The Next Frontier in IBD:

Late-Stage Clinical Advances With Novel Therapeutic Pathways

May 4, 2026

6:00–7:30 PM *(dinner at 6:00 PM and program at 6:30 PM)* • Hyatt Regency McCormick Place

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Faculty

Bruce Sands, MD, MS

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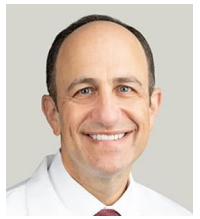

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Disclosures

Prof. Bruce Sands, MD, MS reports consulting fees from Abbvie, Alimentiv , Adiso Therapeutics, Agomab, Amgen, AnaptysBio, Astra Zeneca, Biolojic Design, Biora Therapeutics, Boehringer Ingelheim, Celltrion, Equillium, Ensho Therapeutics, Enthera, Enveda Biosciences, Evommune, Ferring, Fzata, Galapagos, Genentech (Roche), Gilead Sciences, GlaxoSmithKline, Gossamer Bio, Imhotex, Immunyx Therapeutics, Index Pharmaceuticals, Innovation Pharmaceuticals, Kaleido, Kallyope, Merck & Co., Microba, Microbiotica, Mirador Therapeutics, Mitsubishi Tanabe Pharma, Mobius Care, Morphic Therapeutics, MRM Health, Nexus Therapeutics, Nimbus Discovery, Odyssey Therapeutics, Palisade Bio, Prometheus Biosciences, Prometheus Laboratories, Protagonist Therapeutics, Q32 Bio, Rasayana Therapeutics, Recludix Therapeutics, Reistone Biotherapeutics, Sanofi, Sorriso Pharmaceuticals, Surrozen, Target RWE, Teva, TLL Pharmaceutical, TR1X, Union Therapeutics,; consulting and speaking fees from Abivax; consulting and speaking fees and other support from Lilly; research grants, consulting and speaking fees and other support from Bristol Myers Squibb, Janssen/J & J Innovative Medicine, Pfizer, Takeda; research grants and consulting fees from Theravance Biopharma; and consulting fees, stock and stock options from Ventyx Biopharma.

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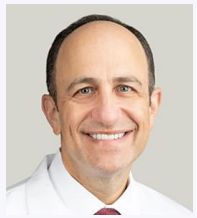
Agenda



David Rubin, MD

University of Chicago Medicine
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Unmet Needs and New Goals in IBD Treatment

6:35–6:50

Parambir Dulai, MD

Feinberg School of Medicine
Northwestern University
Chicago, IL, USA

Mechanistic Rationale and Scientific Evidence for Emerging Therapies

6:50–7:05

Bruce Sands, MD, MS

Mount Sinai Health System
New York, NY, USA

Clinical Data From Late-Stage Investigational Therapies in IBD

7:05–7:25

All

Q&A

7:25–7:30

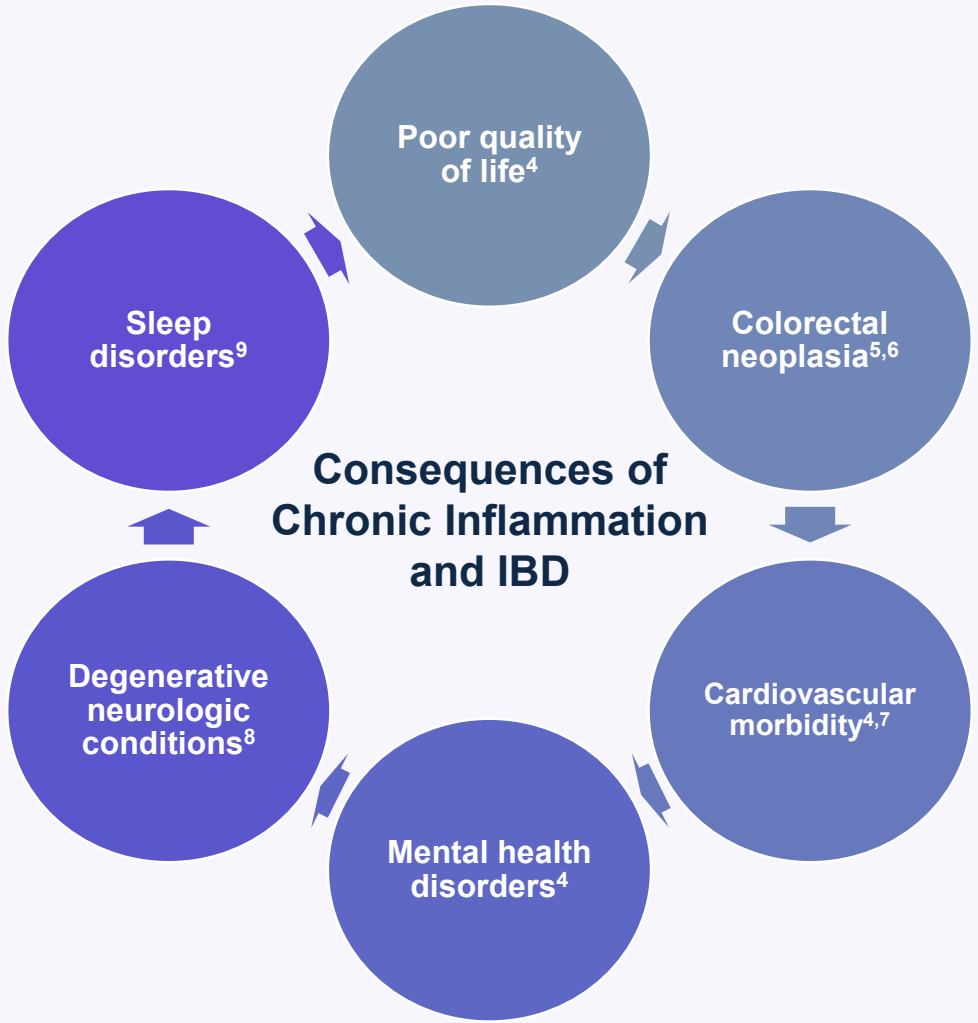
Unmet Needs and New Goals in IBD Treatment

David Rubin, MD

University of Chicago Medicine
Chicago, IL, USA

Challenges in IBD and Chronic Consequences

- Delays in diagnosis[1]
- No cure(s)[1]
- Consideration of extra-intestinal manifestations[2] and systemic problems
- No therapeutic biomarkers[3]
- Imprecise disease monitoring strategies[3]



1. Gordon H, et al. *J Crohns Colitis*. 2024 18: 1531-1555; 2. Rogler G, et al. *Gastroenterology*. 2021;161:1118-1132; 3. Atreya R, Neurath MF. *Clin Gastroenterol Hepatol*. 2024;22:1353-1364; 4. Cabellero-Mateos, et al. *J Clin Med*. 2025;14:1-28; 5. Dulai PS, et al. *Cancer Prev Res*. 2016; 9:887-894; 6. Shahgoli, et al. *Int J Colorectal Dis*. 2024;39:173; 7. Jaiswal, et al. *Medicine*. 2023; 102:6; 8. Zamani M, et al. *Inflamm Bowel Dis*. 2024;30:2195-2204; Kinnucan JA, et al. *Gastroenterol Hepatol*. 2013;9:718-726.

Disease Classification Beyond Phenotypic Assessment

- Clarification of known IBD subtypes
- Broad inclusion of other chronic inflammatory bowel conditions
  - Microscopic colitis
  - Monogenic and very early onset IBD
  - Checkpoint inhibitor IBD
  - Common variable immunodeficiency enteropathy
- Immunotypes and molecular biomarkers
- Response (or lack of) response to therapy
- Develop validated damage index (Lémann Index)

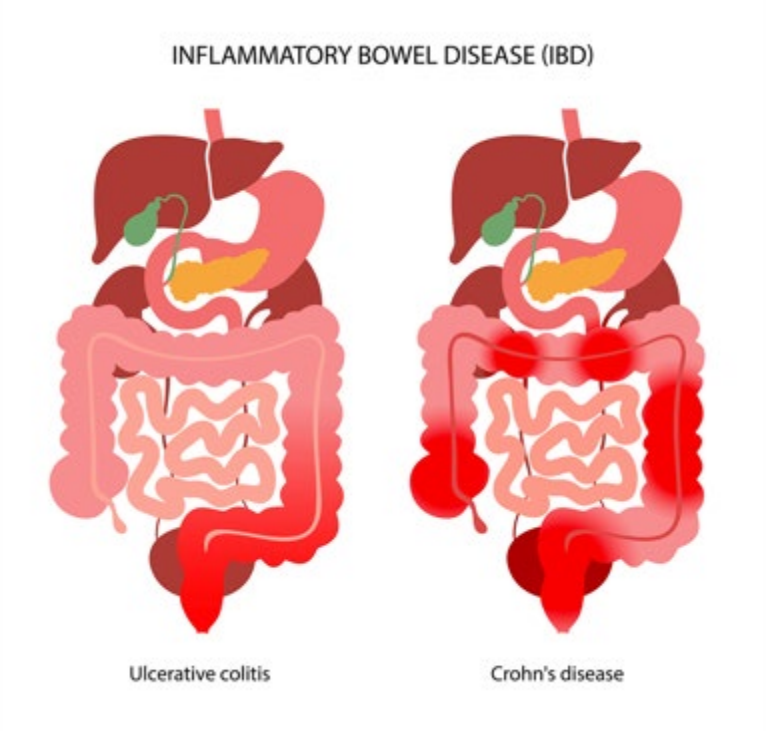
Examples of Mimics of IBD and Potential VEOs with Specific Therapeutic Implications

Disease	Cause
Chronic granulomatous disease	**Neutrophil defect**
Leukocyte adhesion-1	**Neutrophil migration defect**
Common variable immunodeficiency	**Impaired T-cell function**
Agammaglobulinemia	**Impaired B-cell function**
Hyperimmunoglobulin M syndrome	**Deficiency of IgG, IgA and IgE**
Wiskott-Aldrich Syndrome	**Impaired leukocyte migration/function**

VEO, very early onset.
Ouahed J. *Inflamm Bowel Dis.* 2020;26(6):820-842; Kelsen JR, et al. *Inflamm Bowel Dis.* 2020 May; 12;26(6):909-918; Pariente B et al. *Gastroenterology*. 2015 Jan;148(1):52-63.e3.

Reclassification of IBD is Needed … and Happening

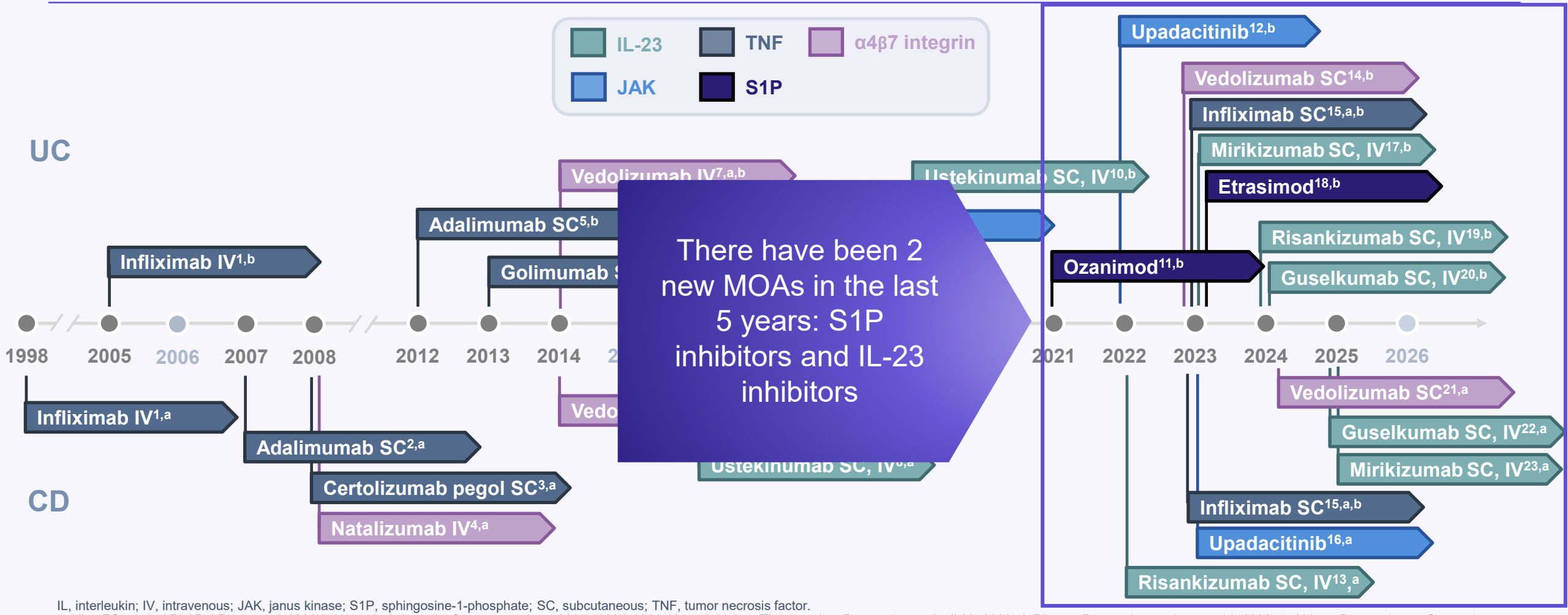
- There is (important) heterogeneity across the IBDs
- Current classifications are imprecise and there is inter- (and intra!) observer disagreements
- Creation of data dictionary
- Broad effort with prospective and retrospective efforts
  - Clinically useful NOW
  - Molecular classifications LATER
- **IOIBD25 Classification** due this year!



IOIBD

Information provided by David T. Rubin, MD, IOIBD Executive Committee Chair.

Advanced Treatment Options Approved for Crohn's Disease (CD) and Ulcerative Colitis (UC) Have Been Expanding in Recent Years



IL, interleukin; IV, intravenous; JAK, janus kinase; S1P, sphingosine-1-phosphate; SC, subcutaneous; TNF, tumor necrosis factor.

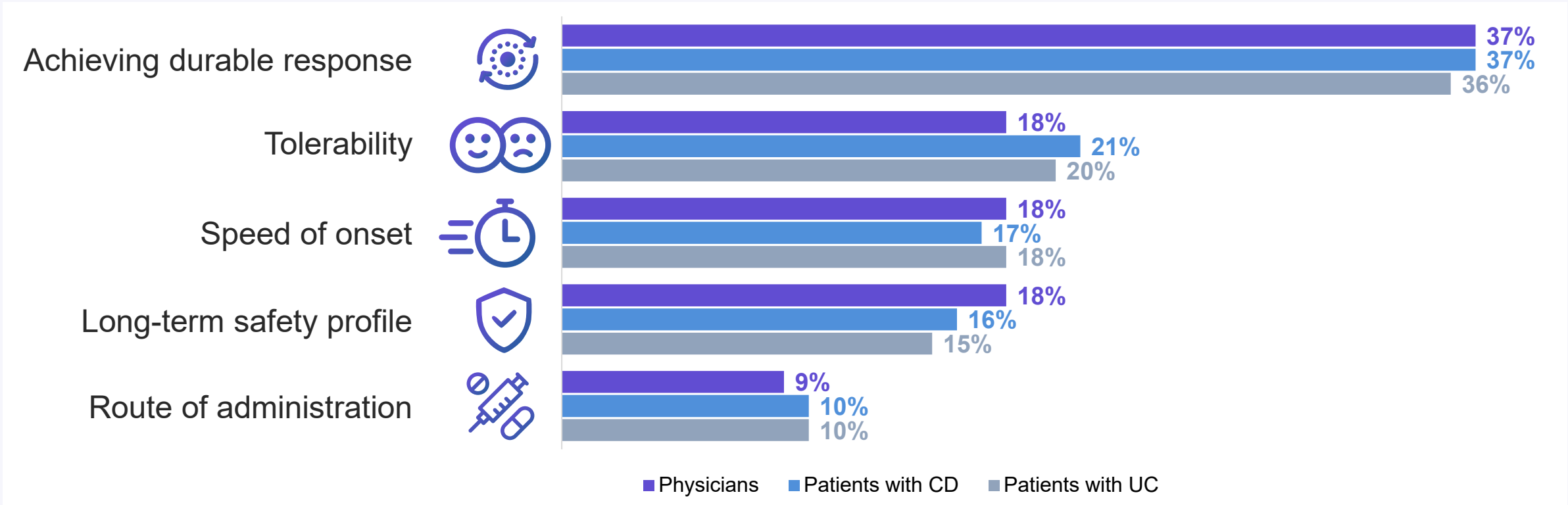
1. Hisa EC, et al. *APLAR J Rheumatol.* 2006;9:107-118. 2. Lang L. *Gastroenterology*. 2007;132(5):1644-1645. 3. Nektar Therapeutics. Press release. April 23, 2008. 4. Biogen. Press release. January 14, 2008. 5. Abbott. Press release. September 28, 2012. 6. Johnson & Johnson. Press release. May 15, 2013. 7. Takeda. News release. May 21, 2014. 8. Johnson & Johnson. Press release. September 26, 2016. 9. Pfizer. Press release. May 30, 2018. 10. Johnson & Johnson. Press release. October 21, 2019. 11. Bristol Myers Squibb. Press release. May 27, 2021. 12. AbbVie. News release. March 16, 2022. 13. AbbVie. News release. June 17, 2022. 14. Takeda. Press release. September 27, 2023. 15. Celltrion. Press release. October 23, 2023. 16. AbbVie. News release. May 18, 2023. 17. Lilly. News release. October 26, 2023. 18. Pfizer. Press release. October 13, 2023. 19. AbbVie. News release. June 18, 2024. 20. Johnson & Johnson. Press release. September 11, 2024. 21. Takeda. Press release. April 18, 2024. 22. Johnson & Johnson. Press release. March 20, 2025. 23. Lilly. News release. January 15, 2025.

