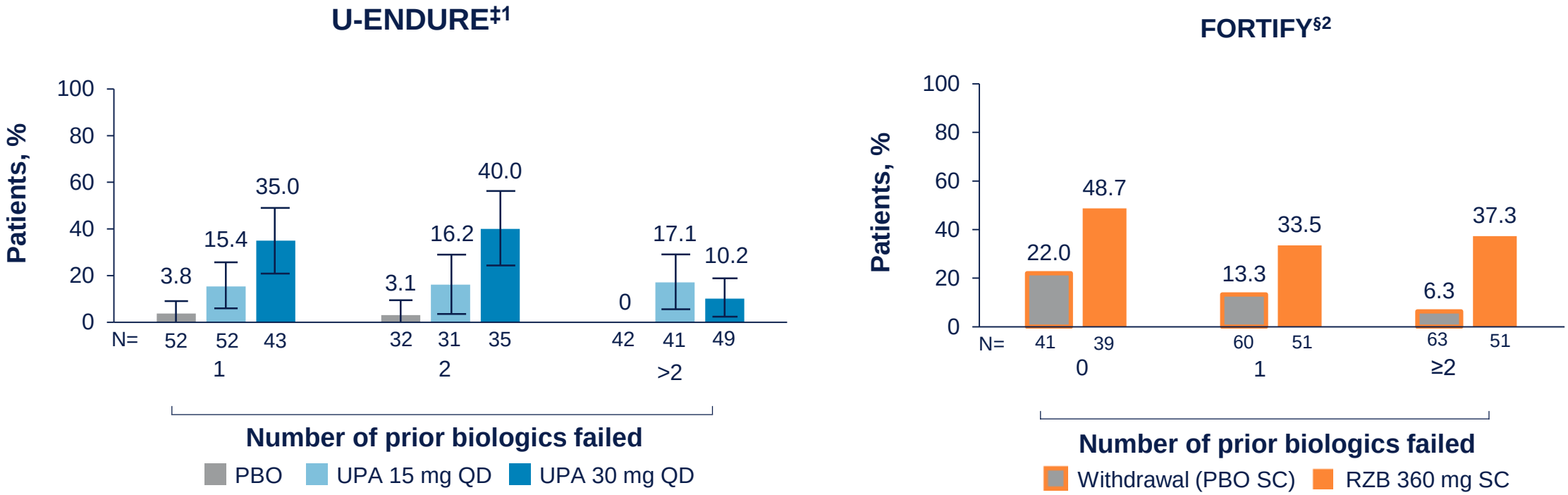


Adapted from 1. Peyrin-Biroulet et al. Clinical gastroenterology and hepatology. 2024. Incl. Suppl. All p-values are nominal.
Endoscopic response: decrease in SES-CD >50% from baseline (or for patients with a BL SES-CD of 4, at least a 2-point reduction from BL), as scored by central reviewer (Co-primary Endpoint)
Endoscopic remission: SES-CD ≤ 4 and at least a 2-point reduction versus BL and no subscore greater than 1 in any individual variable, as scored by a central reviewer (ranked sec. Endpoint)
Bio-IR, Biologics inadequate responders; BL, baseline; CI, confidence interval; COVID-19, coronavirus disease 2019; NRI-C, nonresponder imputation–COVID-19; SES-CD, Simple Endoscopic Score in Crohn's Disease; UPA, Upadacitinib; CD, Crohn's disease.
1. Peyrin-Biroulet, Laurent et al. Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association vol. 22,10 (2024): 2096-2106.

UPA and RZB in CD: Endoscopic remission† at Week 52

Prior Biologic Failure vs No Prior Biologic Failure

***Post-hoc* analysis**



No comparative conclusions regarding clinical efficacy and safety can be drawn from these data.

Error bars represent 95% CI.

Data Limitations: Subgroup analyses were not powered or tested to demonstrate a statistically significant difference between UPA and PBO.

†**Endoscopic remission:** SES-CD ≤4 and ≥2-point reduction from BL, with no subscore >1 in any individual variable.[1,2] ‡ITT1 population includes randomized patients who received at least one dose of study drug in Part 1. Efficacy outcomes were based on non-responder imputation incorporating MI to handle missing data due to COVID-19. §Includes randomized patients who responded to 12 weeks of IV RZB induction therapy in ADVANCE or MOTIVATE and received at least one dose of study drug in FORTIFY substudy 1.

BL, baseline; CI, confidence interval; ITT, intent-to-treat; MI, multiple imputation; PBO, placebo; QD, once daily; RZB, risankizumab; SES-CD, Simple Endoscopic Score for Crohn's Disease; UPA, Upadacitinib; SC; subcutaneous.

1. Peyrin-Biroulet L, et al. *Clin Gastroenterol Hepatol.* 2024;S1542–3565;00253-2 and supplementary data; 2. Ferrante M, et al. Presented at the United European Gastroenterology Week, 12–15 October 2024, Vienna, Austria: OP083.

Upadacitinib in CD: AE of special interest through 52 weeks of maintenance

Bio-IR and Bio-naïve Population

AE (E/100 PY)	U-ENDURE		
	PBO (N = 223; PY = 107.0)	UPA 15 mg QD (N = 221; PY = 148.2)	UPA 30 mg QD (N = 229; PY = 166.5)
Serious infection	9 (8.4)	9 (6.1)	13 (7.8)
Opportunistic infection (excluding TB and HZ)‡	0	1 (0.7)	1 (0.6)
Herpes Zoster (HZ)	5 (4.7)	6 (4.0)	12 (7.2)
Tuberculosis (TB)	0	0	0
Anemia§	13 (12.2)	15 (10.1)	11 (6.6)
Lymphopenia	10 (9.3)	4 (2.7)	10 (6.0)
Neutropenia	1 (0.9)	3 (2.0)	5 (3.0)
Creatine phosphokinase elevation	3 (2.8)	5 (3.4)	8 (4.8)
Hepatic disorder†	3 (2.8)	11 (7.4)	17 (10.2)
Renal disorder	2 (1.9)	0	0
Adjudicated cardiovascular events¶	0	0	0
Adjudicated thromboembolic event¶	0	0	1 (0.6)
Adjudicated gastrointestinal perforation¶	1 (0.9)	1 (0.7)	1 (0.6)
Malignancies (all types)	0	1 (0.7)	2 (1.2)
Excl. NMSC	0	1 (0.7)	2 (1.2)

Upadacitinib is not approved for bio-naïve CD patients in Switzerland.

Bio-IR, Biologics inadequate responders; AE, adverse event; PY, patient-years; CD, Crohn's disease; UPA, Upadacitinib; PBO, Placebo; QD, once daily

* The safety population includes all the patients who received at least one dose of upadacitinib or placebo during the maintenance period. NMSC denotes nonmelanoma skin cancer. Shown are exposure-adjusted event rates.

‡ Opportunistic infections (excluding tuberculosis and herpes zoster infection) during U-ENDURE were reported in one patient who received 15-mg upadacitinib (*P. jirovecii* pneumonia) and one patient who received 30-mg Upadacitinib (esophageal candidiasis).

§ Anemia (as an adverse event of special interest) was based on customized MedDRA queries, which included other preferred terms in addition to the preferred term "anaemia."

¶ Cardiovascular, thromboembolic, and gastrointestinal events were evaluated by independent adjudication committees.

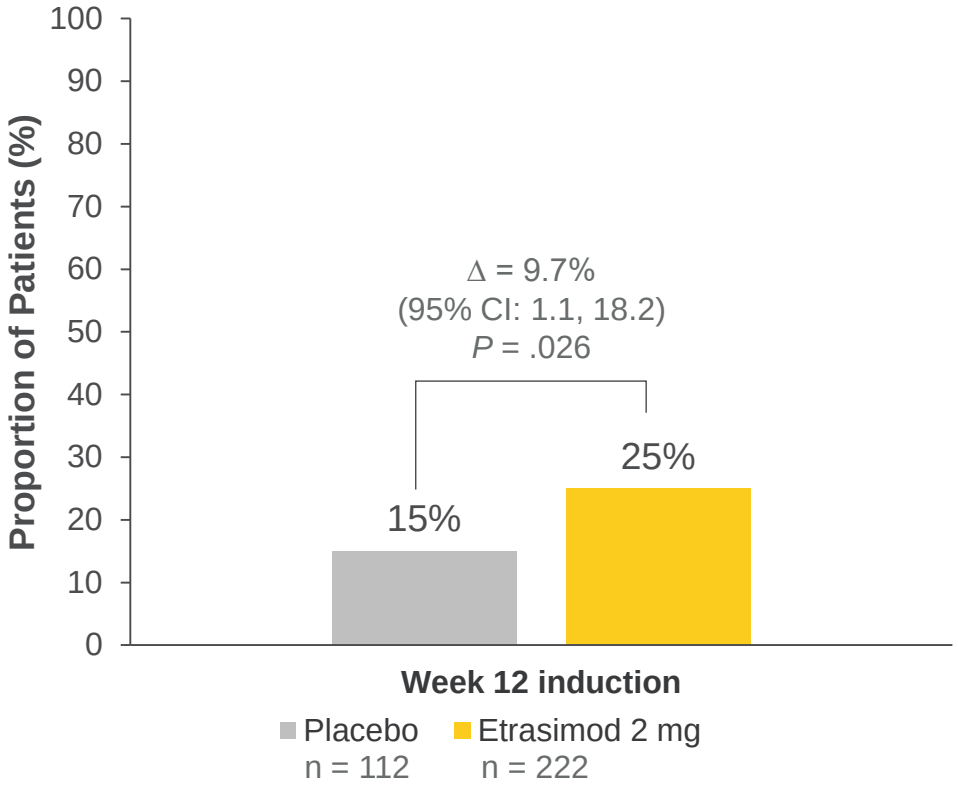
1. Loftus et al. Upadacitinib Induction and Maintenance Therapy for Crohn's Disease. NEJM. 2023;388:1966 1980. Incl. Suppl.

Agenda

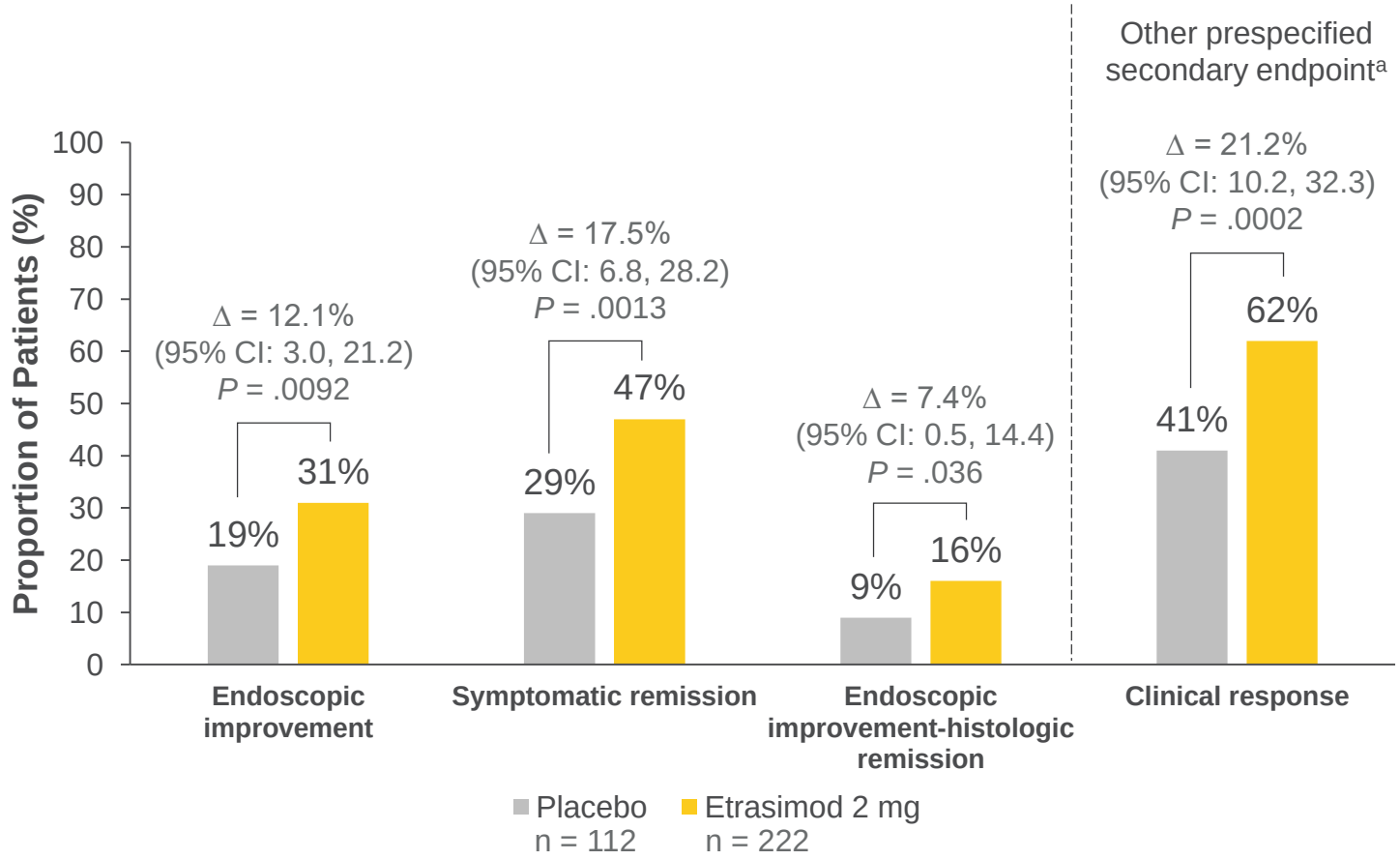
- Meet Emma
- Bottom up or top down? – the window of opportunity
- Unveiling underlying inflammation through holistic monitoring
- **How recent treatment innovations help us aim for higher targets**
    1. CD
    2. **UC**
- Conclusions
- Questions?

Etrasimod in UC: Results from the phase III study ELEVATE UC 12

Clinical Remission



Key Secondary Endpoints: Week 12

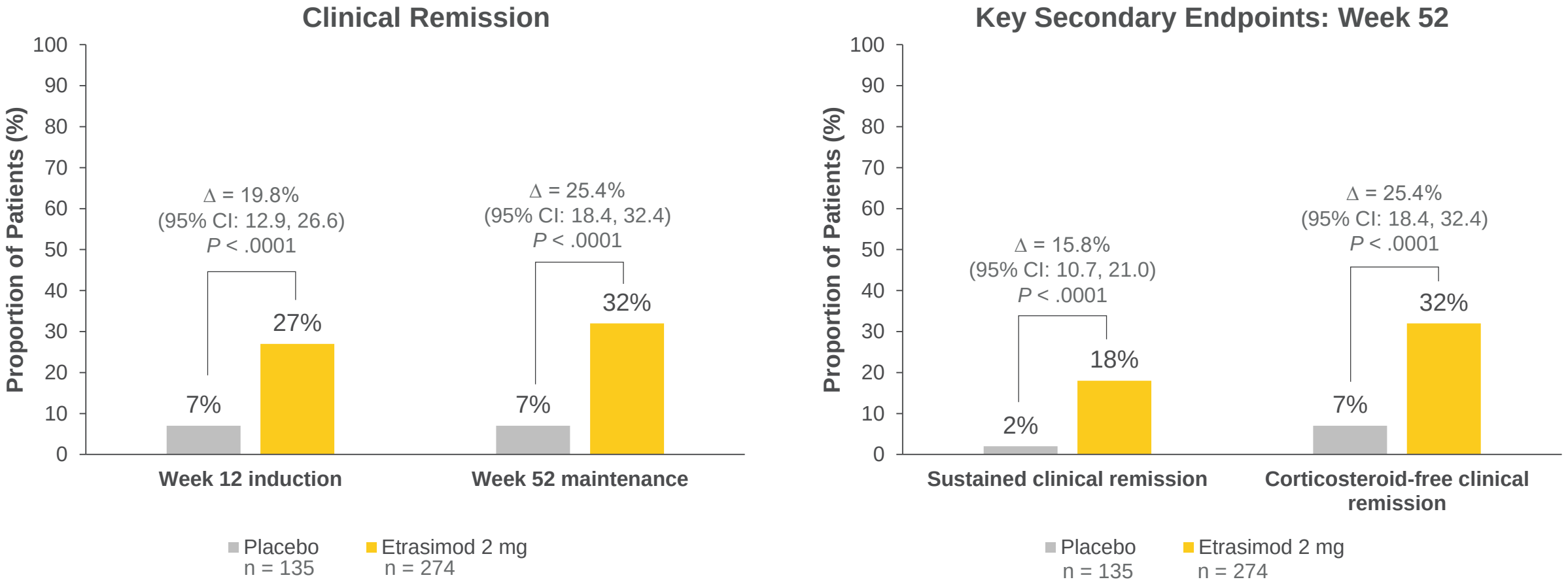


[a]Significance represented using unadjusted *P* values. CI, confidence interval.

Sandborn WJ, et al. Lancet. 2023;401:1159-1171.