What is the main deciding factor that you use when evaluating a new therapy for your patients with ulcerative colitis?

Durable Response Is Key to Therapy Selection for Both Patients and Physicians

Data from the IBD GAPPS survey, including 1368 patients with CD, 1030 patients with UC, and 654 physicians

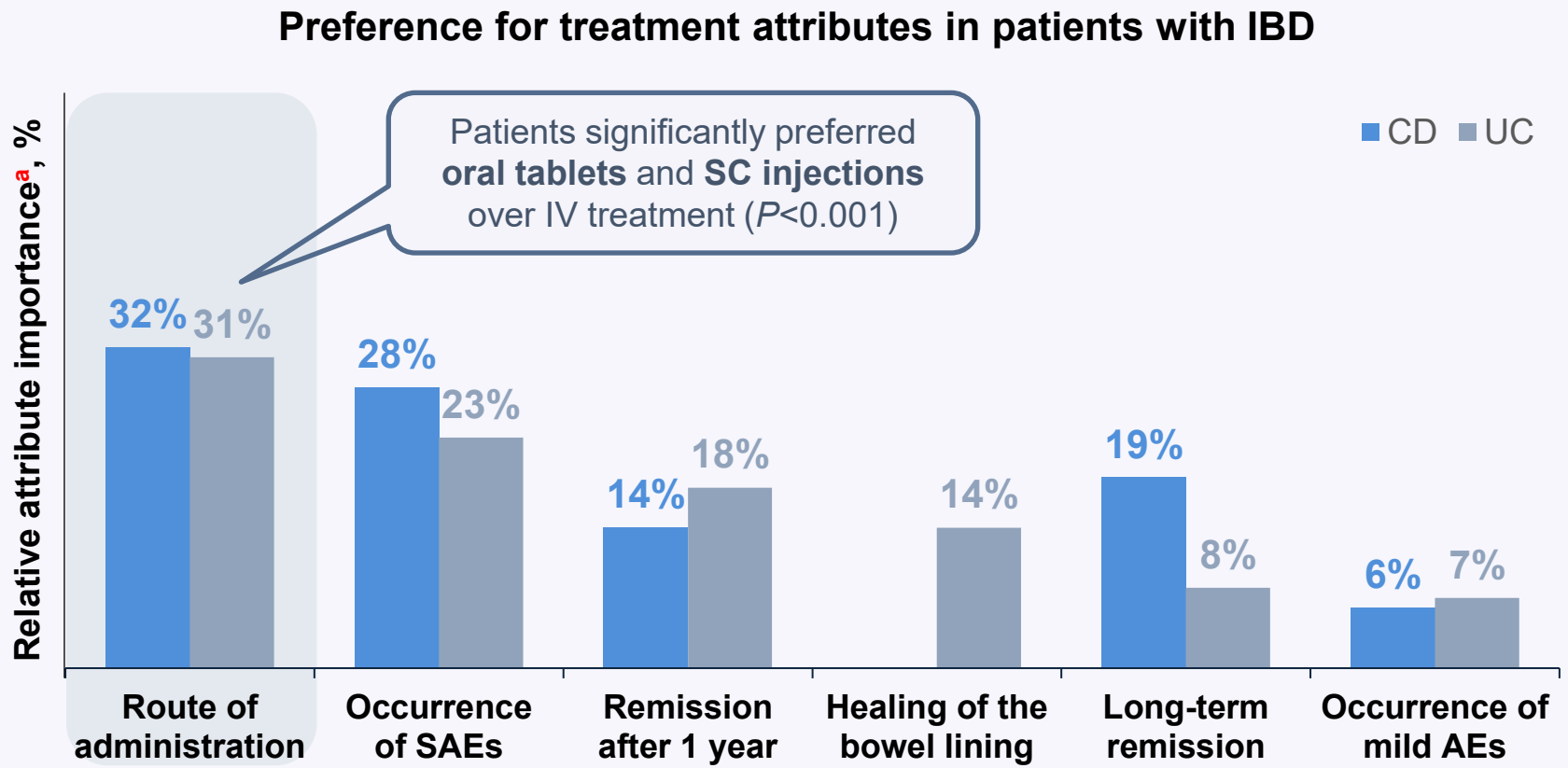
Drivers of Treatment Choice



Rubin DT, et al. *Inflamm Bowel Dis*. 2021;27(12):1942-1953.

Patients Identify Route of Administration as an Important Treatment Attribute

In a recent study on patient preferences, patients with CD (n=360) or UC (n=326) ranked **route of administration** as the most important attribute when selecting a treatment



Descriptive, observational, noninterventional, stated-preference study of 360 patients with CD and 326 patients with UC conducted across 7 European countries; data were collected through an online cross-sectional survey.
[a]Based on a discreet choice experiment conditional logit model.
AE, adverse event; IV, intravenous; SAE, serious adverse event; SC, subcutaneous; UC, ulcerative colitis.
Fiorino G, et al. *Inflamm Bowel Dis*. 2024;30:2380-2394.

Despite New Therapies, Unmet Needs in IBD Remain

A substantial number of patients do not respond to or lose response to current treatments[1-8]

Important limitations remain around safety, tolerability, convenience, and outcomes in difficult-to-treat patients[10]

Clinical improvement does not always translate to full control of underlying disease[11,12]

1. Danese S, et al. *Lancet Gastroenterol Hepatol.* 2021;7:118-127. 2. Hibi T, et al. *J Gastroenterol.* 2017;52:1101-1111. 3. Jyseleca. Summary of product characteristics. 2020. https://www.ema.europa.eu/en/documents/product-information/jyseleca-epar-product-information_en.pdf. Accessed September 2025. 4. Rubin DT, et al. *Lancet Gastroenterol Hepatol.* 2022;7:17-27. 5. Sandborn WJ, et al. *N Engl J Med.* 2017;376:1723-1736. 6. Sandborn WJ, et al. *Gastroenterology.* 2020;158:562-572. 7. Sands BE, et al. *N Engl J Med.* 2019;381:1201-1214. 8. Sandborn WJ, et al. *N Engl J Med.* 2016;374:1754-1762. 9. Kayal M, et al. *Clin Gastroenterol Hepatol.* 2023;21(13):3433-3436.e1. 10. Parigi TL, et al. *J Crohns Colitis.* 2025;19(3):jjae145. 11. Turner D, et al. *Gastroenterology.* 2021;160(5):1570-1583. 12. Centanni, L et al. *Pharmaceuticals (Basel).* 2025;18(1):78.

Future of IBD Treatment

There are an increasing number of drugs with the same molecular target

Additional agents with novel mechanisms of action are needed

There is a need for treatment options that can offer disease modification

This includes preventing relapse, minimizing steroid exposure, preserving bowel integrity, reducing fibrosis-related complications, and avoiding hospitalization and surgery

Treatment goals should consider the patient's perspective

This includes improved quality of life and restoration of daily functioning

Treatment Goals in IBD Have Shifted

New treatment goals go beyond symptom relief to focus on rapid, durable, steroid-free remission; objective control of inflammation; and deeper healing targets

UC: endoscopic and histologic remission

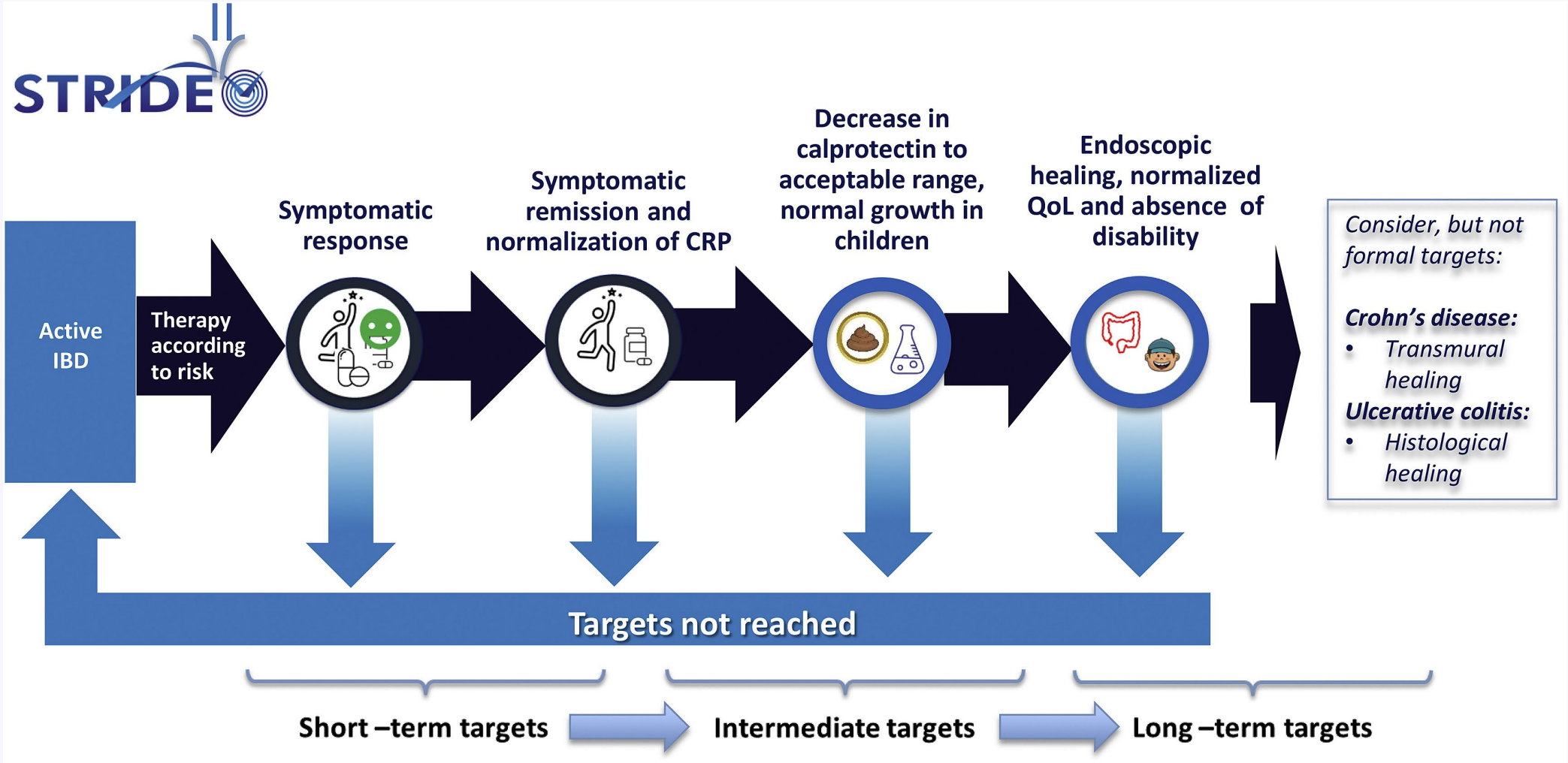
CD: prevention of long-term bowel damage and progression[1,2]

Current therapies are primarily anti-inflammatory and do not reliably prevent, halt, or reverse established fibrotic remodeling

As a result, patients may still progress to fibrostenotic strictures, obstruction, intervention, and surgery[3,4]

1. Turner D, et al. *Gastroenterology*. 2021;160(5):1570-1583. 2. Centanni L, et al. *Pharmaceuticals (Basel)*. 2025;18(1):78. 3. Solitano V, et al. *J Clin Med*. 2023;12(9):3052. 4. Shao YP, et al. *World J Gastroenterol.* 2025;31(33):109938.

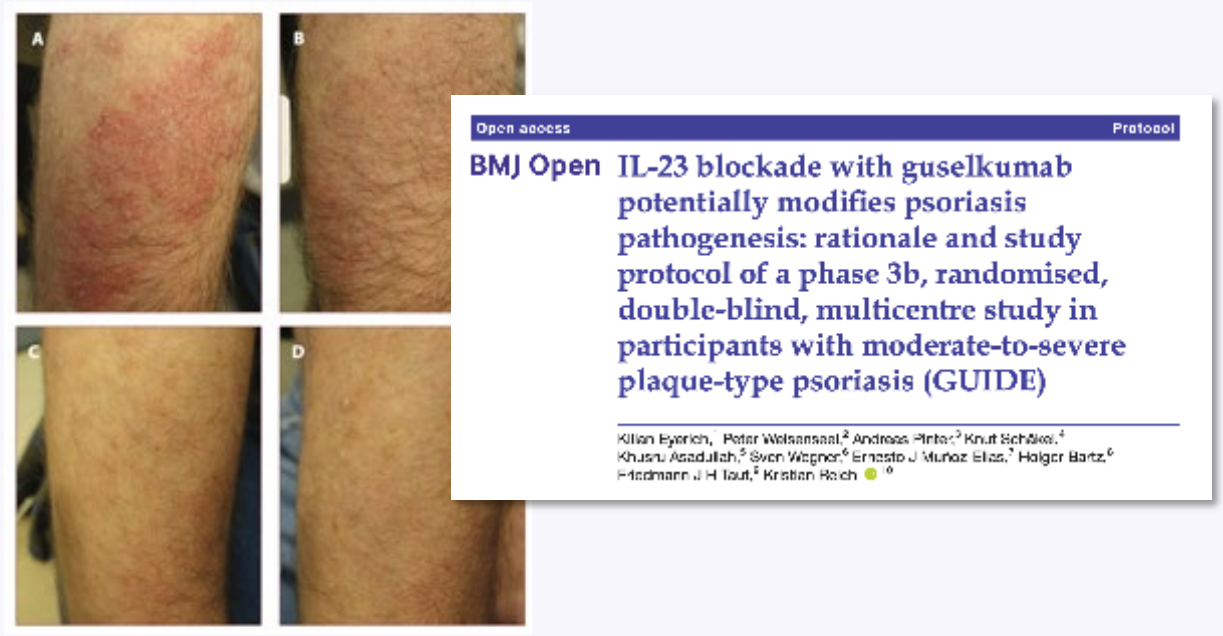
STRIDE-II clarified treatment targets in IBD, but important gaps remain in consistent measurement, monitoring, and achievement of these goals in routine practice



Reprinted from Turner D, et al. STRIDE-II: an update on the selecting therapeutic targets in inflammatory bowel disease (STRIDE) initiative of the International Organization for the Study of IBD (IOIBD): determining therapeutic goals for treat-to-target strategies in IBD, *Gastroenterology.* 2021;160(5):1570-1583. Copyright 2021, with permission from Elsevier.

Can We Achieve a "Clinical Super Response" in IBD?

Disease clearance in dermatology[1]

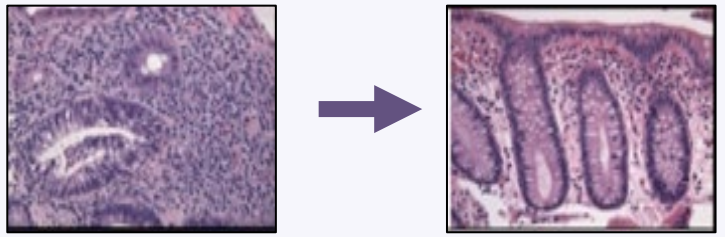


Psoriasis Area and Severity Index 100 (PASI 100) represents total disappearance of skin lesions[2]

Used with permission from Matrix Medical Communications. Fowler JF, et al. Treatment satisfaction, product perception, and quality of life in plaque psoriasis patients using betamethasone dipropionate spray 0.05. *J Clin Aesthet Dermatol.* 2017;10(11):13-18. Permission conveyed through Copyright Clearance Center, Inc.

Disease clearance in IBD

Composite endpoints including endoscopic and histological remission[3] or histological normalization[4]



What will this lead to?