Etrasimod in UC: Results from the phase III study ELEVATE UC 52

Etrasimod Efficacy in ELEVATE UC 52



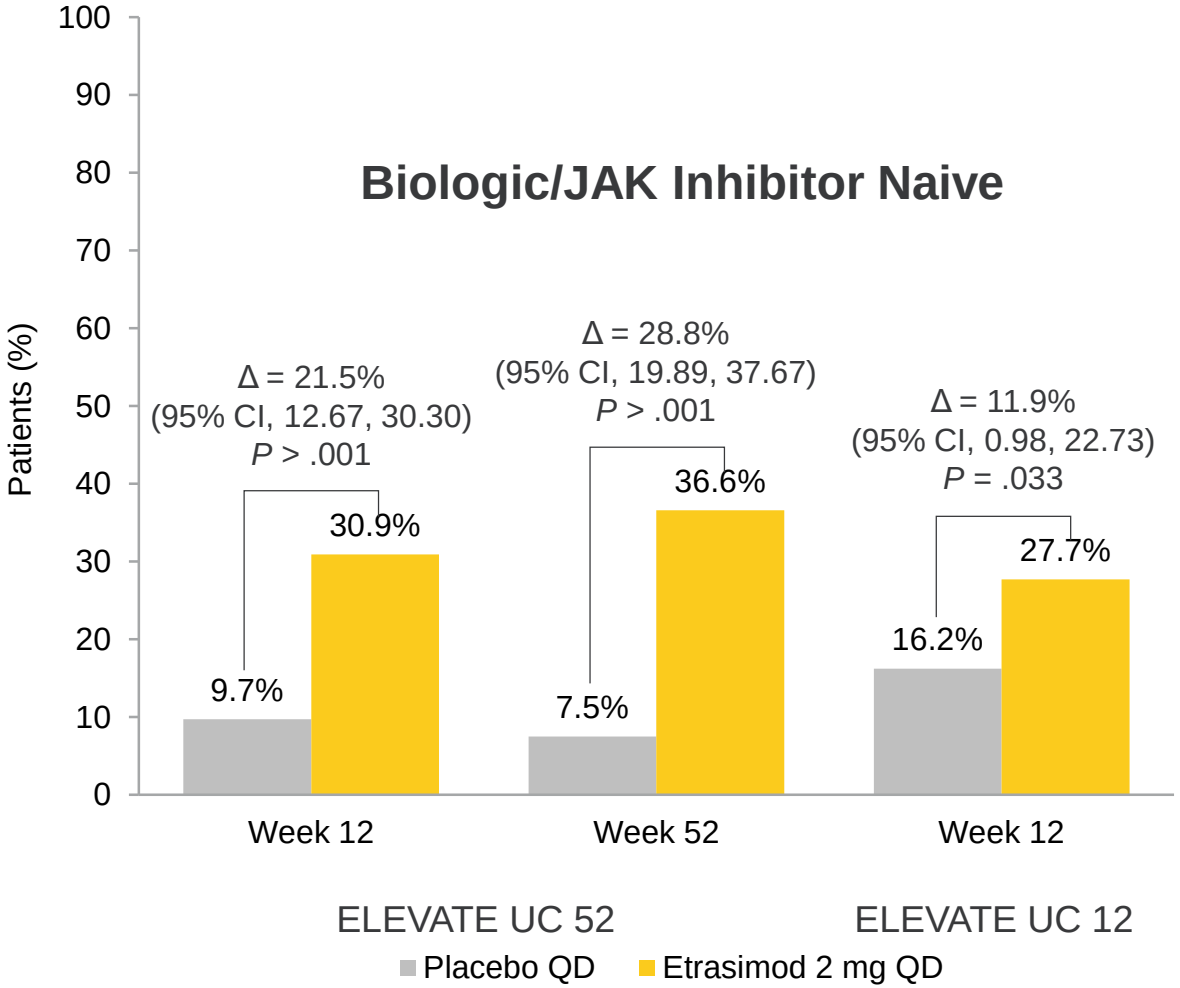
Sandborn WJ, et al. Lancet. 2023;401:1159-1171. CI, confidence interval.

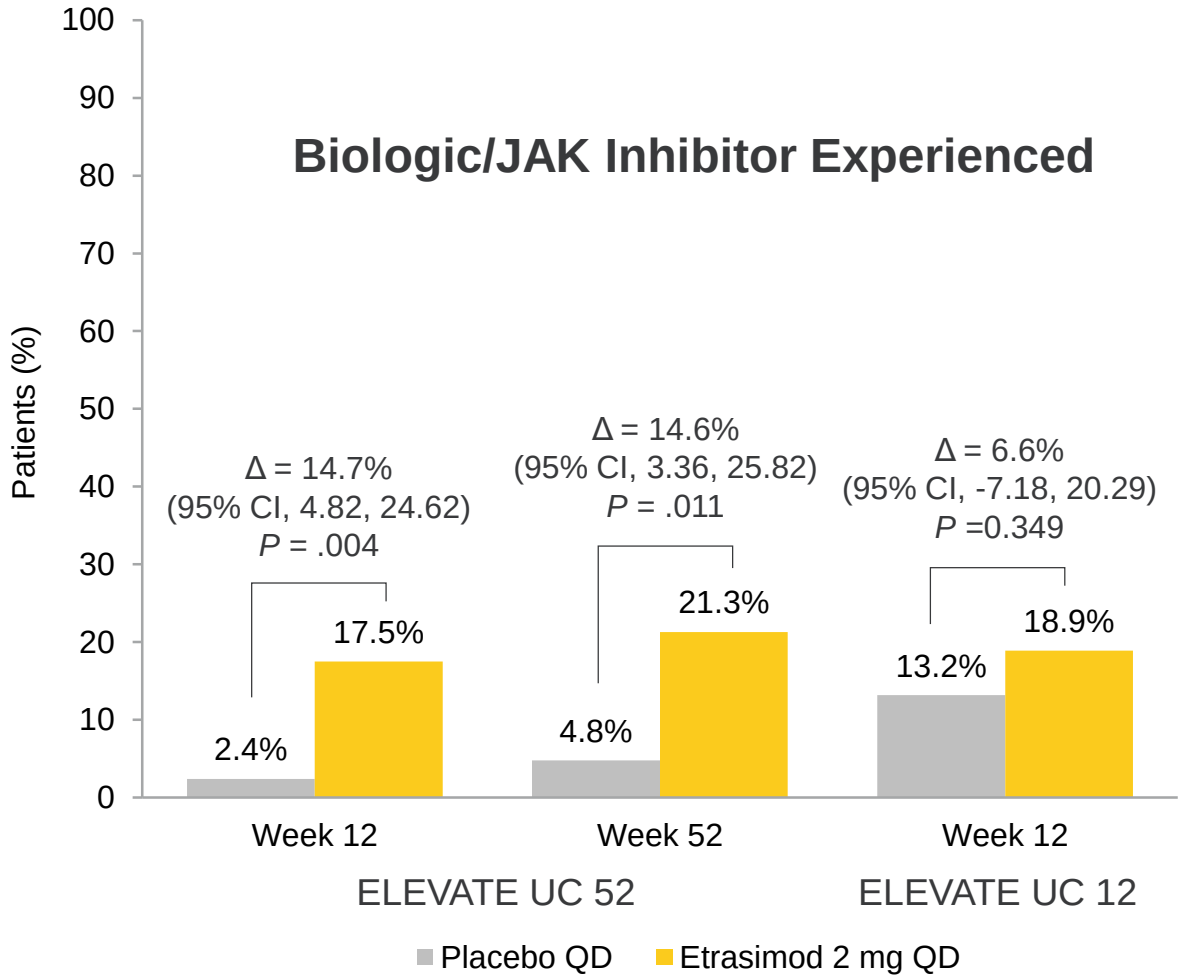
S1P

UC

Etrasimod Efficacy by Prior Biologic/JAK Inhibitor Exposure in ELEVATE UC 12 and ELEVATE UC 52

Clinical Remission





Sandborn WJ, et al. Lancet. 2023;401:1159-1171. QD, once daily; CI, confidence interval; JAK, janus kinase.

Safety of S1P Receptor Modulators

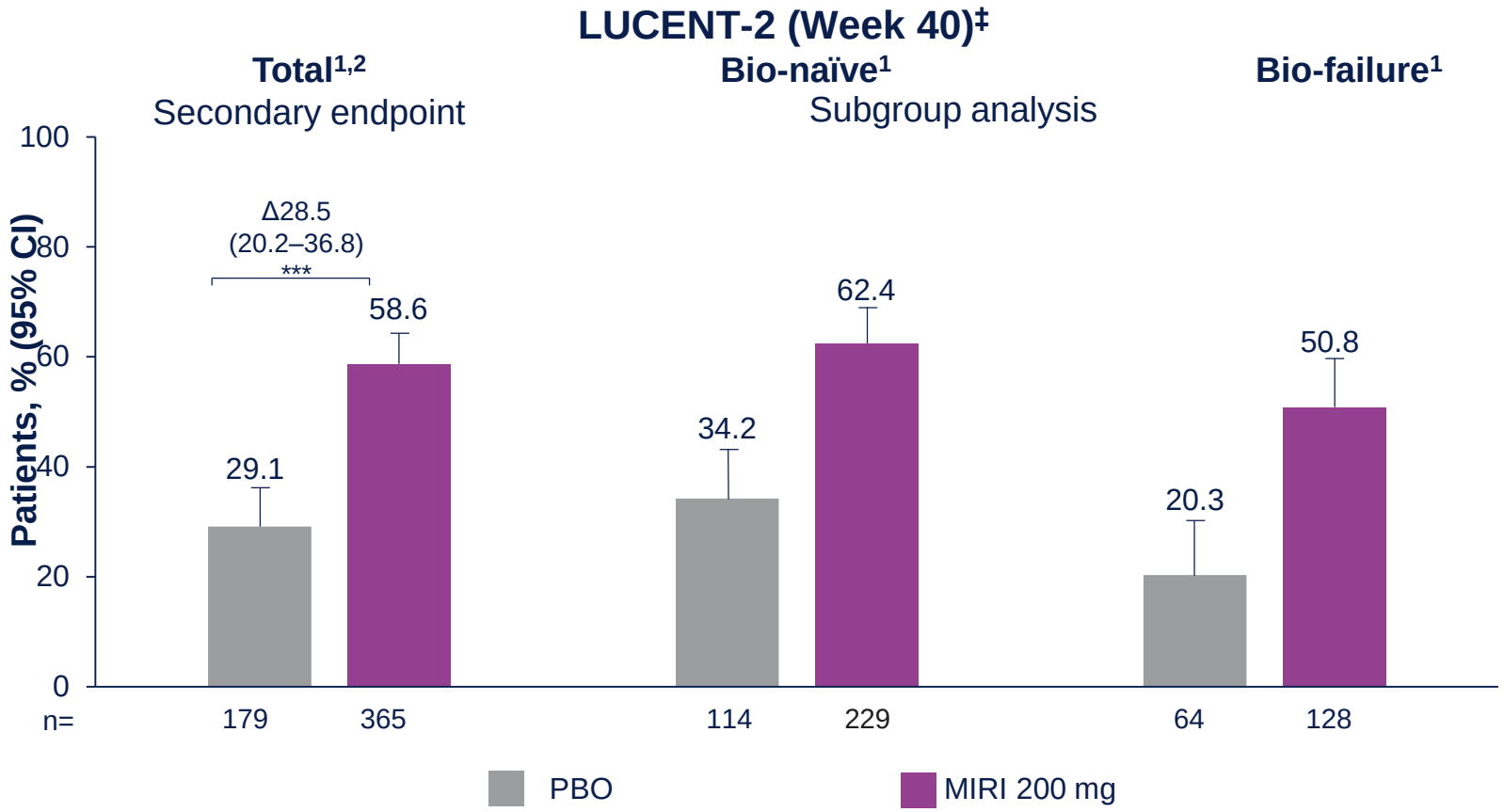
Etrasimod[1], Ozanimod[2]

- Lab monitoring before and during treatment
  - CBC with differential
  - CMP
- Monitor BP during treatment
- Baseline ECG (both agents)
- Baseline skin exam (etrasimod[1])
- Baseline ophthalmic exam (**etrasimod[1]:** required; **ozanimod[2]:** UV/ME)
- Spirometry, if clinically indicated

The information shown here is from the US package insert. Please consult the Swiss professional information for instructions applicable to Switzerland. S1P, sphingosine-1-phosphate; BP, blood pressure; CBC, complete blood count; CMP, comprehensive metabolic panel; ECG, electrocardiogram; ME, macular edema, UV, uveitis.

1. Etrasimod [PI]. Approved 2023. Revised November 2023. 2. Ozanimod [PI]. Approved 2020. Revised August 2023

Mirikizumab in UC: Mucosal healing at Week 40†



***p≤0.001 vs PBO. Total population error bars represent the upper boundary of the 95% CI.

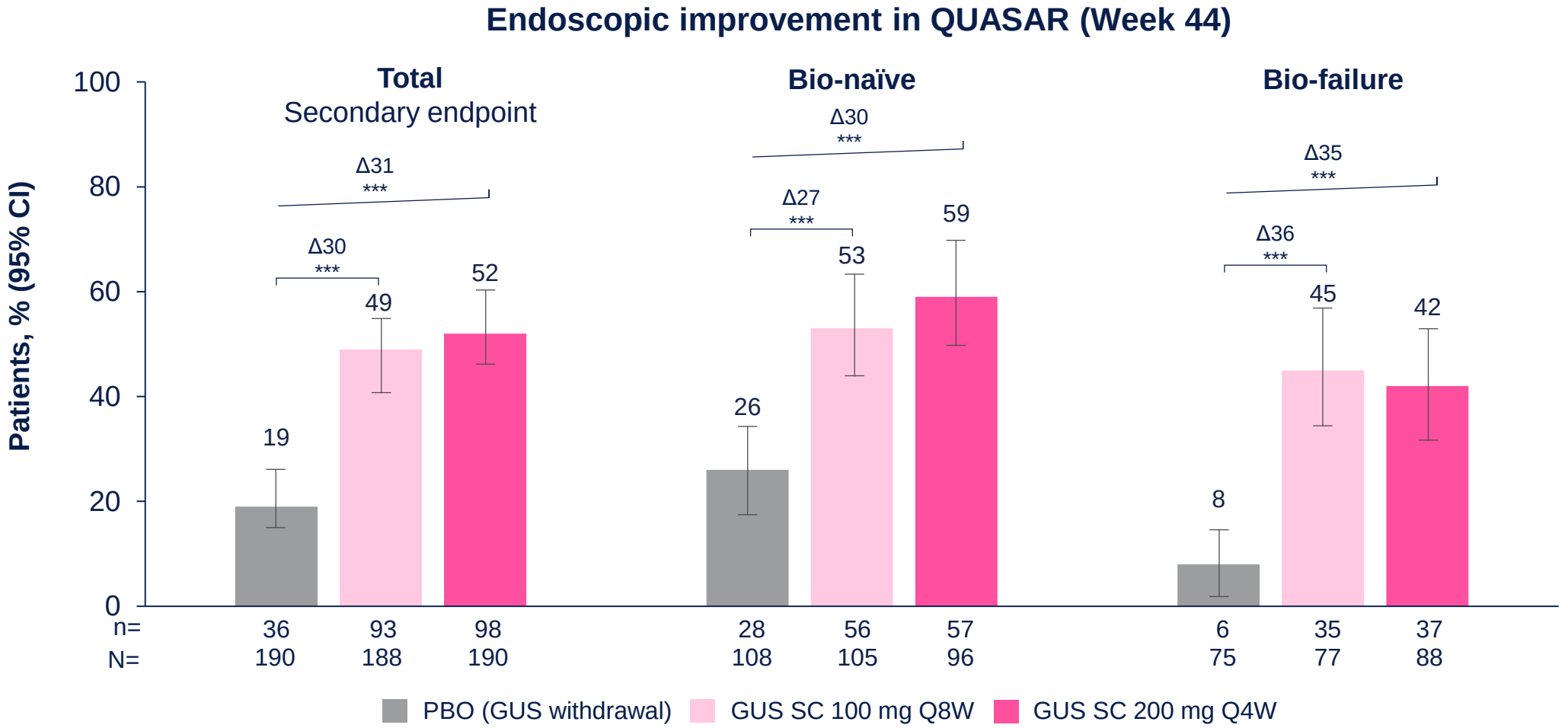
Data limitations: Subgroup analyses were prespecified but were not ranked or controlled for multiplicity, therefore, treatment differences could represent chance findings. No conclusions regarding these comparisons can be made.

†**Mucosal healing:** ESS ≤1 excluding friability. Mucosal healing was rereferred to as "endoscopic improvement" in the Omvoh SmPC and "endoscopic remission" in the Phase III clinical trials of MIRI in UC. ‡In the Phase III, maintenance trial, patients with a response to MIRI induction therapy were randomized 2:1 to receive MIRI 200 mg or PBO SC Q4W for 40 weeks.[1]

CI, confidence interval; ESS, endoscopic subscore; IL-23i, interleukin 23 inhibitor; MIRI, mirikizumab; PBO, placebo; Q4W, every 4 weeks; SmPC, Summary of Product Characteristics.