Images provided by David T. Rubin, MD

1. Fowler JF, et al. *J Clin Aesthet Dermatol*. 2017;10:13-18. 2. Reich K, et al. *Lancet*. 2019;394:576-86. 3. Colombel JF. *Gastroenterol Hepatol*. 2021;17:233-35. 4. Christensen B, et al. Clin *Gastroenterol Hepatol*. 2017;15:1557-64.e1.

In Progress: STRIDE III

1. Clarifying clinical practice vs clinical trial endpoints
2. More patient-centred outcomes
3. Discussion of transmural healing and histological healing
4. Adaptations for low-resource settings
5. Integration of AI-based tools
6. Special populations (the elderly, paediatric patients, relevant comorbidities), patients with stoma, patients with proctitis, following pouch surgery

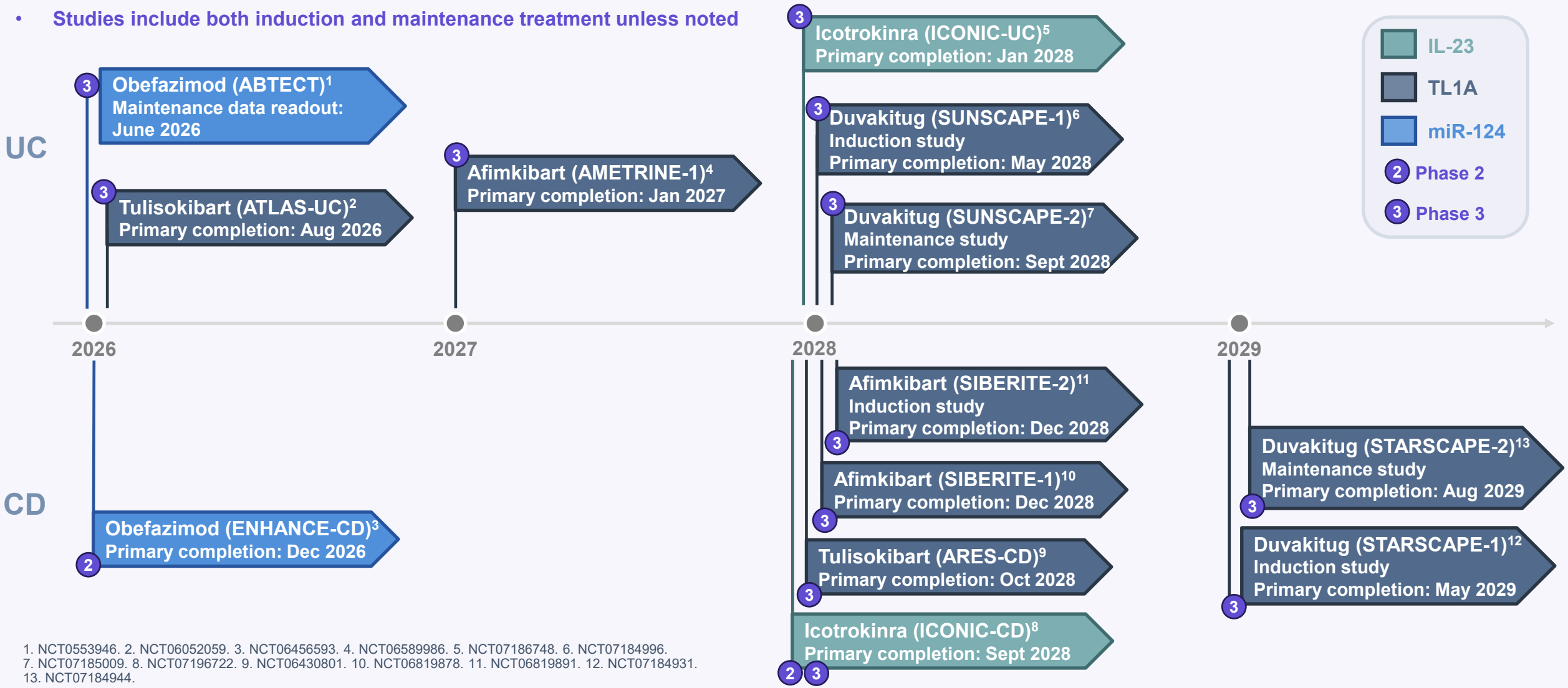
Steering committee: Dan Turner, Axel Dignass, David T. Rubin, Iris Dotan

Information provided by David T. Rubin, MD, IOIBD Executive Committee Chair.

What do you feel is the most important unmet need with current IBD treatment?

Several Therapies With a Novel Mechanism of Action Are in Later Stages of Development

- Studies include both induction and maintenance treatment unless noted



1. NCT0553946. 2. NCT06052059. 3. NCT06456593. 4. NCT06589986. 5. NCT07186748. 6. NCT07184996. 7. NCT07185009. 8. NCT07196722. 9. NCT06430801. 10. NCT06819878. 11. NCT06819891. 12. NCT07184931. 13. NCT07184944.

Mechanistic Rationale and Scientific Evidence for Emerging Therapies

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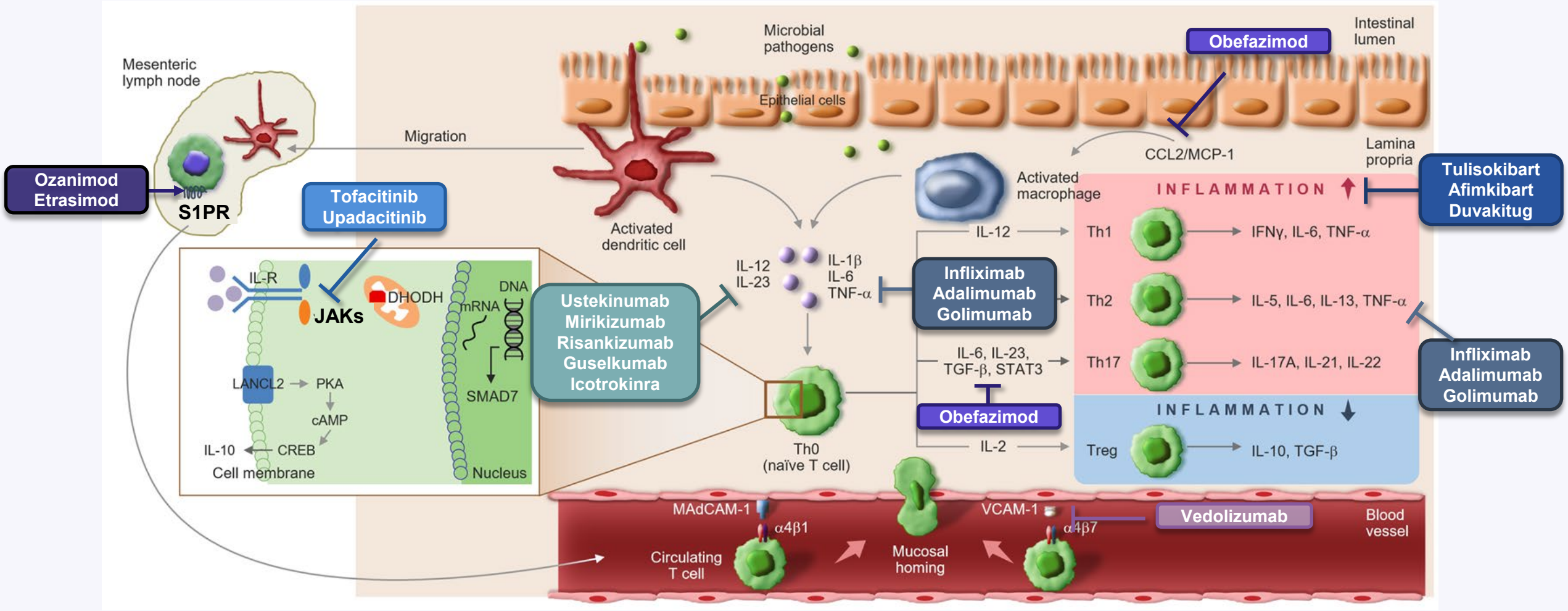
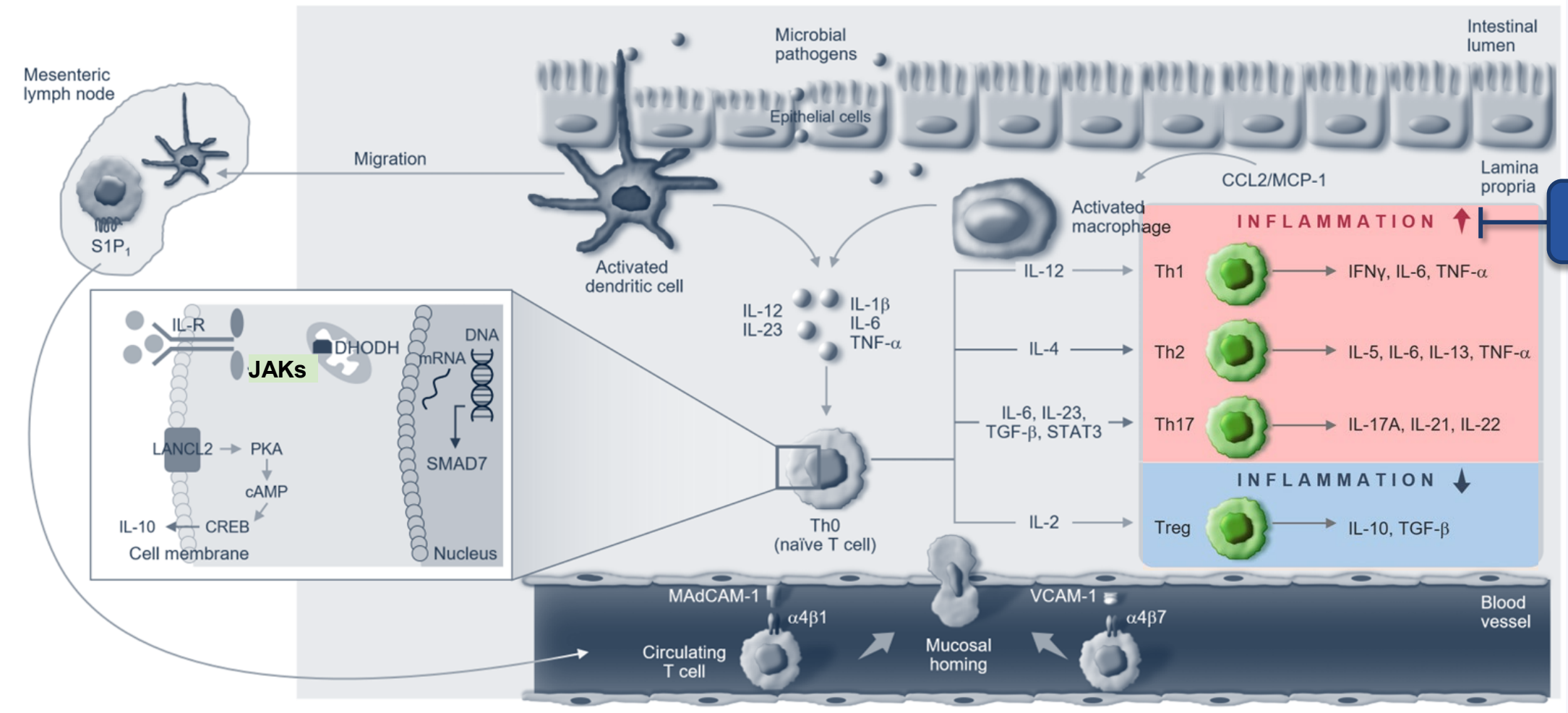
The Pathogenesis of UC Provides Many Therapeutic Targets



cAMP, cyclic adenosine monophosphate; CCL, C-C motif chemokine ligand; CREB, cAMP response element binding protein; DHODH, dihydroorotate dehydrogenase; IFN, interferon; IL, interleukin; JAK, Janus kinase; LANCL2, lanthionine synthetase C-like 2; MAdCAM, mucosal addressin cell-associated molecule; MCP-1, monocyte chemoattractant protein-1; PKA, protein kinase; S1PR, sphingosine-1-phosphate receptor; STAT3, signal transducer and activator of transcription 3; TGF, transforming growth factor; Th0, naive T cell; Th1, T-helper 1 cell; Th2, T-helper 2 cell; Th17, T-helper 17 cell; TNF, tumor necrosis factor; Treg, regulatory T cell; UC, ulcerative colitis; VCAM-1, vascular cell adhesion molecule.

Highlighting the Mechanism of Action of TL1A Inhibitors



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TL1A Inhibitors: Tulisokibart, Afimkibart, Duvakitug

- Activate innate, adaptive immune pathways through binding DR3[1,2]
- Proinflammatory effects include T-cell activation and enhanced fibrosis[1,2]
- **TL1A inhibitors:** tulisokibart, afimkibart (RVT-3101), and duvakitug (TEV-48574)[1,3-5]

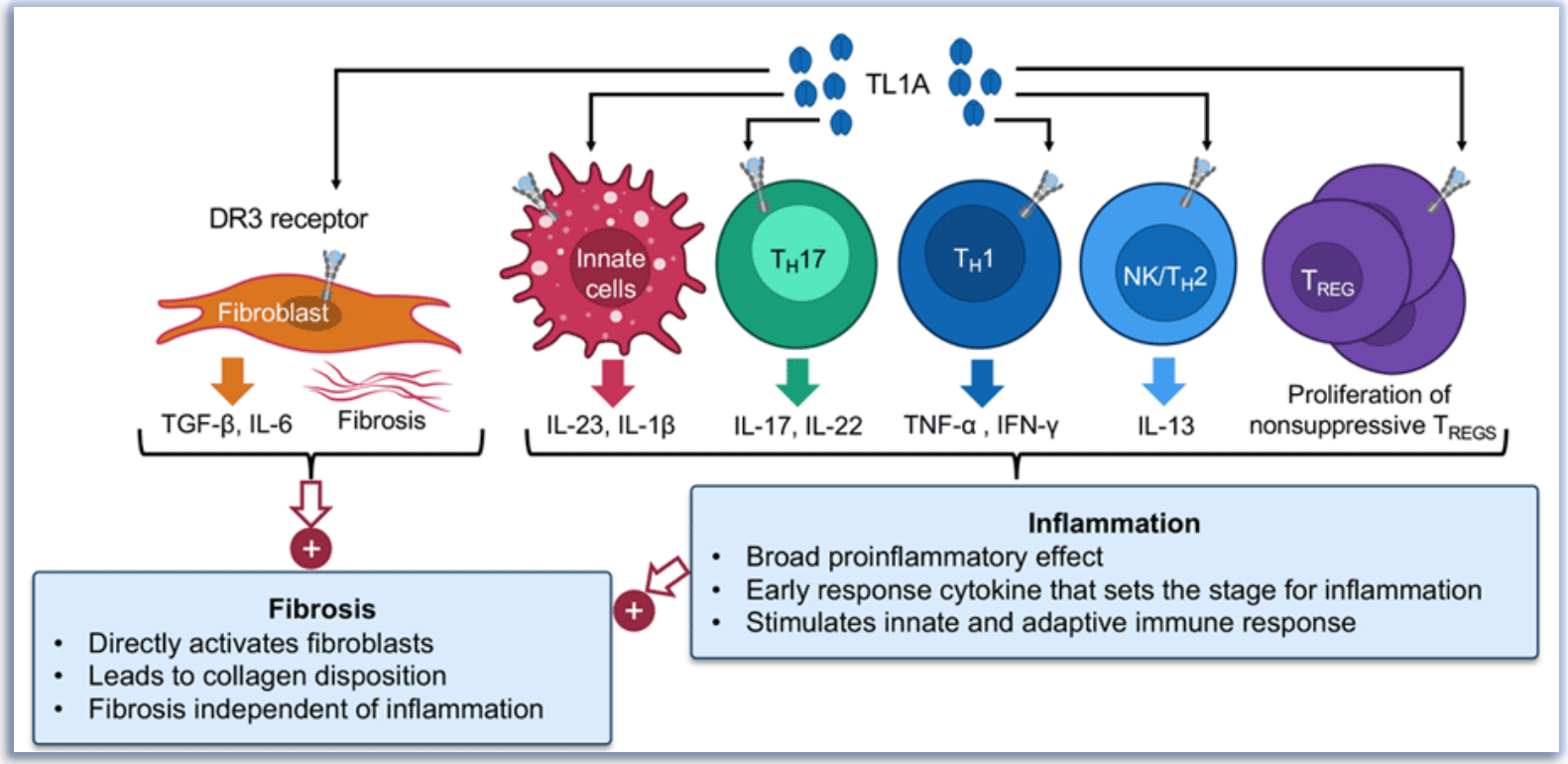
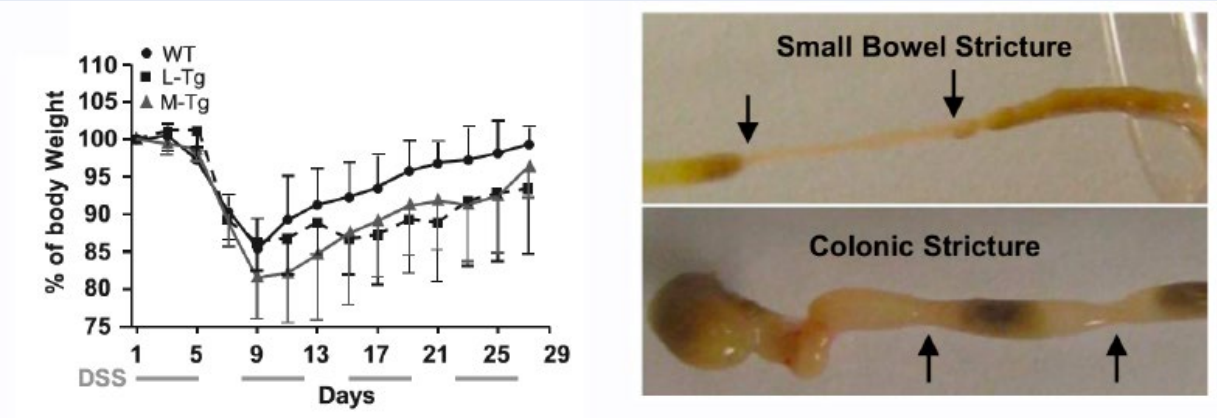
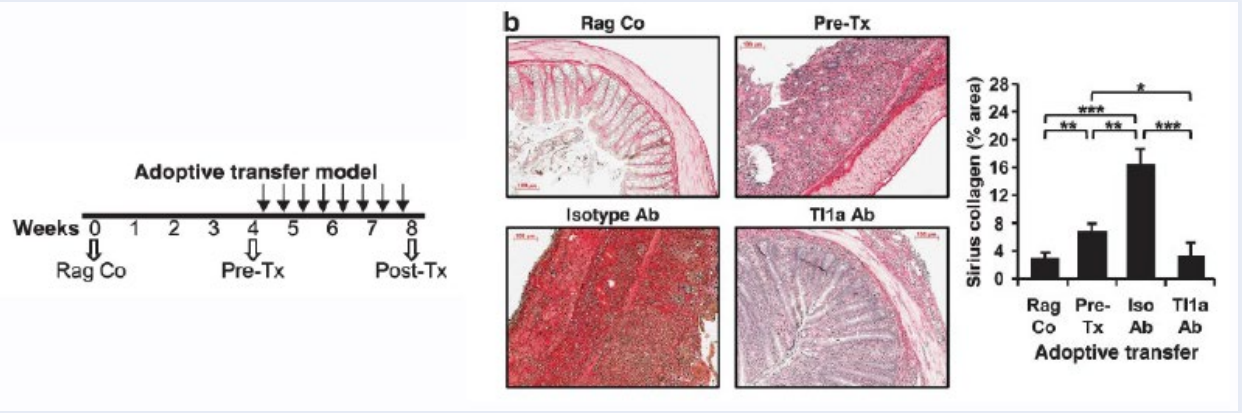