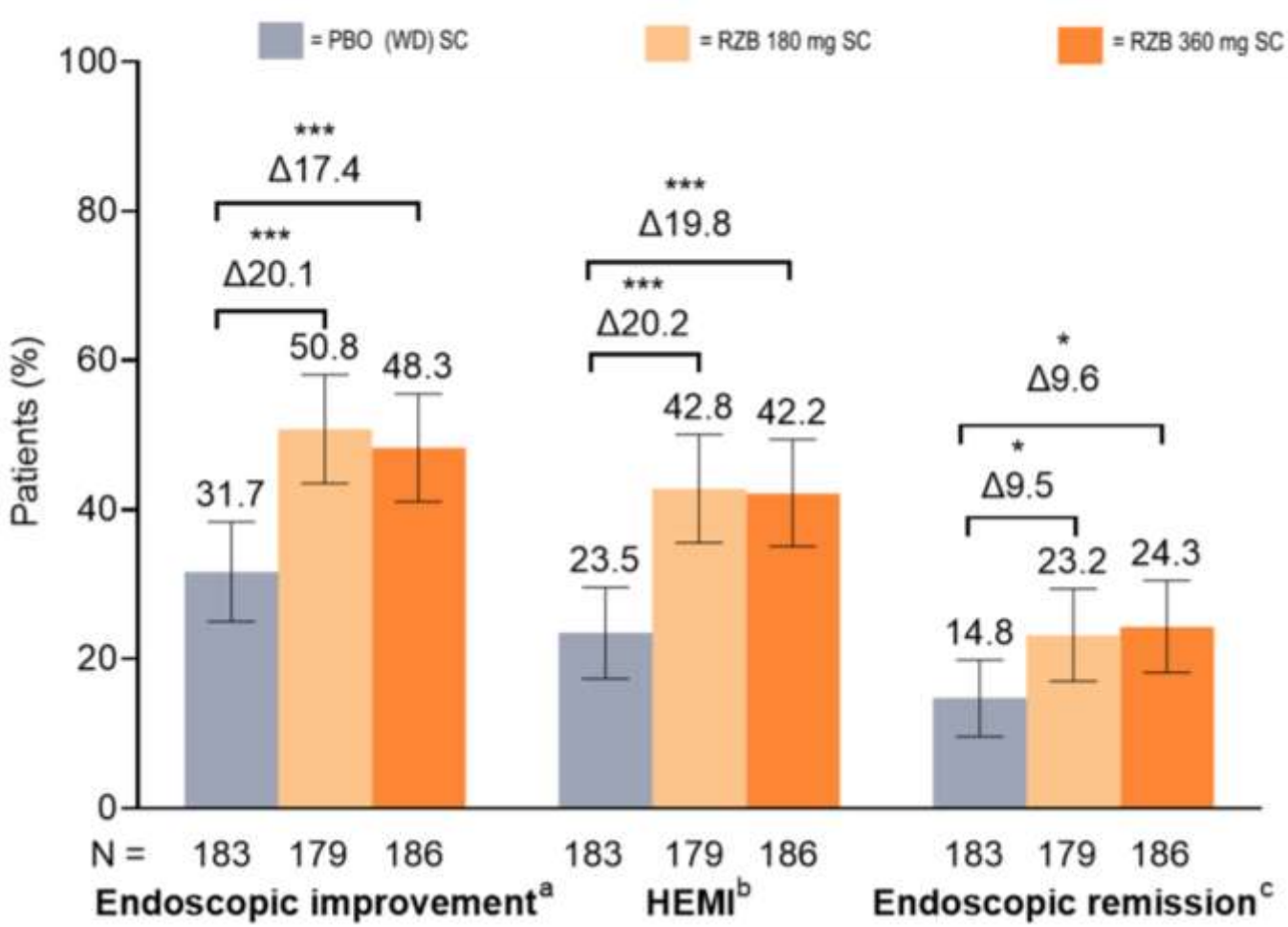
1. D'Haens G, et al. *N Engl J Med*. 2023;388:2444–55 and supplementary data; 2. Omvoh [Summary of Product Characteristics]. Eli Lilly and Company Ltd; Current SmPC.

Guselkumab in UC: Mucosal healing† at Week 44

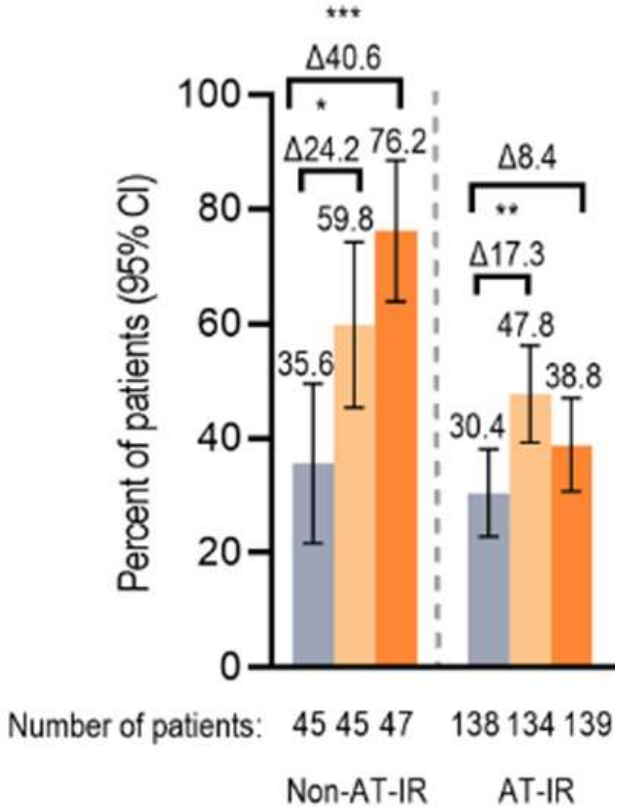


***p<0.0001 vs PBO.
CI, confidence interval; GUS, guselkumab; MES, Mayo endoscopic score; PBO, placebo; Q4/8W, every 4/8 weeks.
†**Endoscopic improvement:** MES of 0 or 1 with no friability present on endoscopy.
Rubin DT, et al. *Lancet*. 2024;405:33–49.

Risankizumab in UC: Endoscopic outcomes at Week 52[1]



Endoscopic improvement by IR status[2]



AT-IR, advanced therapy-inadequate response; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; HEMI, histological-endoscopic mucosal improvement; Non-AT-IR, nonadvanced therapy-inadequate response NRI-MI, nonresponding multiple imputation; PBO, placebo; RZB, Risankizumab; SC, subcutaneous; WD, withdrawal.
Results reported as adjusted treatment difference RZB vs PBO (WD) SC % (95% CI) and are based on NRI-MI to handle missing data due to COVID-19 or due to geopolitical conflict in Ukraine or surrounding areas. P values for treatment difference between RZB and PBO were calculated using CMH test for categorical endpoints, controlling for stratification factors. Error bars are % 95 CI. *p ≤ 0.05; ** p ≤ 0.01; *** p ≤ 0.001 versus PBO (WD) SC. *P*-values for non-AT-IR/AT-IR are nominal and statistical comparisons were made using Pearson's Chi-Square test.
[a] Endoscopic improvement: Endoscopic subscore of 0 or 1 without friability. [b] HEMI: Endoscopic subscore of 0 or 1 without friability and Geboes score ≤ 3,1. [c] Endoscopic remission. Endoscopic subscore of 0.

1. Louis E, et al. JAMA. 2024 Sep 17;332(11):881-897. doi: 10.1001/jama.2024.12414. Supplement.
2. Panaccione R, et al. Efficacy of Risankizumab in Patients With Moderately to Severely Active Ulcerative Colitis by Prior Advanced Therapy Failure and Mechanism of Action: A Post Hoc Analysis of INSPIRE and COMMAND Phase 3 Studies. Poster at ECCO congress, Feb 21-24, 2024.

Risankizumab in UC: Adverse events of Special Interest Through 52 Weeks of maintenance with both doses[a]

AE, n (%)	PBO (WD) SC N = 196	RZB 180 mg SC N = 193	RZB 360 mg SC N = 195
Serious infections[b]	4 (2.0)	2 (1.0)	1 (0.5)
Opportunistic infection (excluding tuberculosis and herpes zoster)	0	0	1 (0.5)[c]
Herpes zoster	3 (1.5)	2 (1.0)	1 (0.5)
Hypersensitivity[d]	10 (5.1)	20 (10.4)	10 (5.1)
Injection site reactions	2 (1.0)	7 (3.6)	5 (2.6)
Hepatic events	1 (0.5)	3 (1.6)	13 (6.7)
Malignancies (all types)	1 (0.5)	0	2 (1.0)[e]
Nonmelanoma skin cancer	1 (0.5)	0	0

No active tuberculosis, serious hypersensitivity, adjudicated anaphylactic reactions, or adjudicated MACE occurred in any treatment group

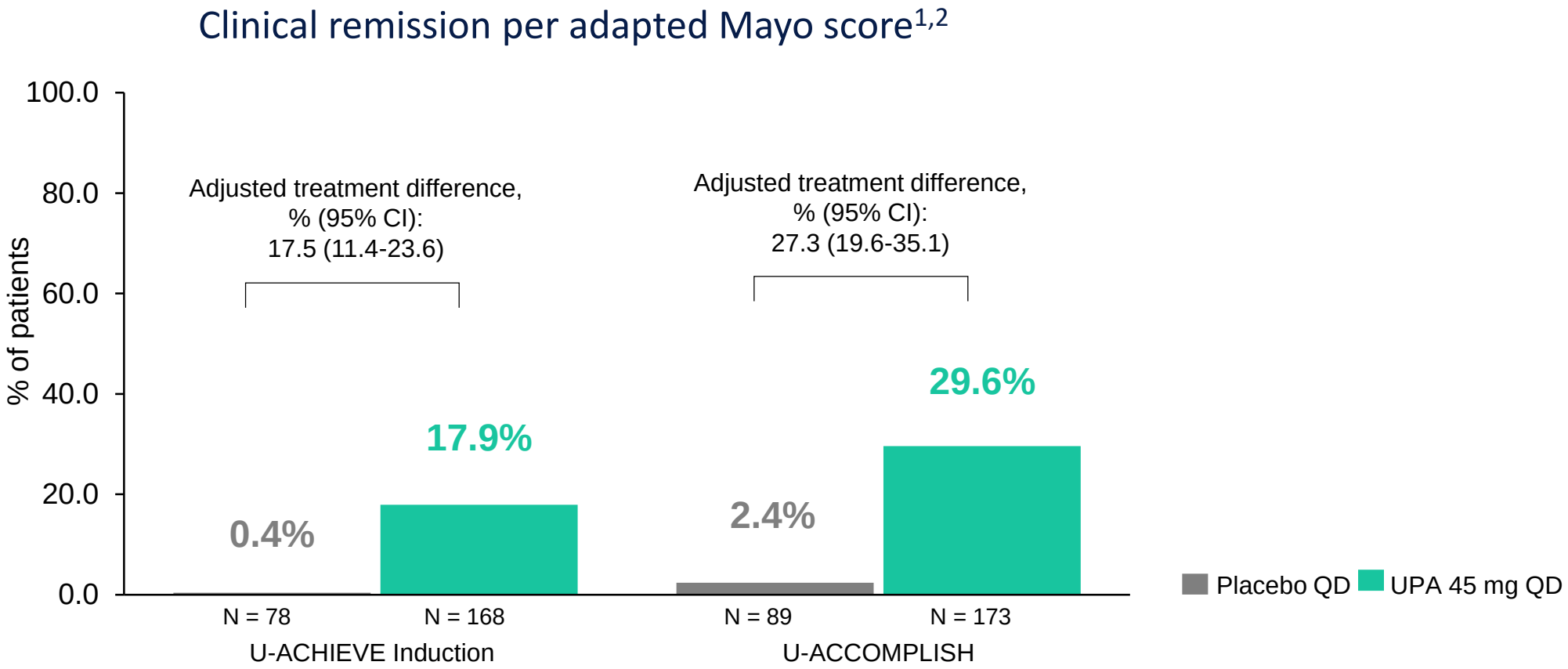
Most hepatic events in the RZB groups were mild, asymptomatic liver test increases, did not lead to treatment discontinuation, and resolved; No cases met the criteria for Hy's law

AE, adverse event; IV, intravenous; MACE, major adverse cardiovascular event; PBO, placebo; RZB, risankizumab; SC, subcutaneous; WD, withdrawal.
[a]The safety population included all patients who clinically responded to IV RZB at 12 or 24 weeks, were randomised to COMMAND at maintenance week 0, and received ≥ 1 dose of study drug during 52-week maintenance period.
[b]Serious infections in RZB-treated patients included COVID-19, COVID-19 pneumonia, abscess limb, and pneumonia.
[c]A nonserious eczema herpeticum.
[d]Events identified with Hypersensitivity SMQ, a broader medical concept, including terms overlapping with these in Injection site reaction CMQ.
[e]Invasive ductal breast carcinoma and nontreatment emergent adenocarcinoma of the colon.

Louis E, et al. JAMA. 2024 Sep 17;332(11):881-897. doi: 10.1001/jama.2024.12414. Supplement.

Upadacitinib in UC: Clinical remission at week 8[1]

Bio-IR Population



Graph adapted from Danese et al. Lancet. 2022;399(10341):2113-2128.

Induction Primary Endpoint = Clinical remission per adapted Mayo score: adapted Mayo score ≤2, with SFS ≤1 and not greater than BL, RBS of 0, and endoscopic subscore ≤1 without friability.

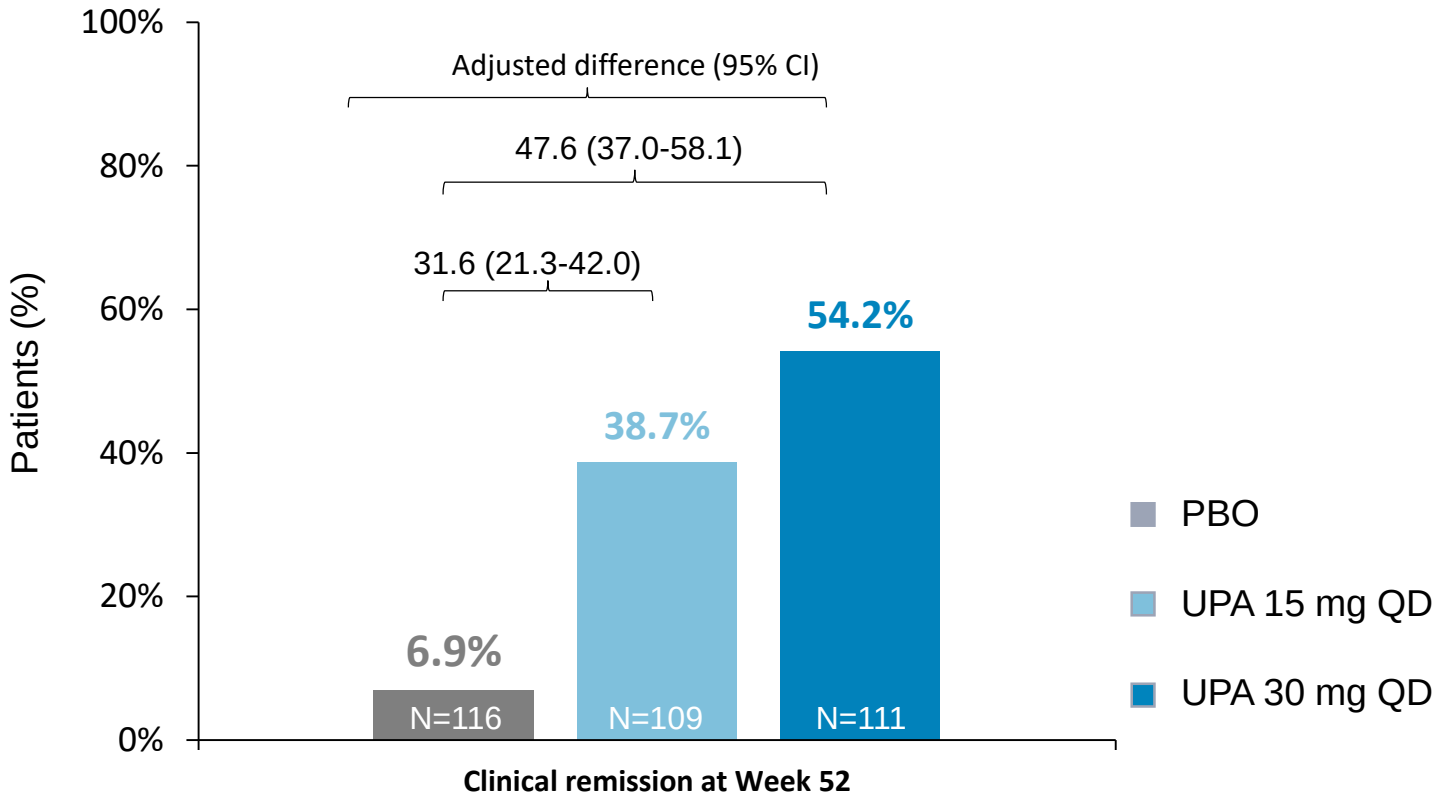
BL, baseline; CI, confidence interval; QD, once daily; RBS, rectal bleeding subscore; SFS, stool frequency subscore; UPA, upadacitinib.

1. Danese S et al. Lancet. 2022;399(10341):2113-2128. 2. Rinvoq Fachinformation, www.swissmedicinfo.ch

Upadacitinib in UC: Clinical remission at week 52[1]

Bio-IR Population

Clinical remission per adapted Mayo score[1]