Image adapted from Ma C et al. UEG 2025. Presentation MP315.
DR3, death receptor 3; TL1A, TNF-like cytokine 1A.
1. Higashiyama M, et al. *Digestion*. 2023;104(1):74-81. 2. Gomez-Bris R, et al. *Int J Mol Sci*. 2023;24:2696. 3. Strober W, et al. *Gastroenterology*. 2011;140(6):1756-1767. 4. NCT06052059. 5. *PharmaPhorum*. Press release. October 5, 2023.

Inhibition of TL1A Signaling Protects Against Fibrosis in Mouse Models of IBD



Reprinted from Barrett R, et al, Constitutive TL1a expression under colitogenic conditions modulates the severity and location of gut mucosal inflammation and induces fibrostenosis. *Am J* Pathol. 2012;180(2):636-649. Copyright 2012, with permission from Elsevier.

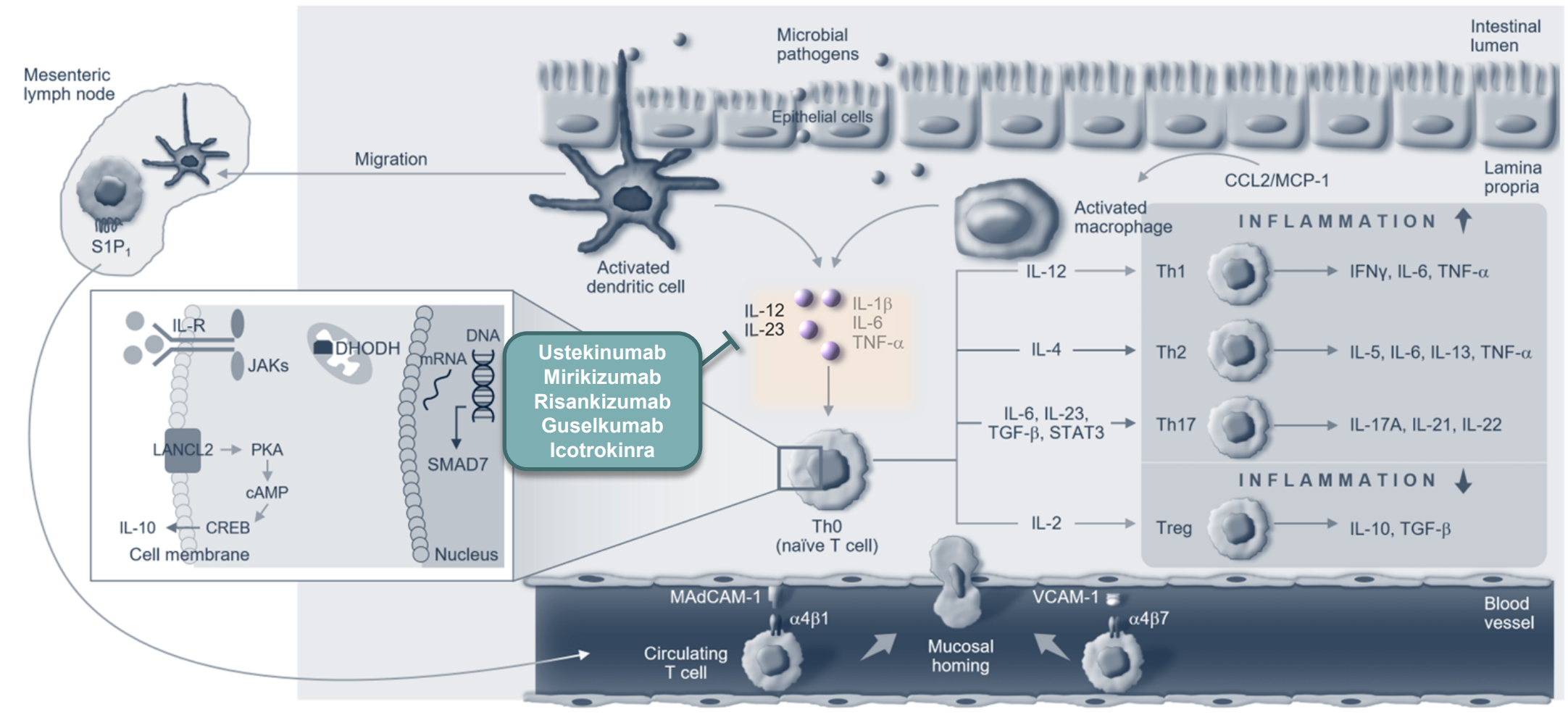


Reprinted from Shih DQ, et al. Inhibition of a novel fibrogenic factor Tl1a reverses established colonic fibrosis. *Mucosal Immunol.* 2014;7(6):1492-1503. Copyright 2014, with permission from Elsevier.

- In mouse models of colitis, TL1A overexpression results in increased collagen deposition and the development of intestinal strictures[1]
- TL1A antibody treatment reverses established fibrosis in mouse models of chronic colitis[2]

1. Barrett R, et al. *Am J Pathol.* 2012;180(2):636-649. 2. Shih DQ, et al. *Mucosal Immunol.* 2014;7(6):1492-503.

Highlighting the Mechanism of Action of IL-23 Inhibitors



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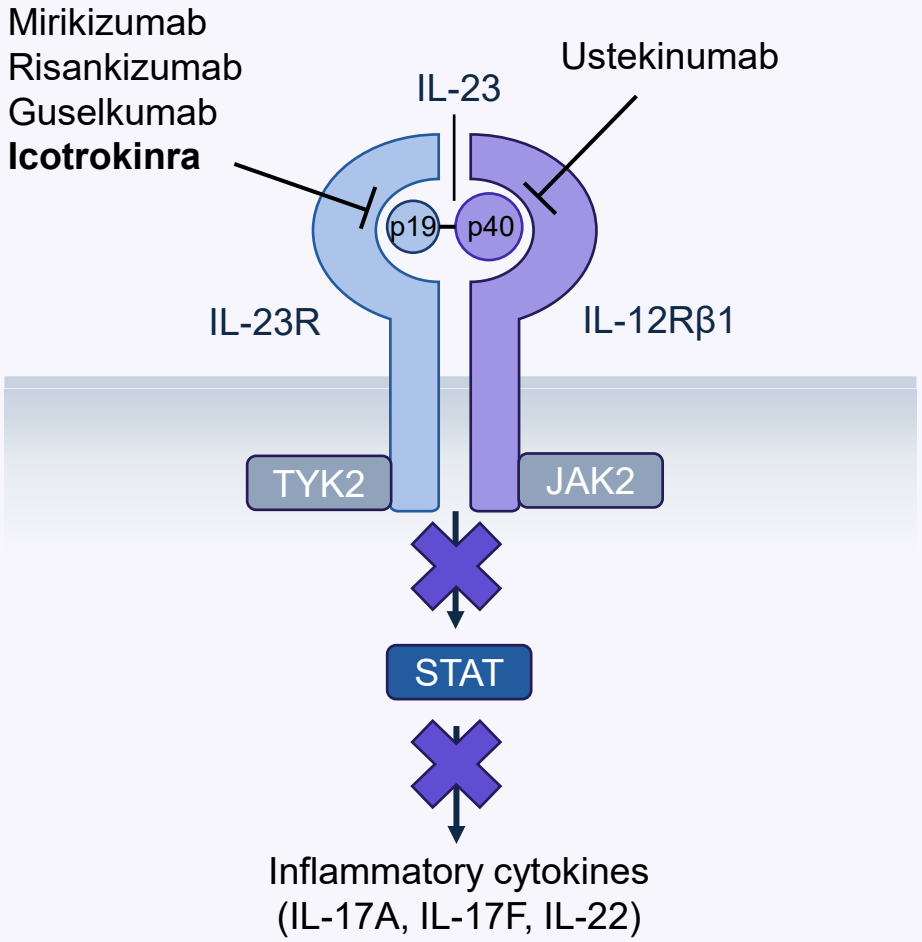
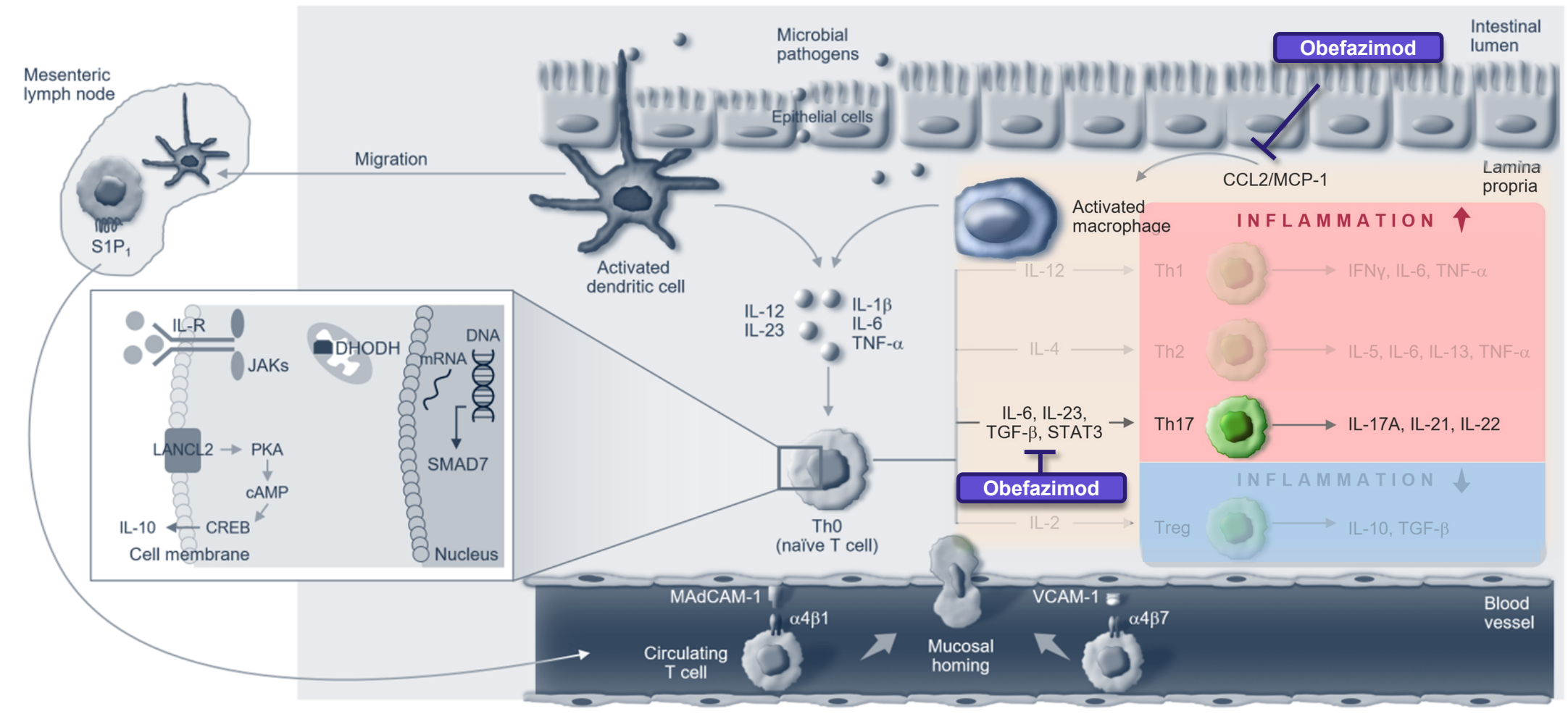
IL-23 Inhibitors: Ustekinumab, Mirikizumab, Risankizumab, Guselkumab, Icotrokinra

- IL-23 binding to its receptor stimulates activation of the JAK-STAT pathway[1]
- Results in production of inflammatory cytokines[1]
- Icotrokinra is the first IL-23R targeted oral peptide[2]



1. Verstockt B, et al. *Nat Rev Gastroenterol Hepatol.* 2023;20(7):433-446. 2. Stein Gold L, et al. *Adv Ther.* 2025;42(7):3158-3172.

Highlighting the Mechanism of Action of a miR-124 Enhancer



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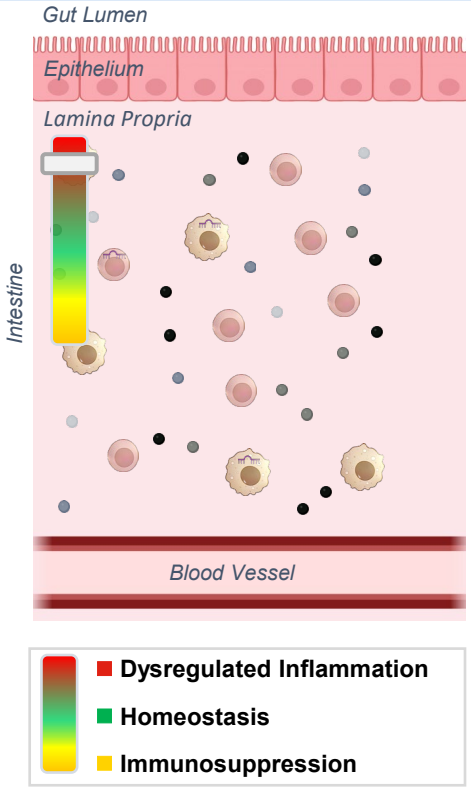
Obefazimod May Potentially Restore Mucosal Immune Balance in UC Through Physiologic Immunoregulation

Obefazimod Is Thought to Address Multiple Hallmarks of IBD Pathology and Chronic Inflammation

Active UC

Inflammatory Th17 cells and macrophages are elevated in the mucosa: key disease drivers



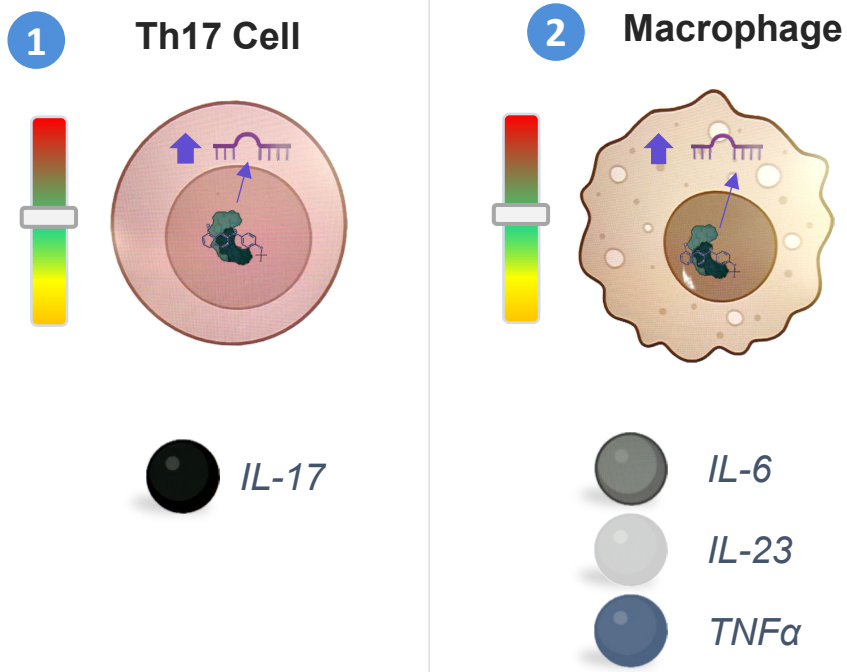
Obe ↑ miR-124

miR-124 is an endogenous regulator of cell behavior

↑ miR-124 normalizes the levels of proinflammatory cells

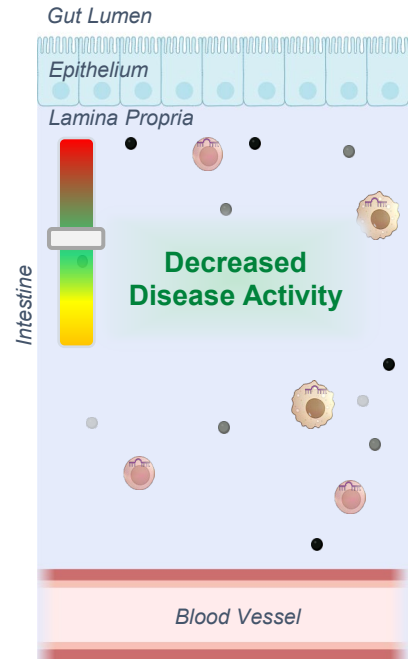
Normalizes inflammatory Th17 T cells and IL-17 levels

Reduces macrophage recruitment while balancing levels of IL-23, IL-6, and TNFα



Balance restored

Restores mucosal immune balance

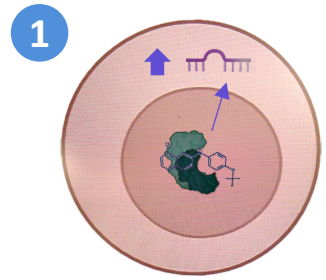
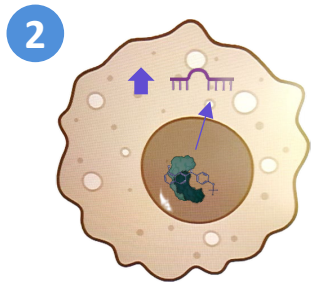
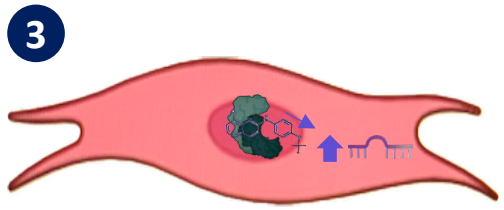


Images made with BioRender. Apolit C, et al. *Clin Transl Gastroenterol.* 2023;14(4):e00560. Vermeire S, et al. *J Crohns Colitis.* 2023;17(10):1689-1697. Abivax. Data on file.

Obefazimod Function Across Key Cell Types

Obefazimod binds to the cap-binding complex (CBC) to induce miR-124, an endogenous regulator of cell behavior

Mechanism:

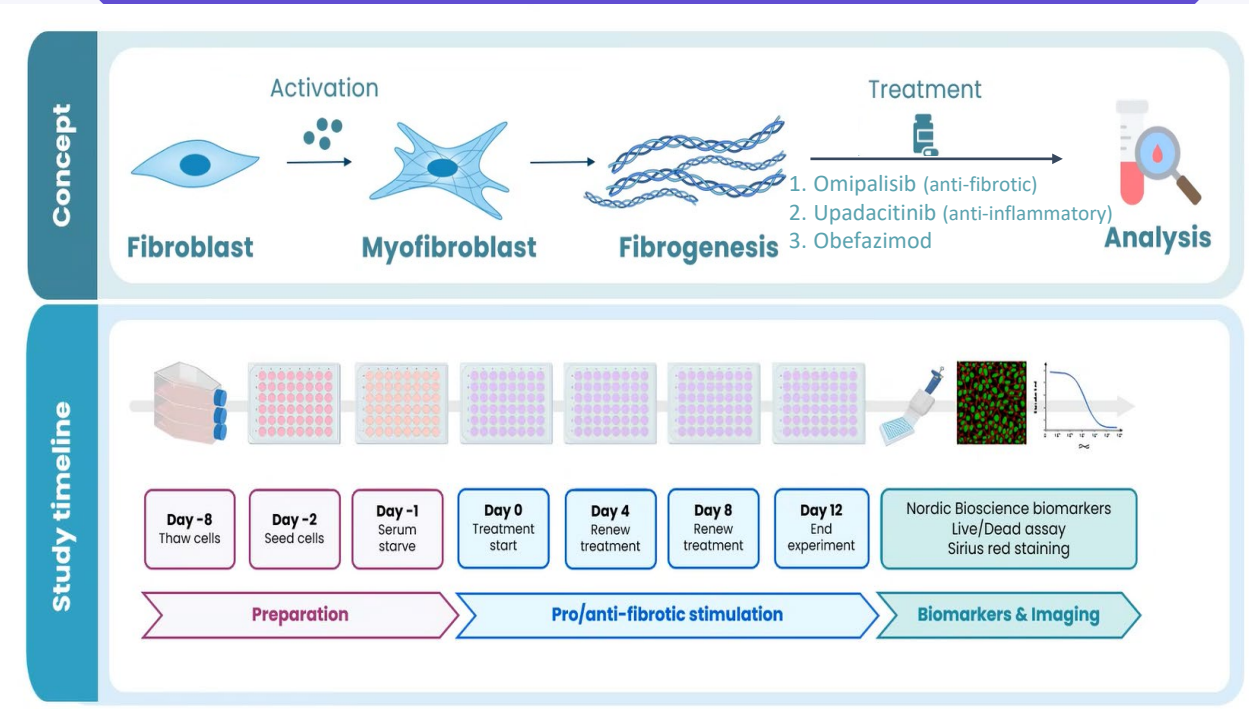
	Th17 Cell	Macrophage	Fibroblast
Cell Type:			
Targets:	STAT3, IL6R	CCL2	TGFβ, MMPs
Effects:	• Reduces Th17 differentiation • Reduces IL-17 expression	• Reduces IL-6 expression • Reduces IL-23 expression • Reduces TNFα expression • Reduces macrophage recruitment	• Reduces collagen deposition • Reduces αSMA expression • Reduces proliferation

Inflammation | **Fibrosis[a]**

Images made with BioRender.
[a]Additional cell types beyond fibroblasts can also play a role in fibrosis.
Apolit C et al. *Clin Transl Gastroenterol.* 2023;14(4):e00560. Vermeire S, et al. *J Crohns Colitis.* 2023;17(10):1689-1697. Abivax. Data on file.

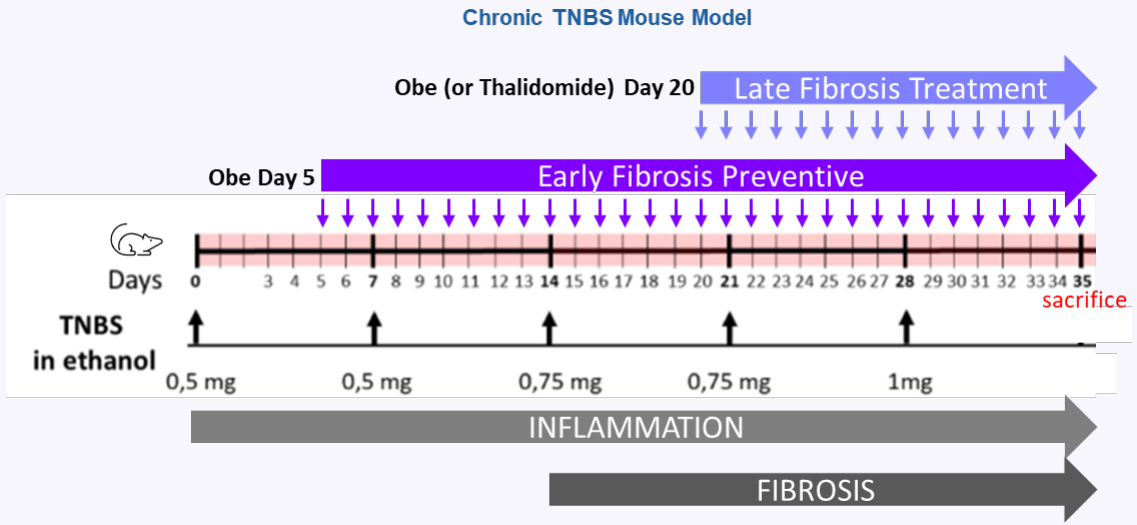
Two Well-Established Models Were Used to Assess Obefazimod's Anti-fibrotic Effects

Model 1
In Vitro Scar-in-a-Jar Assay



Scar-in-a-Jar is an in vitro assay that forms a 3D extracellular matrix in a dish, mimicking fibrotic scarring in tissues, and can be used to explore whether compounds show anti-fibrotic activity by assessing collagen formation and maturation.

Model 2
In Vivo Chronic TNBS Colitis Mouse Model

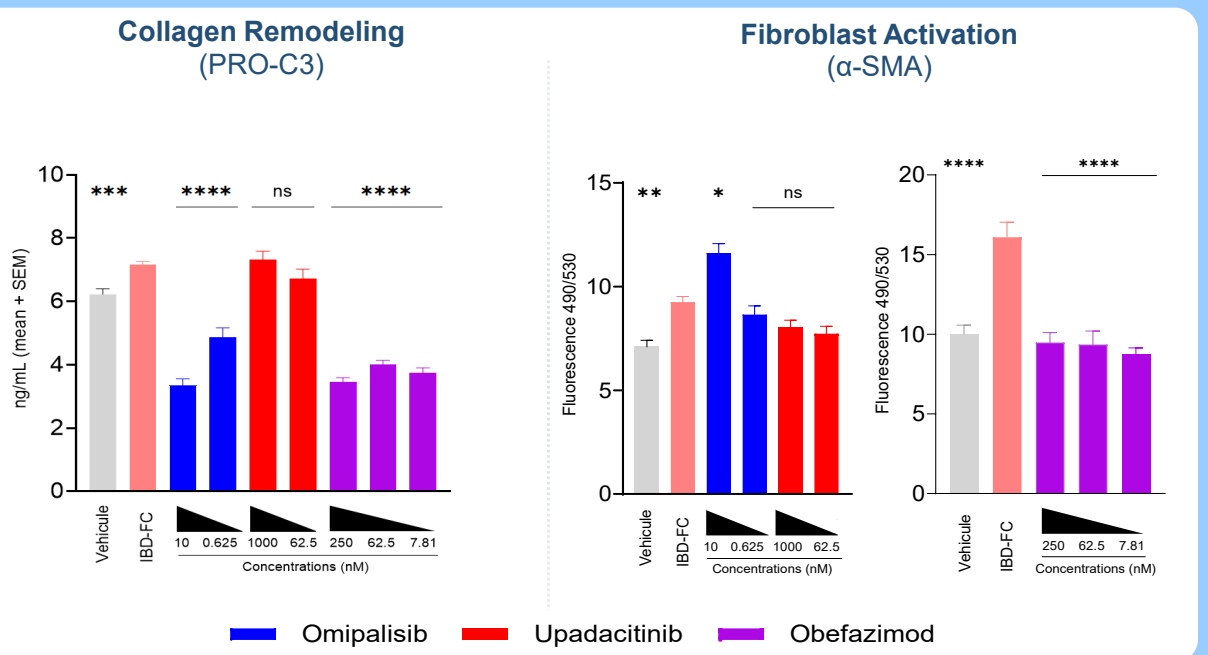


The chronic TNBS colitis mouse is a standard model used to study CD. It causes long-lasting intestinal inflammation in mice that mimics key features of CD in humans, including tissue damage and scarring (fibrosis).

Danese S, et al. Oral presentation. 21st Congress of ECCO; February 18-21, 2026; Stockholm, Sweden.

Model 1: Obefazimod Showed an Anti-fibrotic Effect on Human Small Intestine Fibroblasts in the Scar-in-a-Jar Model

Results



Conclusions

Obefazimod reduced human fibroblast populations and activation status

- **≈50% reduction in Pro-C3** (fibrogenesis marker)
- **≈30% reduction in αSMA** (fibroblast activation marker)

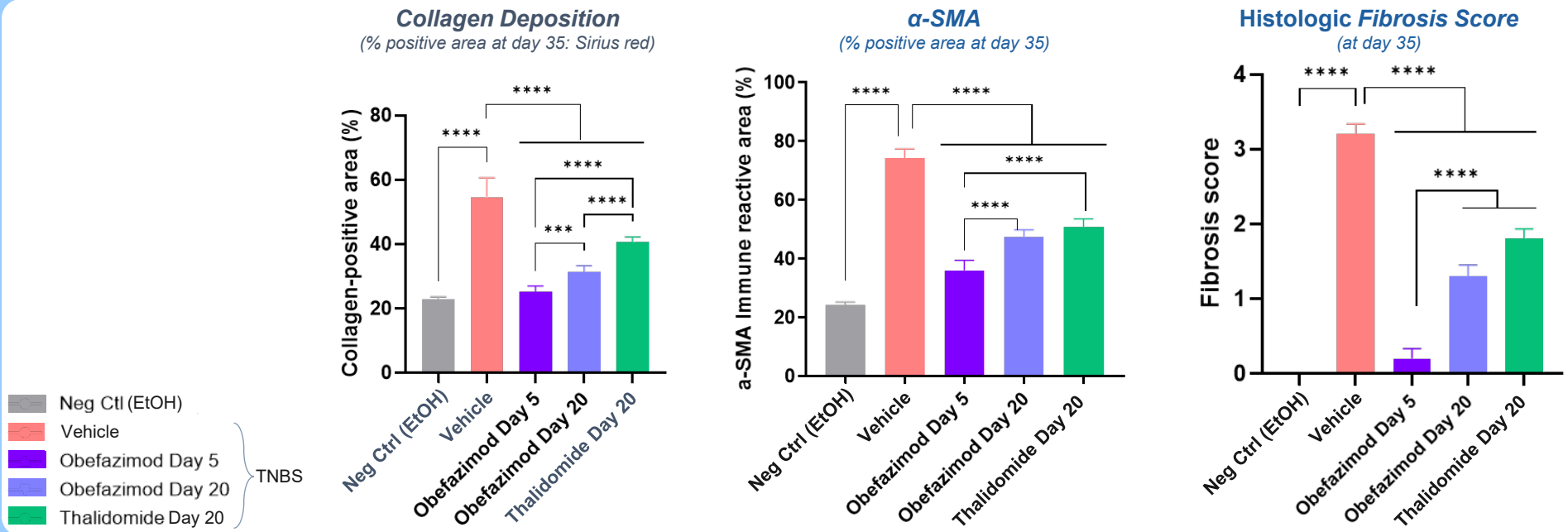
Profound effect of obefazimod *suggests* ***dual anti-inflammatory and anti-fibrotic effects***
that are greater than singular anti-fibrotics (omipalisib) or anti-inflammatories (upadacitinib)

*$P<0.05$, **$P<0.01$, ***$P<0.001$, ****$P<0.0001$; 1-way ANOVA with Tukey's multiple comparisons test.

Danese S, et al. Oral presentation. 21st Congress of ECCO; February 18-21, 2026; Stockholm, Sweden.