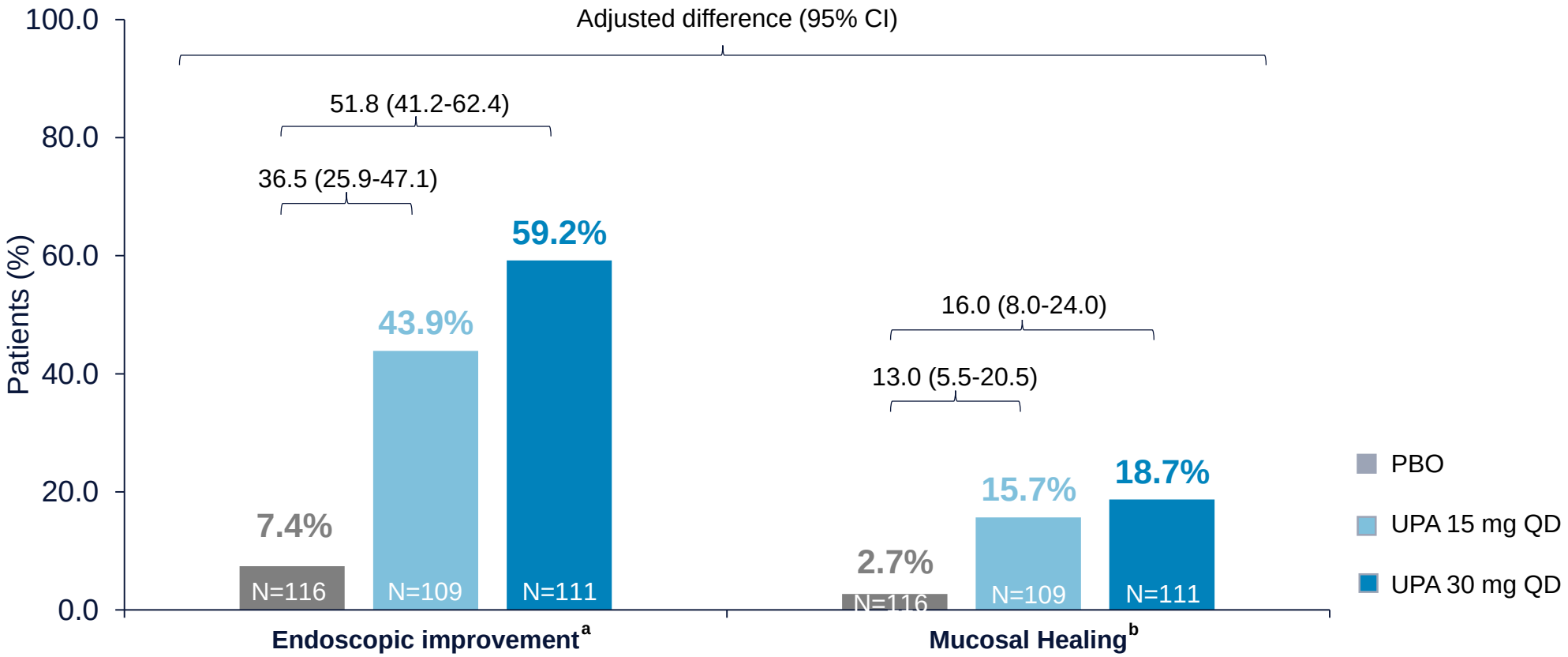


Adapted from Vermeire et al. *Lancet Gastroenterol Hepatol*. 2023;8(11):976-989.
Maintenance Primary endpoint = Clinical remission per adapted Mayo score: adapted Mayo score ≤2, with SFS ≤1 and not greater than BL, RBS of 0, and endoscopic subscore ≤1 without friability.
BL, baseline; CI, confidence interval; QD, once daily; RBS, rectal bleeding subscore; SFS, stool frequency subscore; UPA, upadacitinib.
The efficacy analysis was performed in the non-bio-IR, bio-IR, and anti-TNF-IR subgroups of the ITT population (UPA 45 mg QD 8-week induction responders who were enrolled per protocol for the 52-week maintenance treatment period and received ≥1 dose of study drug [placebo, UPA 15 mg QD, or UPA 30 mg QD]).
1. Vermeire S et al. *Lancet Gastroenterol Hepatol*. 2023;8(11):976-989.

Upadacitinib in UC: Endoscopic outcomes at week 52[1]

Bio-IR Population

Mucosal healing endpoints at week 52[1]



[a]ES ≤1 without friability. [b]Mucosal healing= endoscopic score of 0 and a Geboes score <2

1. Vermeire S et al. Lancet Gastroenterol Hepatol. 2023;8(11):976-989.

Long-term safety of JAK inhibitors: Tofacitinib and Upadacitinib

Bio-IR and Bio-naïve population

	TOFA[1] OCTAVE Open LTE study (7 years of follow-up)			UPA[2] U-ACTIVATE LTE (Week 144, interim analysis)†	
	5 mg BID (n=175)	10 mg BID (n=769)	Total (N=944)	UPA 15 mg QD n=142; 397.4 PYs	UPA 30 mg QD n=227; 646.1 PYs
	n, (%)			E (E/100 PYs) [95% CI]	
Overall TEAEs‡	154 (88.0)	626 (81.4)	780 (82.6)	854 (214.9) [200.5–229.3]	1398 (216.4) [205.0–227.7]
Serious TEAEs	39 (22.3)	147 (19.1)	186 (19.7)	42 (10.6) [7.4–13.8]	75 (11.6) [9.0–14.2]
Severe TEAEs	25 (14.3)	104 (13.5)	129 (13.7)	N/R	N/R
AEs leading to discontinuation	20 (11.4)‡§	80 (10.4)‡§	100 (10.6)‡	18 (4.5) [2.4–6.6]	30 (4.6) [3.0–6.3]
Death	0 (0.0)	6 (0.8)¶	6 (0.6)	0	1†† (0.2) [0.0–0.5]
Serious infections	8 (4.6)‡‡	31 (4.0)§§	39 (4.1	10 (2.5) [1.0–4.1]	29 (4.5) [2.9–6.1]
Herpes zoster	13 (7.4)	60 (7.8)¶¶	73 (7.7)	14 (3.5) [1.7–5.4]	37 (5.7) [3.9–7.6]
MACE†††	2 (1.1)	2 (0.3)	4 (0.4)	1 (0.3) [0.0–0.7]	1 (0.2) [0.0–0.5]
VTE‡‡‡	N/R	N/R	N/R	1 (0.3) [0.0–0.7]	3 (0.5) [0.0–1.0]

No comparative conclusions regarding clinical safety can be drawn from these data. Upadacitinib is not approved by Swissmedic for bio-naïve patients with ulcerative colitis.

†Safety analysis based on data up to 30 June 2024.[2] ‡For TOFA – excluding worsening UC. AEs of worsening UC leading to discontinuation were designated as insufficient clinical response.[1] §Related to study drug in 12 (6.9%) and 46 (6.0%) patients who received TOFA 5 mg BID and TOFA 10 mg BID, respectively.[1]

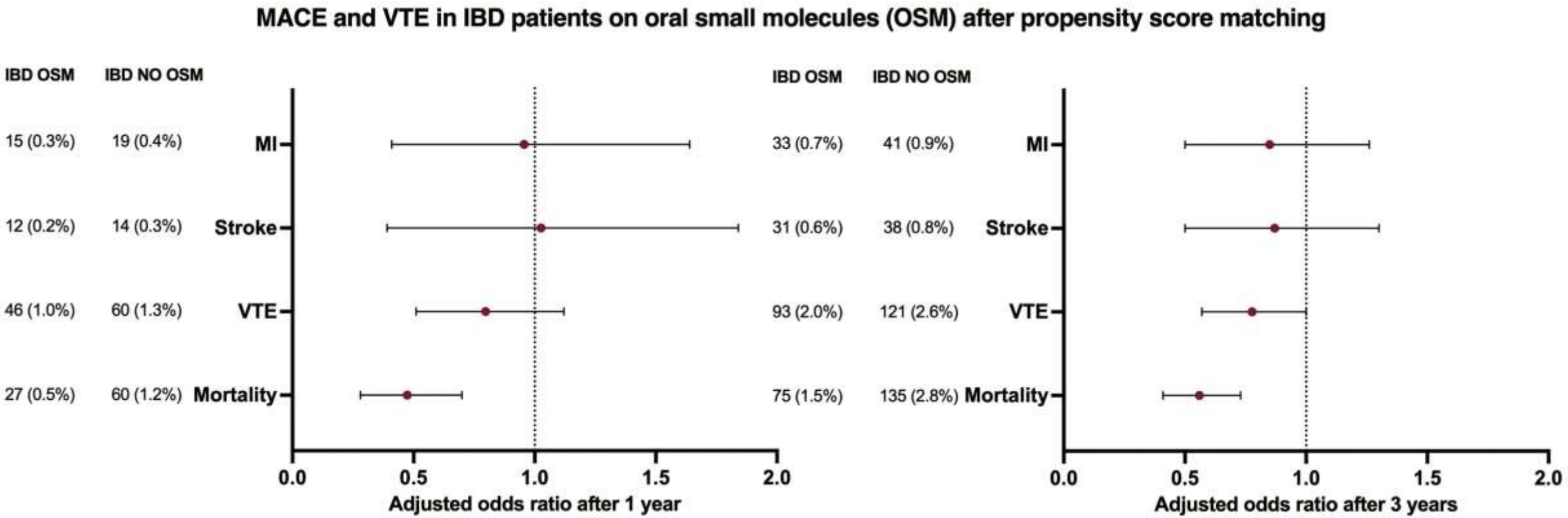
¶All events, including those outside the 28-day risk period were included.[1] ††57-year-old male who experienced a suspected pulmonary thromboembolism event while hospitalized for worsening of COVID-19 infection and acute renal failure. Primary cause of death was pulmonary embolism. Risk factors included medical history of arterial hypertension, former cigarette smoker, concurrent COVID-19 infection and prolonged hospitalization.[2] ‡‡Three events were reported as severe (number of events): complicated appendicitis (1), gastroenteritis norovirus (1), necrotising fasciitis (1).[1]

§§Sixteen events were reported as severe in a total of 13 patients (number of events): appendicitis (3), arthritis bacterial (1), atypical pneumonia (1), herpes zoster (3), herpes zoster meningitis (1), mastoiditis (1), meningitis viral (1), ophthalmic herpes zoster (1), osteomyelitis (1), perirectal abscess (1), sinusitis (1), wound infection (1).[1] ¶¶Five events were reported as severe.[1] †††Defined as cardiovascular death, nonfatal myocardial infarction, and nonfatal stroke in Panaccione R, et al.[2] ‡‡‡Defined as DVT and PE (fatal and nonfatal) in Pannacione R, et al.[2]

AE, adverse event; CI, confidence interval; BID, twice daily; cPYE, censored patient-years of exposure; DVT, deep vein thrombosis; EAIR, exposure-adjusted incidence rate; JAK, Janus kinase; LTE, long-term extension; N/R, not reported; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PE, pulmonary embolism; PYE, patient-years of exposure; TEAE, treatment-emergent adverse event; TOFA, tofacitinib; VTE, venous thromboembolism.

1. Sandborn WJ, et al. *Aliment Pharmacol Ther*. 2022;55:464–78;; 2. Panaccione R, et al. Presented at the European Crohn's and Colitis Organisation (ECCO), 19–22 February 2025, Berlin, Germany: DOP002 .

A retrospective analysis of a large multi-institutional US data base for MACE and VTE in IBD patients treated with small molecules (93% JAK inhibitors)[1]



MACE, major adverse cardiovascular event; VTE, venous thromboembolic event; IBD, inflammatory bowel disease; MI, myocardial infarction; VTE, venous thromboembolic event; JAK, janus kinase inhibitor.

1. Qapaja, Thabet et al. Inflammatory bowel diseases, izae267. 13 Nov. 2024.

Putting It All Together: Positioning IBD therapy[1]

UC
CD

Modifier	First drug consideration	Reason
Psoriasis	Anti-TNF or IL-12/23, IL23	On label
Anti-TNF induced psoriasiform dermatitis	IL-12/23,IL23, UPA*, S1P#	On label
>60 yrs., cardiovascular comorbidity	Vedolizumab or IL12/23, IL23	Older patients have higher risk of infections and malignancy and cardiovascular risks
Synovitis Arthritis	anti-TNF or JAKs*#	On label
Enthesitis	Anti-TNF, JAKs*# or IL-12/23, IL23	Most common IBD related joint symptoms (like PsA)
Low albumin, high BMI, High CRP	JAKs*#, S1P#	Non-protein-based therapies (not a biologic)
Need for speed	IFX, JAKs*# > S1P#, IL23	Rapidity of onset
Preconception and Pregnancy	BIOLOGICS	Established safety and not cross placenta in 1st trimester**
Isolated Proctitis	S1P#	Efficacy in Phase 3
Extensive Small Bowel CD	Anti-TNF	Evidence suggests best healing of SB
Fistulas	Anti-TNF	Infliximab RCT

1. Opinion of Dr. Bruce Sands. *Upadacitinib is not approved by Swissmedic for bio-naïve IBD patients. **Per Swissmedic label, no biologic is recommended for use during pregnancy. #S1P Modulators and Tofacitinib are approved by Swissmedic only for UC. TNF, tumor necrosis factor; IL, interleukin; Upa, Upadacitinib; S1P, Sphingosin-1-phosphate; JAK, janus kinase; PsA, psoriatic arthritis; SB, small bowel; RCT, randomized controlled trial;

Emma

Considerations in choice of therapy

- Efficacy after failure of 1 advanced therapy
- She is concerned about safety of advanced therapies
- Still wishes to conceive in the coming year*
- Hesitant to self-inject

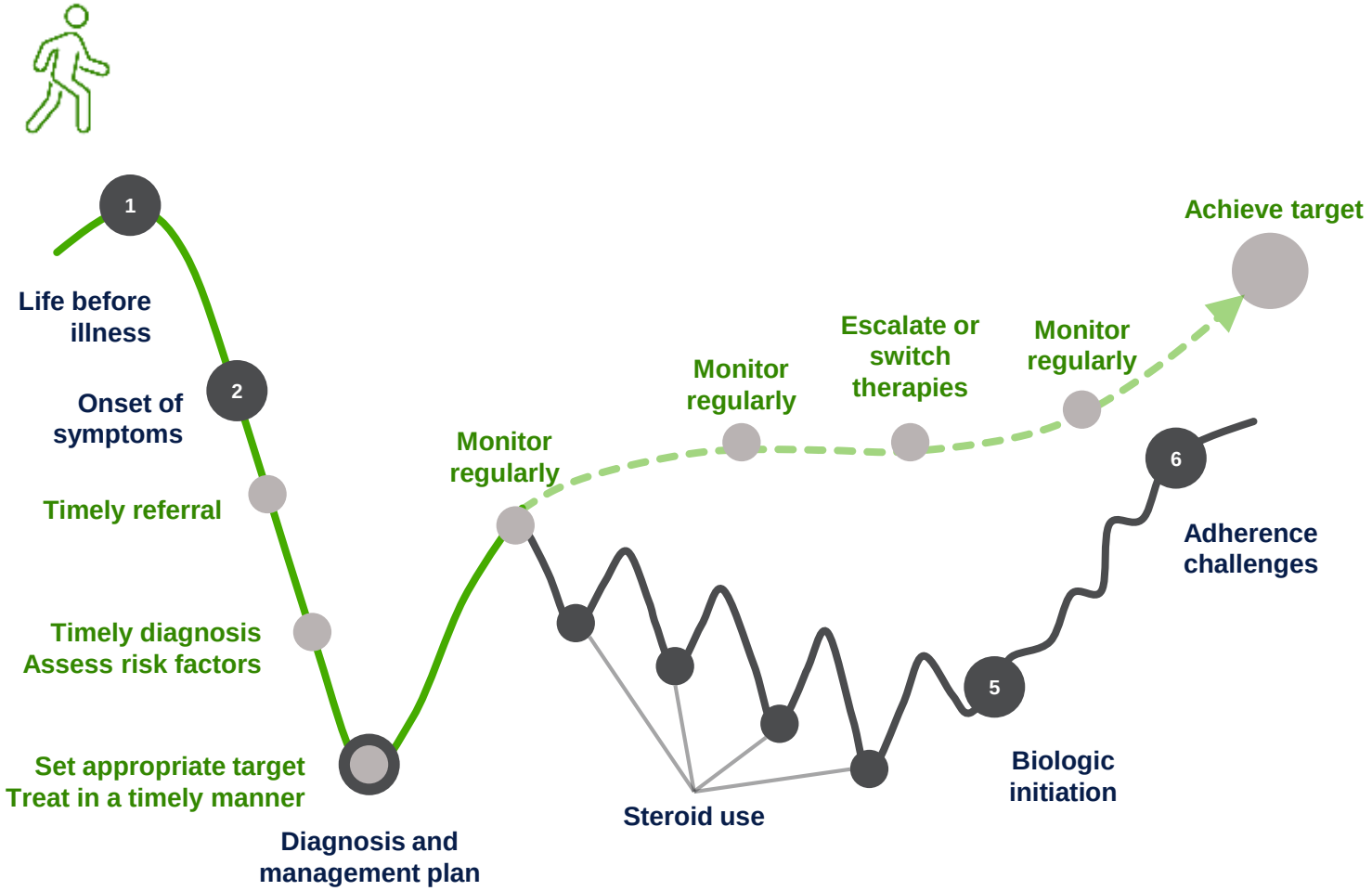
Chooses risankizumab

IUS, intestinal ultrasound.
This is a hypothetical patient case for discussion. *Women of childbearing age should use effective contraception during and for at least 20 weeks after treatment with Risankizumab. Risankizumab should not be used during pregnancy.

Putting it all together to achieve disease modification[1]

Principles[1]:

- Early diagnosis
- Timely treatment
- Effective therapy
- Meaningful targets
- Tailored to the patient
- Monitoring
- Treatment optimization to achieve targets



1. Opinion of Dr. Bruce Sands.

Agenda

- Meet Emma
- Bottom up or top down? – the window of opportunity
- Unveiling underlying inflammation through holistic monitoring
- How recent treatment innovations help us aim for higher targets
- **Conclusions**
- Questions?

Conclusions

1. High burden of disease: greater than most healthcare providers appreciate[1]
2. Timely interventions in a “window of opportunity” improve the course of the disease[2-3]
3. STRIDE II sets specific goals in a treat-to-target approach to optimize care of IBD patients[4]
4. Holistic monitoring includes subjective (symptoms, quality of life) and objective (biomarkers, endoscopy, histology and imaging) evaluation[4-6]
5. Monitoring helps achieve tight control[7]
6. Early treatment/top-down approaches should use the most efficacious treatment that is appropriate for that individual[8]
7. New agents with novel mechanisms of action offer progress in both safety and efficacy[8]

1. D'Amico F, et al. United European Gastroenterol J. 2024;12:705–16. 2. Colombel JF, et al. Gastroenterology. 2017;152:351–361. 3. Fumery M, et al. Clin Gastroenterol Hepatol. 2018;16:343–56. 4. Turner D, et al. Gastroenterology. 2021;160:1570–83. 5. Le Berre C, et al. Gastroenterology. 2022;162:1424–38. 6. Garcia NM, et al. United European Gastroenterol J. 2022;10:1121–8. 7. Colombel JF, et al. Lancet. 2017;390:2779–89. 8. Opinion of Dr. Bruce Sands.