Model 2: Obefazimod and Fibrosis in the Chronic TNBS Mouse Model

Results: Day 35



Conclusions

Obefazimod effects when initiated as a **fibrosis preventative** or **fibrosis treatment:**

- **≈45% and ≈55% reduction** in **collagen deposition** (fibrogenesis marker) with late and early treatment, respectively
- **≈40% and ≈50% reduction** in **αSMA** (fibroblast activation marker) with late and early treatment, respectively
- **≈60% and ≈90% reduction** in histologic **fibrosis score** with late and early treatment, respectively

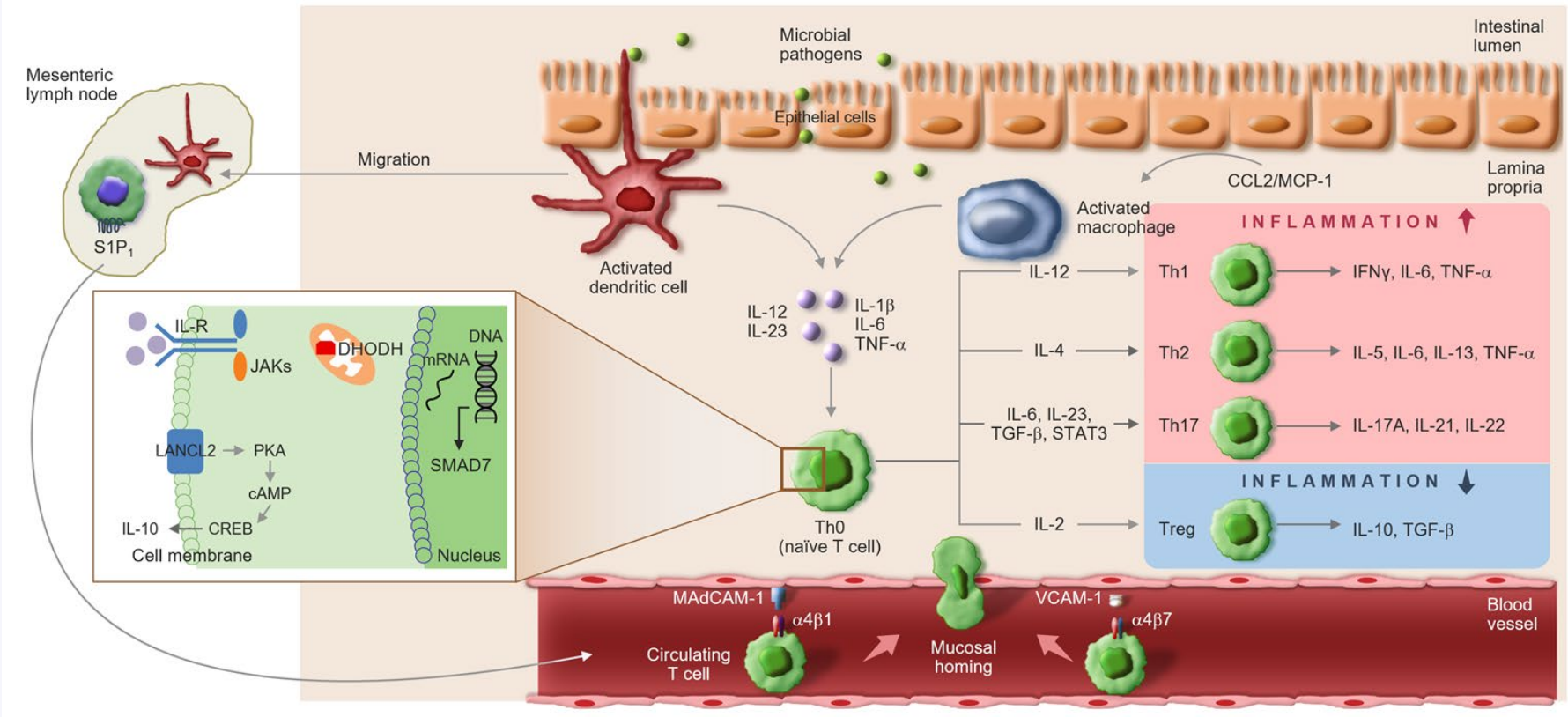
***Obefazimod effects** were **more profound** than **dual anti-inflammatory/anti-fibrotic** thalidomide positive control*

***p<0.001, ****p<0.0001 1-way ANOVA with Tukey's multiple comparisons test.

Danese S, et al. Oral presentation. 21st Congress of ECCO; February 18-21, 2026; Stockholm, Sweden.

Summary of Emerging Therapies

- The breadth of new drugs in development underscores the complex biology involved in UC[1]
- New approaches include enhancing miR-124 expression and inhibiting TL1A
- Clinical trials are currently underway to determine the impact of these novel therapies on UC[2-6]

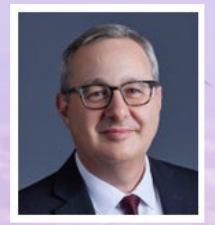


s, mechanisms of action. Image adapted from Ben Ghezala I, et al. *Pharmaceuticals*. 2021;14(7):637. Reprinted and licensed under Creative Commons Attribution License 4.0 (CC BY; https://creativecommons.org/licenses/by-nc/4.0/).

1. Bretto E, et al. *Biomedicines*. 2023;11:2249. 2. NCT05507203. 3. NCT06052059. 4. NCT06588855. 5. NCT07184996. 6. NCT07196748.

Which of these emerging therapies were you aware of prior to this symposium? Select all that apply.

Clinical Data From Late-Stage Investigational Therapies in IBD



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Mount Sinai Health System
New York, NY, USA

TL1A inhibitors

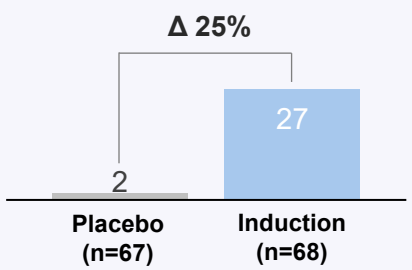
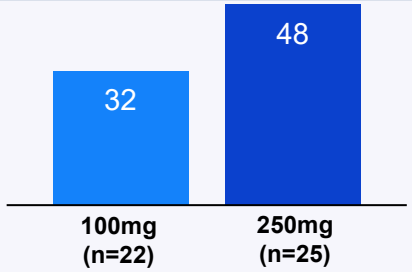
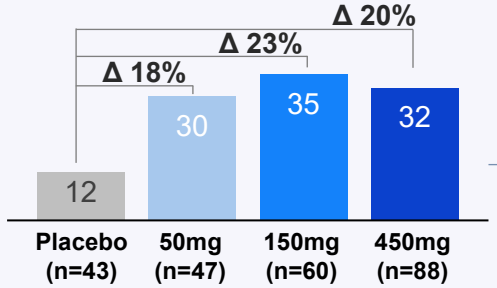
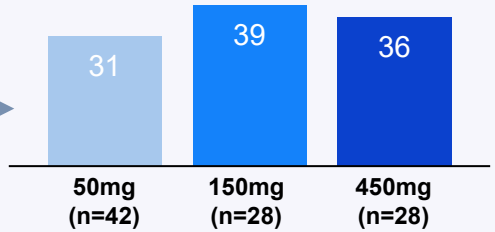
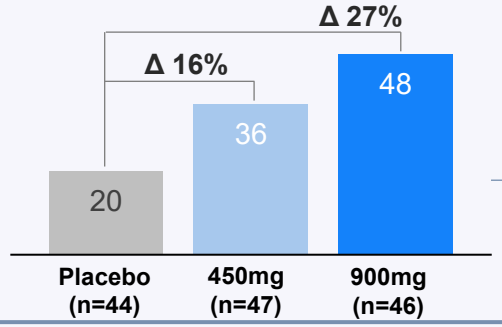
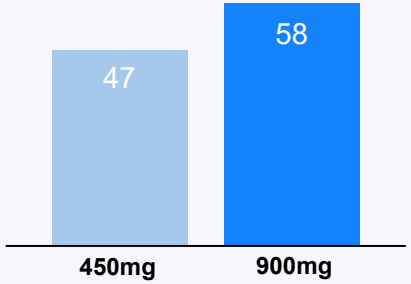
Tulisokibart (MK7240, PRA023), Afimkibart (RVT-3101), Duvakitug (TEV-48574)

TL1A Inhibitors with Positive Phase 2 data

Tulisokibart	**ARTEMIS-UC** Placebo-controlled, 12-week induction -> open-label extension Primary endpoint: clinical remission	**APOLLO-CD** Open-label, 12-week induction -> open-label extension Primary endpoint: clinical remission
Afimkibart	**TUSCANY-2** Placebo-controlled, 14-week induction -> open-label extension Primary endpoint: clinical remission by tMS	
Duvakitug	**RELIEVE UCCD** Placebo-controlled, 14-week induction basket trial for both UC and CD -> long-term extension UC primary endpoint: clinical remission	CD primary endpoint: endoscopic response

ClinicalTrials.gov. Accessed December 1, 2025. https://clinicaltrials.gov/study/NCT04090411; https://clinicaltrials.gov/study/NCT04996797; https://clinicaltrials.gov/study/NCT05013905; https://clinicaltrials.gov/study/NCT05499130.

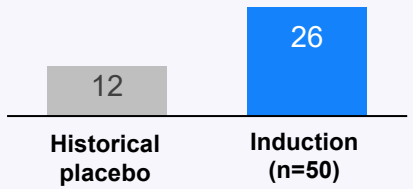
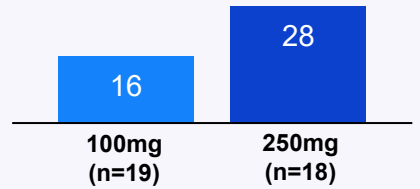
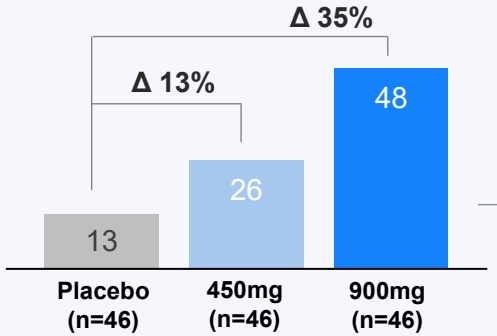
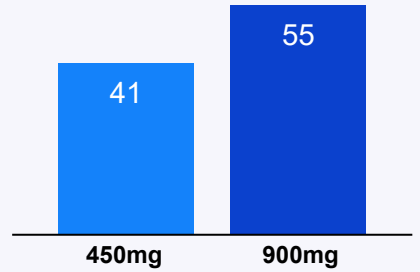
TL1A Inhibitors in UC - Efficacy

Proportion of patients, %	UC Trial: Induction	UC Trial: Maintenance
Tulisokibart[1,2] *Clinical remission* **47% to 48% AT-experienced**	*Week 12* 	*Tulisokibart responders* *Week 50* 
Afimkibart[3] *Clinical remission by mMS** **42% AT-experienced**	*Week 14* 	*All patients (treat-through)* *Week 56* 
Duvakitug[4,5] *Clinical remission* **39% AT-experienced**	*Week 14* 	*Duvakitug responders* *Week 44* 

*Clinical remission by mMS was a secondary endpoint. The primary endpoint was clinical remission by tMS.

1. Sands BE, et al. *N Engl J Med.* 2024;391(12):1119-1129. 2. Ma C, et al. *Am J Gastroenterol.* 2024;119(10S):p S1046-S1047. 3. Danese S, et al. *Lancet Gastroenterol Hepatol.* 2025;10(10):882-895. 4. Reinisch W, et al. ECCO 2025. Presentation OP40. 5. Sanofi. Press release. February 17, 2026.

TL1A Inhibitors in CD - Efficacy

Proportion of patients, %	CD Trial	
	Induction	**Maintenance**
Tulisokibart[1,2] *Endoscopic response* **71% AT-experienced**	***Week 12***  	***Week 50*** ***Tulisokibart responders*** 
Duvakitug[3,4] *Endoscopic response* **63% AT-experienced**	***Week 14***  	***Week 44*** ***Duvakitug responders*** 

1. Feagan, BG et al. *Lancet Gastroenterol Hepatol.* 2025;10(8):715-725. 2. Siegel CA, et al. DDW 2025. Presentation Tu1883. 3. Jairath V, et al. ECCO 2025. Presentation OP41. 4. Sanofi. Press release. February 17, 2026.

TL1A Inhibitor Safety Summary

Across phase 2 trials, there were no safety or tolerability signals

There were no strong signals for immunosuppression, malignancy, or MACE

Injection site/infusion reactions were low

1. Sands BE, et al. *N Engl J Med.* 2024;391(12):1119-1129. 2. Feagan, BG et al. *Lancet Gastroenterol Hepatol.* 2025;10(8):715-725. 3. Danese S, et al. *Lancet Gastroenterol Hepatol.* 2025;10(10):882-895. 4. Reinisch W et al. ECCO 2025. Presentation OP40. 5. Jairath V et al. ECCO 2025. Presentation OP41

IL-23 Receptor Blocker

Icotrokinra

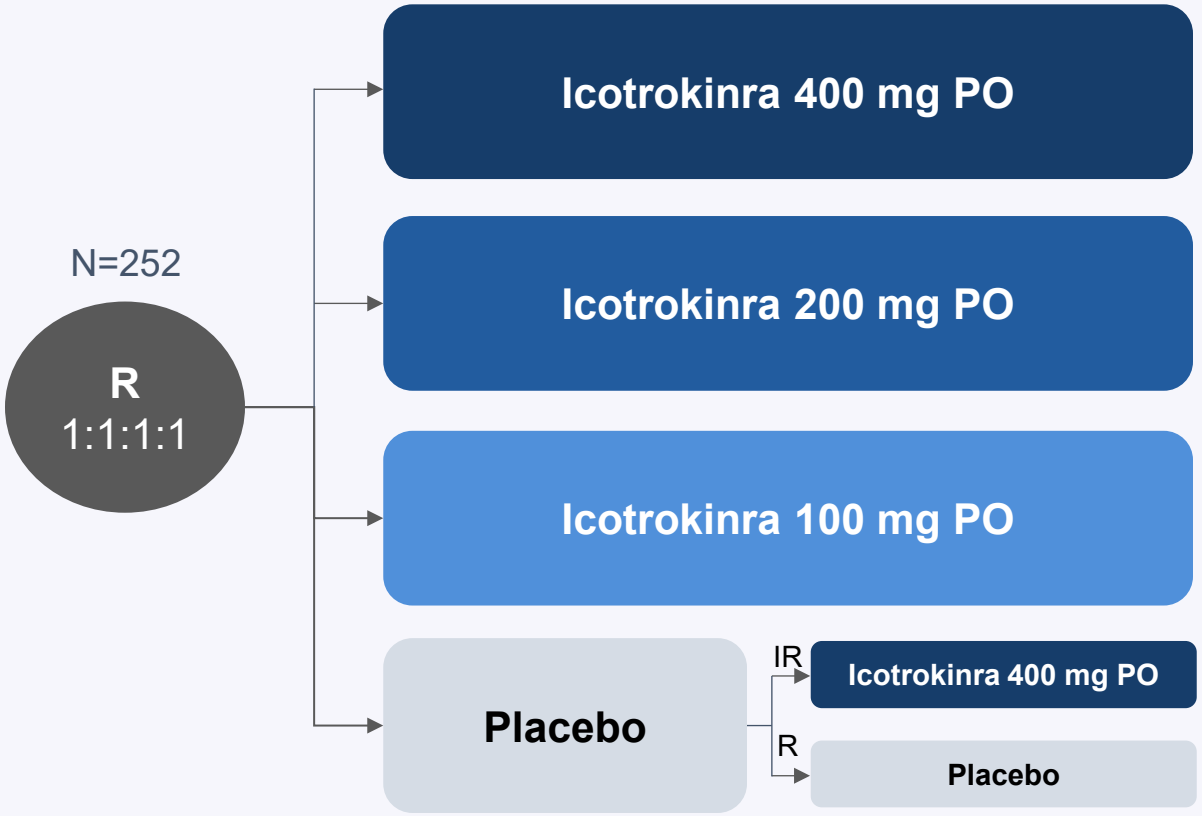
Icotrokinra: Phase 2b Study Design (ANTHEM-UC)

Randomized, Double-blind, Placebo-Controlled Study

Inclusion Criteria

- Adults with documented diagnosis of moderately to severely active UC ≥12 weeks prior to screening
- MMS=5–9, with MES ≥2
- Inadequate response or an intolerance to advanced therapy[a]

Induction (28 Weeks)



Primary Endpoint

- Clinical response at week 12

IR, inadequate responder; JAK, Janus kinase; MES, Mayo endoscopic subscore; MMS, modified Mayo score; R, responder; S1PRM, sphingosine type-1 receptor modulator; TNF, tumor necrosis factor.
[a]TNF-alpha inhibitors, vedolizumab, ustekinumab, JAK inhibitors, S1PRMs, or conventional therapy (corticosteroids, azathioprine, mercaptopurine).

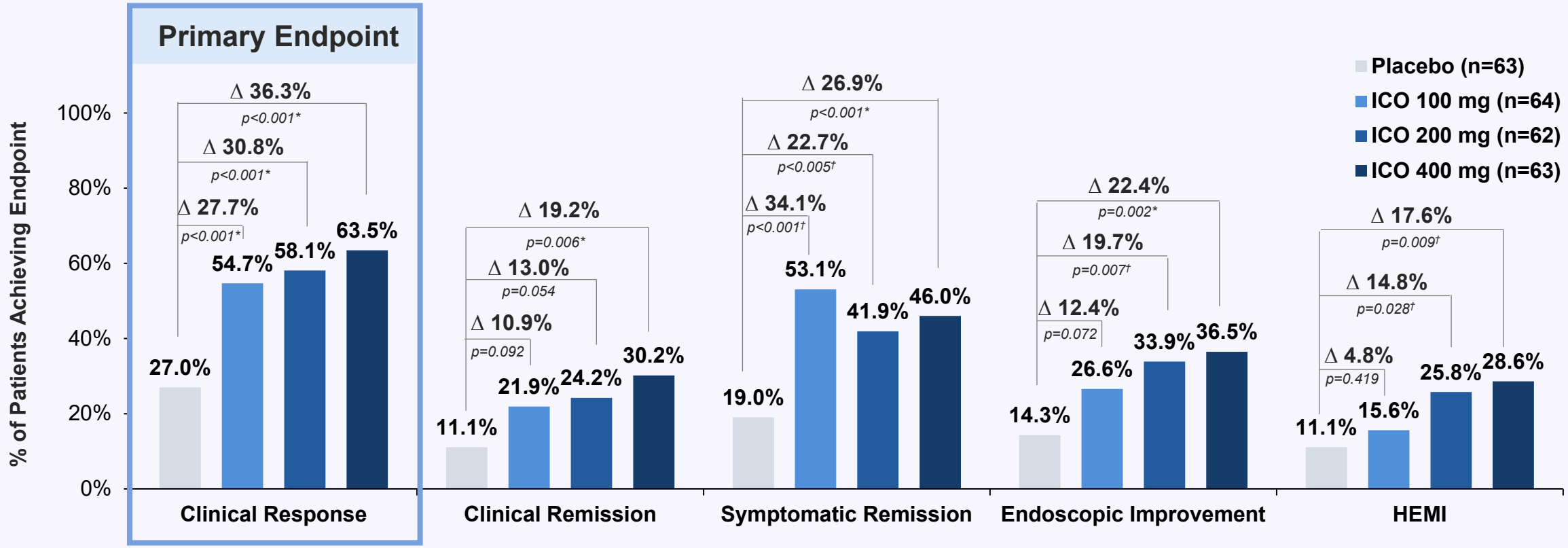
1. NCT06049017. 2. Abreu M, et al. Oral Presentation. United European Gastroenterology Week; October 4-7, 2025; Berlin, Germany. 3. Jairath V, et al. *Am J Gastroenterol*. 2025;120(Suppl):S1449.

Baseline Characteristics

	Placebo (n=63)	100 mg (n=64)	200 mg (n=62)	400 mg (n=63)
Age, years, mean (SD)	38.3 (13.8)	45.8 (14.6)	41.8 (14.6)	40.6 (14.8)
Extensive disease, n (%)	27 (42.9%)	23 (35.9%)	23 (37.1%)	29 (46.0%)
Modified Mayo score (max=9), mean (SD)	6.75 (1.231)	6.55 (1.296)	6.75 (1.386)	6.49 (1.401)
Mayo endoscopic subscore of 3 (severe), n (%)	36 (57.1%)	38 (59.4%)	37 (59.7%)	37 (58.7%)
Fecal calprotectin, mg/kg, median [IQR]	1467.0 [420.5; 3622.0]	1433.3 [698.0; 3121.2]	2467.0 [646.4; 4599.6]	1421.3 [584.6; 4978.6]
No history of BIO/JAKi/S1Pm-IR, n (%)	35 (55.6%)	38 (59.4%)	36 (58.1%)	34 (54.0%)
BIO/JAKi/S1Pm-IR, n (%)	28 (44.4%)	26 (40.6%)	26 (41.9%)	29 (46.0%)
IR to 1 class/mechanism[a]	22 (78.6%)	19 (73.1%)	21 (80.8%)	15 (51.7%)
IR to 2 classes/mechanisms[a]	6 (21.4%)	6 (23.1%)	5 (19.2%)	14 (48.3%)
IR to >2 classes/mechanisms[a]	0	1 (3.8%)	0	0

AT, advanced therapy; BIO, TNFα antagonists, ustekinumab, or vedolizumab; IR, prior inadequate response or intolerance; MOA, mechanism of action.
[a]Denominator was number of participants with a history of inadequate response or intolerance to biologics, JAK inhibitors, or S1P modulators (BIO/JAKi/S1Pm-IR).
Abreu M, et al. Oral presentation. United European Gastroenterology Week; October 4-7, 2025; Berlin, Germany.

Icotrokinra: Efficacy at Week 12



Clinical remission was defined as stool frequency subscore of 0 or 1, rectal bleeding score of 0, and MES of 0 or 1. Symptomatic remission was defined as a stool frequency subscore of 0 or 1 and a rectal bleeding score of 0. Endoscopic improvement was defined as MES of 0 or 1. HEMI was defined as histologic remission (absence of neutrophils from the mucosa [both lamina propria and epithelium], no crypt destruction, and no erosions, ulcerations, or granulation tissue according to the Geboes grading system) and endoscopic improvement (MES of 0 or 1).

AT-IR, advanced therapy inadequate response; HEMI, histologic-endoscopic mucosal improvement; ICO; icotrokinra; MES, Mayo endoscopic subscore.

*Significant *P* value based on the testing procedure. †Nominal *P* value <0.05 based on the testing procedure.

Abreu M, et al. Oral Presentation. United European Gastroenterology Week; October 4-7, 2025; Berlin, Germany.

Icotrokinra: Safety Through Week 28

	Icotrokinra ANTHEM-UC			
Treatment-emergent adverse events (TEAEs), n (%)	**Placebo (N=63)**	**100mg (N=64)**	**200mg (N=62)**	**400mg (N=63)**
Any TEAE	39 (61.9)	42 (65.6)	41 (66.1)	38 (60.3)
TEAE leading to study drug discontinuation	7 (11.1)	0	4 (6.5)	2 (3.2)
Serious TEAE	6 (9.5)	0	3 (4.8)	1 (1.6)
Death	0	0	0	0
Infection	17 (27.0)	18 (28.1)	24 (38.7)	15 (23.8)
Most common TEAEs ≥5%				
Worsening of ulcerative colitis	8 (12.7)	4 (6.3)	9 (14.5)	5 (7.9)
Upper respiratory tract infection	1 (1.6)	8 (12.5)	4 (6.5)	6 (9.5)
Nasopharyngitis	4 (6.3)	5 (7.8)	4 (6.5)	6 (9.5)
Headache	1 (1.6)	6 (9.4)	3 (4.8)	4 (6.3)

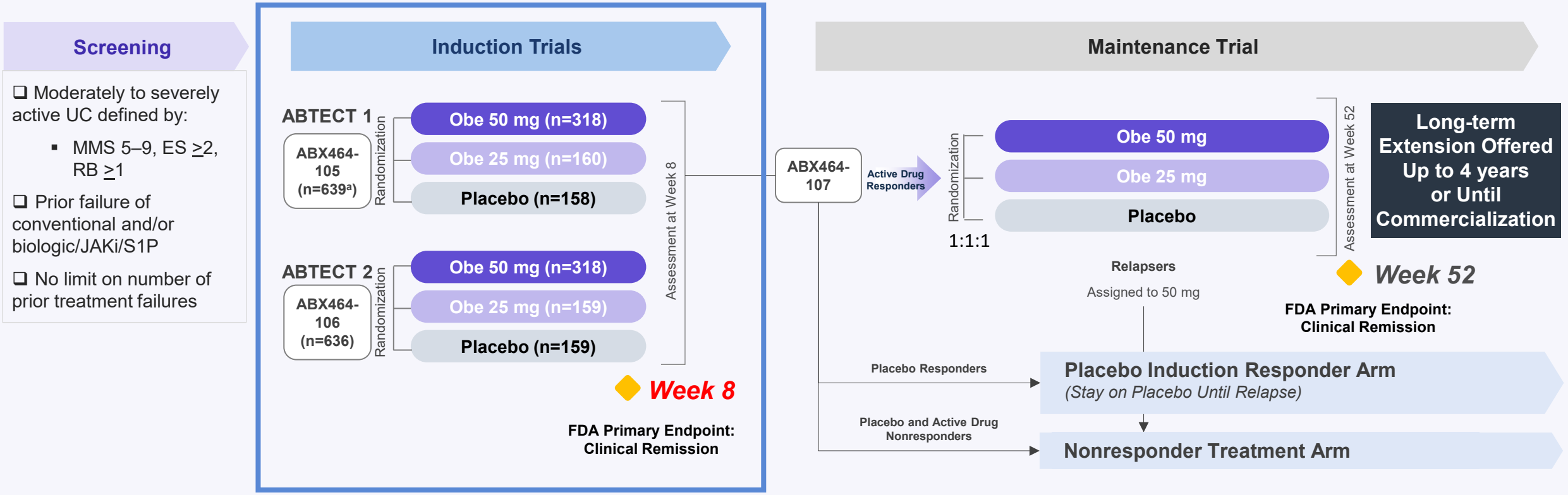
Jairath V, et al. ACG 2025. Presentation 65.

miR-124 Enhancer

Obefazimod

ABTECT Phase 3 Program: Obefazimod in UC

Two 8-week Induction Trials and 1 Maintenance Trial



This presentation will focus on the safety and efficacy results of patients from ABTECT 1 and 2 induction trials

Sands BE et al. Oral presentation presented at: United European Gastroenterology Week, October 4–7 2025, Berlin, Germany.
Placebo responders from induction are not re-randomized and do not contribute to the primary endpoint in the maintenance study. Clinical remission is defined as SFS=0 or 1, and RBS=0 and MES=0 or 1 (MES of 1 modified to exclude friability).
[a]Three patients in ABTECT 1 were randomized but not treated.
ES, endoscopic Mayo score; MES, Mayo endoscopic subscore; MMS, modified Mayo score; Obe, obefazimod.

Baseline Characteristics: Generally Well Balanced

Slightly more severe and refractory population randomized to 25mg group in ABTECT 2 vs. ABTECT 1

	Pooled ABTECT 1 & 2			ABTECT 1 (105)			ABTECT 2 (106)		
	Placebo (N=317)	Obe 25 mg (N=319)	Obe 50 mg (N=636)	Placebo (N=158)	Obe 25 mg (N=160)	Obe 50 mg (N=318)	Placebo (N=159)	Obe 25 mg (N=159)	Obe 50 mg (N=318)
Age (years), mean (SD)	42.3 (14.1)	41.4 (13.2)	42.1 (14.0)	43.1 (13.6)	41.5 (13.5)	42.7 (14.3)	41.6 (14.7)	41.3 (12.8)	41.4 (13.6)
Baseline MMS, mean (SD)	6.9 (1.0)	6.9 (1.0)	6.9 (1.1)	6.9 (1.0)	6.8 (1.0)	6.9 (1.1)	6.8 (1.0)	7.0 (1.0)	6.9 (1.1)
Endoscopic subscore 3, n (%)	189 (59.6)	194 (60.8)	378 (59.4)	94 (59.5)	91 (56.9)	190 (59.7)	95 (59.7)	103 (64.8)	188 (59.1)
Extensive Colitis	130 (41.0)	131 (41.1)	236 (37.1)	59 (37.3)	63 (39.4)	110 (34.6)	71 (44.7)	68 (42.8)	126 (39.6)
Fecal Calprotectin (μg/g), median	1902	1762	1564	1969	1499	1581	1792	2041	1499
Concomitant Corticosteroids	126 (39.7)	120 (37.6)	262 (41.2)	61 (38.6)	61 (38.1)	132 (41.5)	65 (40.9)	59 (37.1)	130 (40.9)
AT-IR Yes	148 (46.7)	146 (45.8)	308 (48.4)	69 (43.7)	70 (43.8)	149 (46.9)	79 (49.7)	76 (47.8)	159 (50.0)
Number of prior JAK-IR (% of AT-IR Yes Patients)	35 (23.6)	34 (23.3)	55 (17.9)	15 (21.7)	15 (21.4)	22 (14.8)	20 (25.3)	19 (25.0)	33 (20.8)
Number of prior AT-IR by medication name†, n (%)									
1	62 (19.6)	45 (14.1)	150 (23.6)	31 (19.6)	23 (14.4)	70 (22.0)	31 (19.5)	22 (13.8)	80 (25.2)
2	34 (10.7)	45 (14.1)	64 (10.1)	16 (10.1)	20 (12.5)	35 (11.0)	18 (11.3)	25 (15.7)	29 (9.1)
3	28 (8.8)	33 (10.3)	52 (8.2)	12 (7.6)	18 (11.3)	25 (7.9)	16 (10.1)	15 (9.4)	27 (8.5)
4+	24 (7.6)	23 (7.2)	42 (6.6)	10 (6.3)	9 (5.6)	19 (6.0)	14 (8.8)	14 (8.8)	23 (7.2)

Highly refractory population with ~21% of AT-IR failing a JAK inhibitor

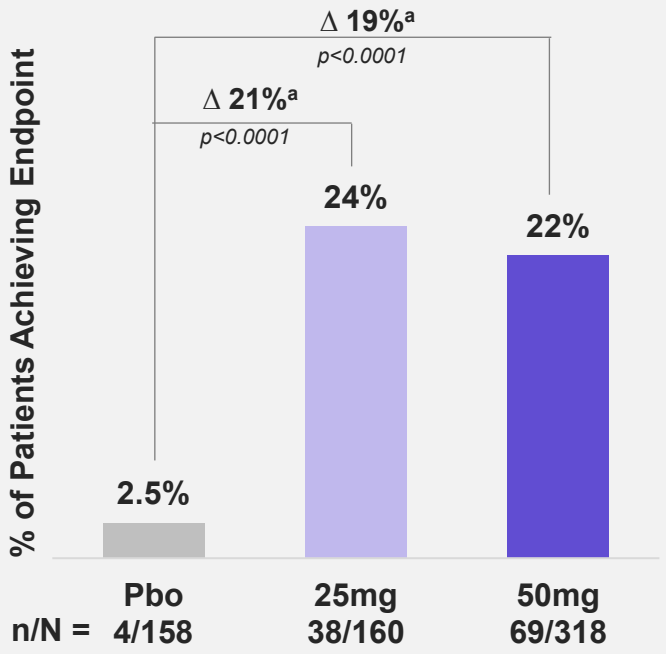
Sands BE et al. Oral presentation presented at: United European Gastroenterology Week, October 4–7 2025, Berlin, Germany.

† Medication name results in each individual advanced therapy being counted as a unique medication; e.g. infliximab + adalimumab would be counted as 2

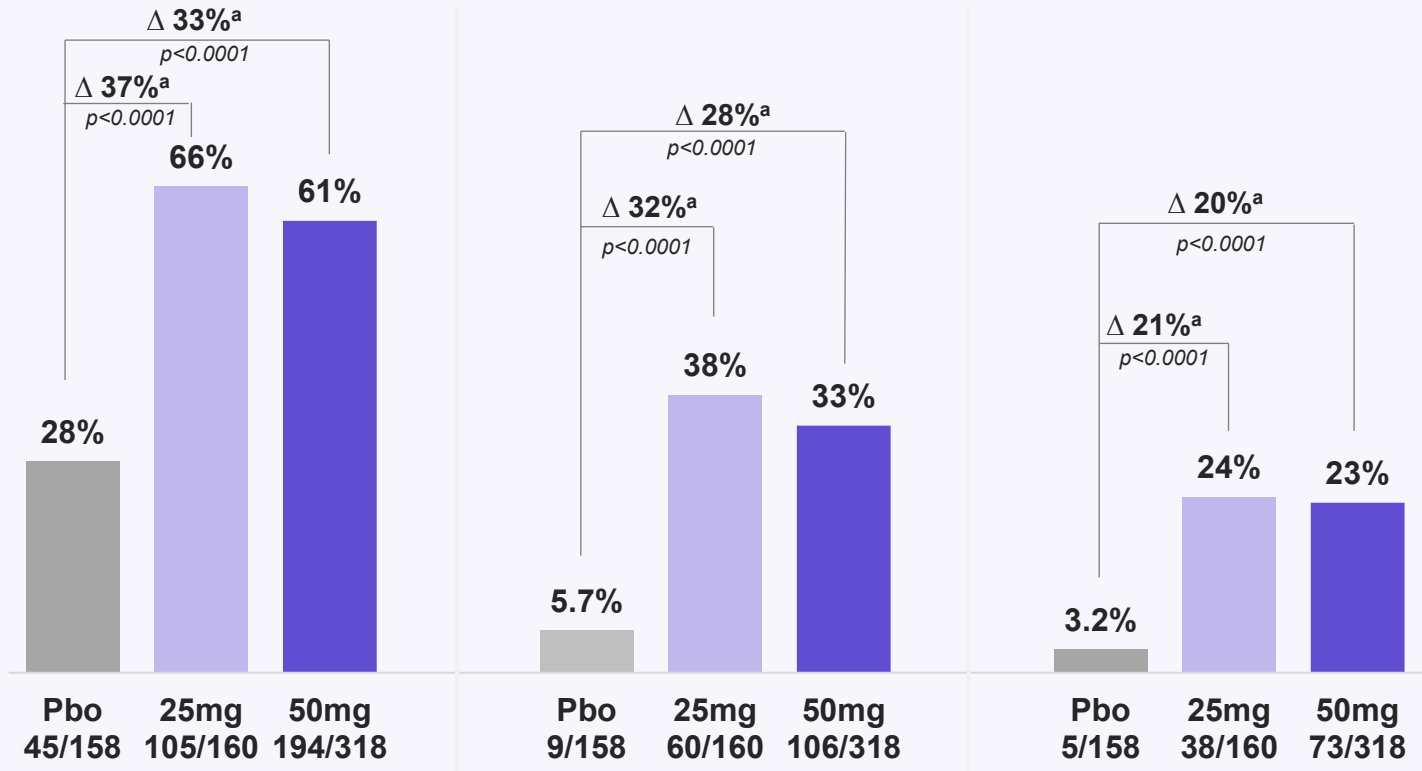
ABTECT-1: Both doses met primary and all key secondary endpoints at week 8

Clinical Remission – ABTECT-1

Primary Endpoint at Week 8



Key Secondary Endpoints at Week 8 – ABTECT-1



Sands BE et al. Oral presentation presented at: United European Gastroenterology Week, October 4–7 2025, Berlin, Germany.

[a] % Difference is for ABX464 minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: inadequate response to advanced therapies (yes/no), Baseline oral corticosteroids usage (yes/no). P-values are two sided. NRI is used for subjects with missing outcome at Week 8 and subjects reporting any IE prior to Week 8.

[b] Clinical remission is defined as SFS = 0 or 1, and RBS = 0 and MES = 0 or 1 (MES of 1 modified to exclude friability).

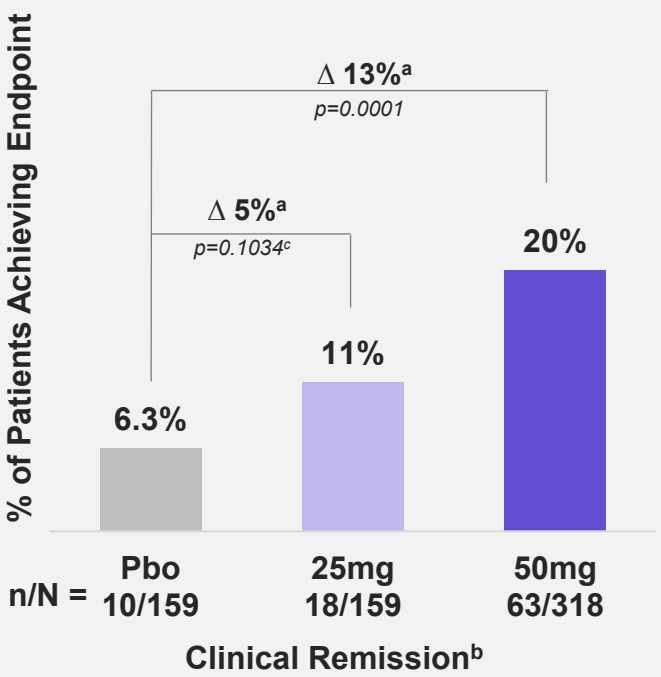
Endoscopic improvement is defined as MES = 0 or 1 (MES of 1 modified to exclude friability).

Clinical response is defined as a reduction from Baseline in MMS >= 2 points and a relative reduction from Baseline in MMS >= 30%, and a reduction from Baseline in RBS >= 1 point and/or RBS = 0 or 1. HEMI is defined as MES = 0 or 1 and Geboes Index score <3.1

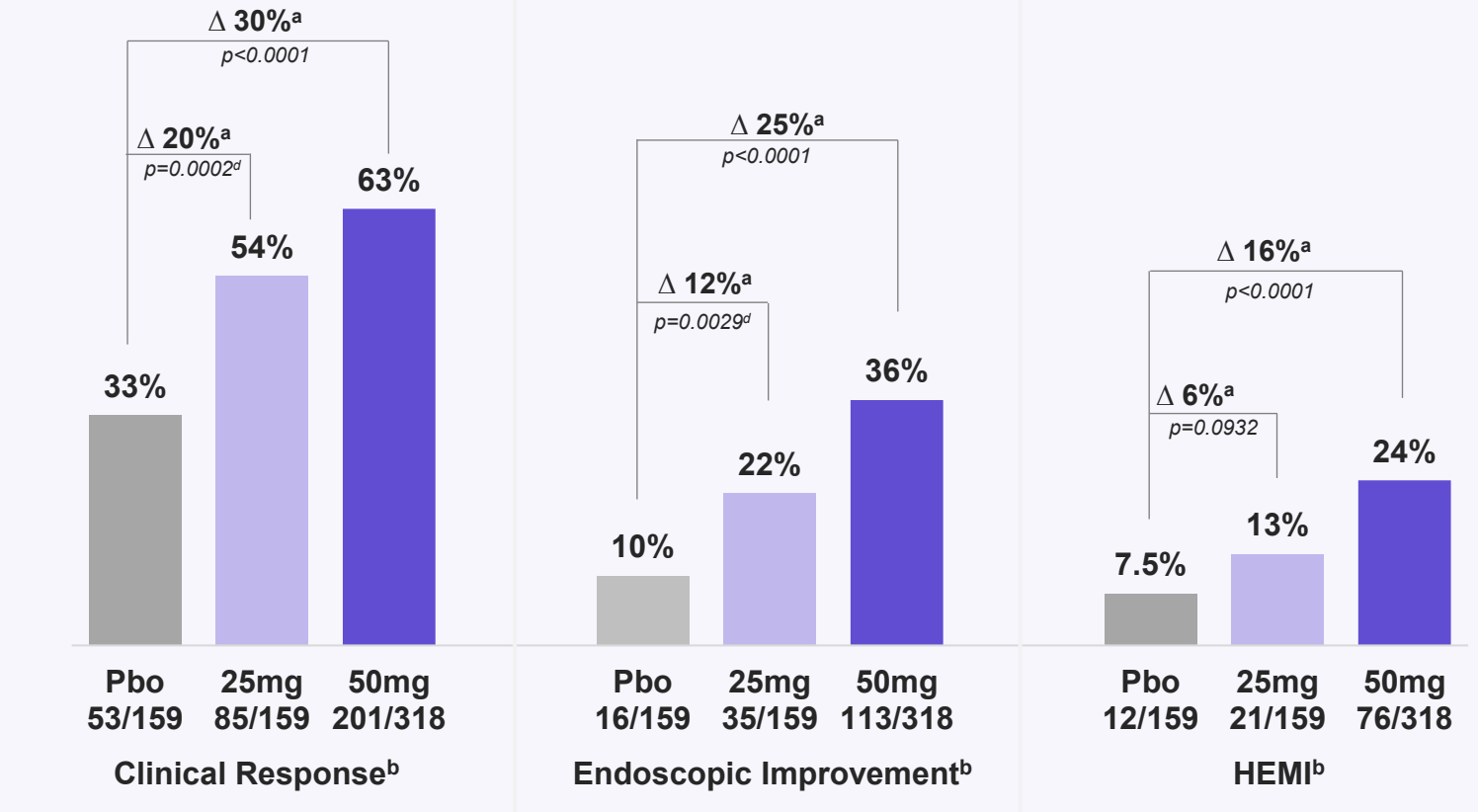
ABTECT-2: Obefazimod 50 mg met primary and all key secondary endpoints

Clinical Remission – ABTECT 2

Primary Endpoint at Week 8



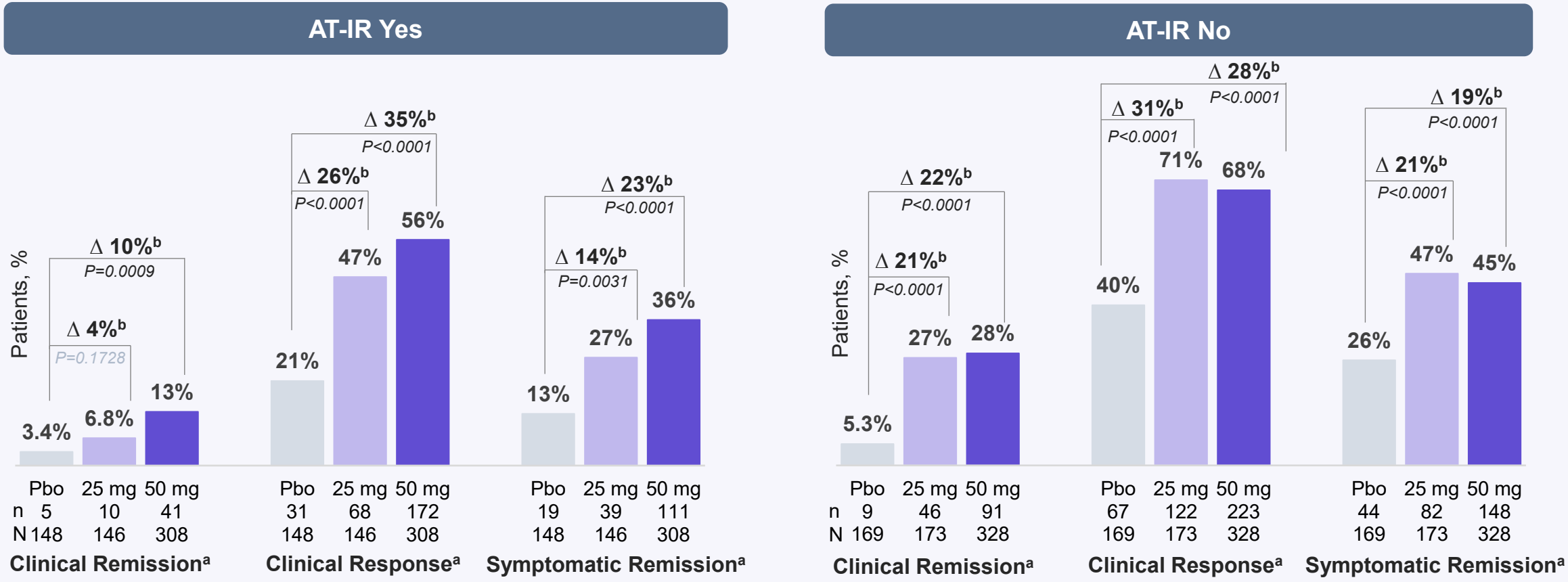
Key Secondary Endpoints at Week 8 – ABTECT 2



Sands BE et al. Oral presentation presented at: United European Gastroenterology Week, October 4–7 2025, Berlin, Germany.
[a] % Difference is for ABX464 minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: inadequate response to advanced therapies (yes/no), Baseline oral corticosteroids usage (yes/no). P-values are two sided. NRI is used for subjects with missing outcome at Week 8 and subjects reporting any IE prior to Week 8.
[b] Clinical remission is defined as SFS = 0 or 1, and RBS = 0 and MES = 0 or 1 (MES of 1 modified to exclude friability).
Endoscopic improvement is defined as MES = 0 or 1 (MES of 1 modified to exclude friability).
[c] 25mg did not show statistical significance at 8 weeks [d] p values for 25mg are nominal on key FDA secondary endpoints of HEMI and Clinical Response
Clinical response is defined as a reduction from Baseline in MMS >= 2 points and a relative reduction from Baseline in MMS >= 30%, and a reduction from Baseline in RBS >= 1 point and/or RBS = 0 or 1. HEMI is defined as MES = 0 or 1 and Geboes Index score ≤3.1

Pooled ABTECT 1 & 2: Obefazimod 50 mg Achieved Clinically Meaningful Improvements in All Clinical Endpoints Regardless of Prior AT-IR at Week 8

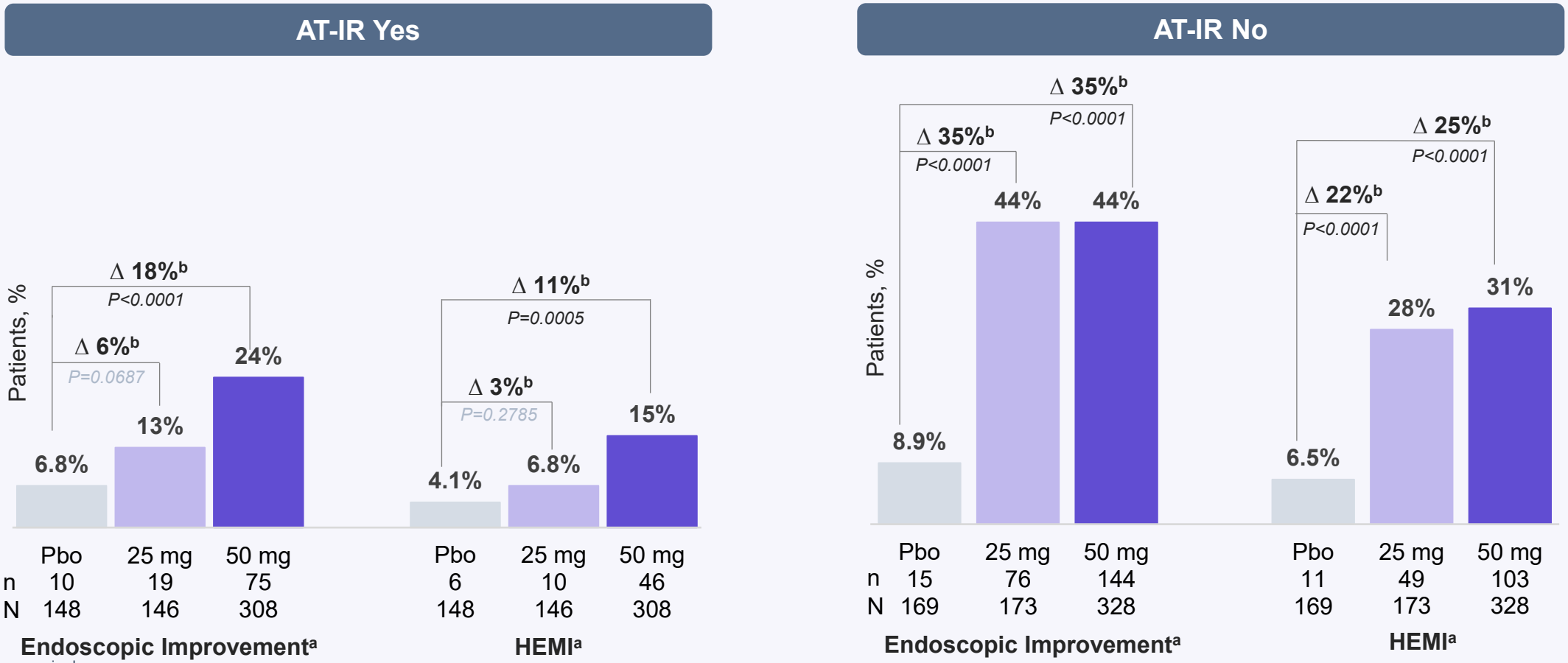
- 25 mg and 50 mg perform similarly in subgroup with no prior AT-IR in pooled data set



All *P* values are nominal.
[a]**Clinical remission** is defined as SFS=0 or 1, and RBS=0 and MES=0 or 1 (MES of 1 modified to exclude friability). **Clinical response** is defined as a reduction from baseline in MMS ≥2 points and a relative reduction from Baseline in MMS ≥30%, and a reduction from baseline in RBS ≥1 point and/or RBS 0 or 1. **Symptomatic remission** is defined as RBS=0 and SFS=0 or 1.
[b]% Difference is for ABX464 minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: inadequate response to advanced therapies (yes/no), Baseline oral corticosteroids usage (yes/no). *P* values are 2-sided. NRI is used for subjects with missing outcome at week 8 and subjects reporting any IE prior to week 8.
Danese , et al. Oral presentation. United European Gastroenterology Week; October 4-7, 2025; Berlin, Germany.

Pooled ABTECT 1 & 2: Obefazimod 50 mg Achieved Clinically Meaningful Improvements in Endoscopic and Histologic Endpoints Regardless of Prior AT-IR at Week 8

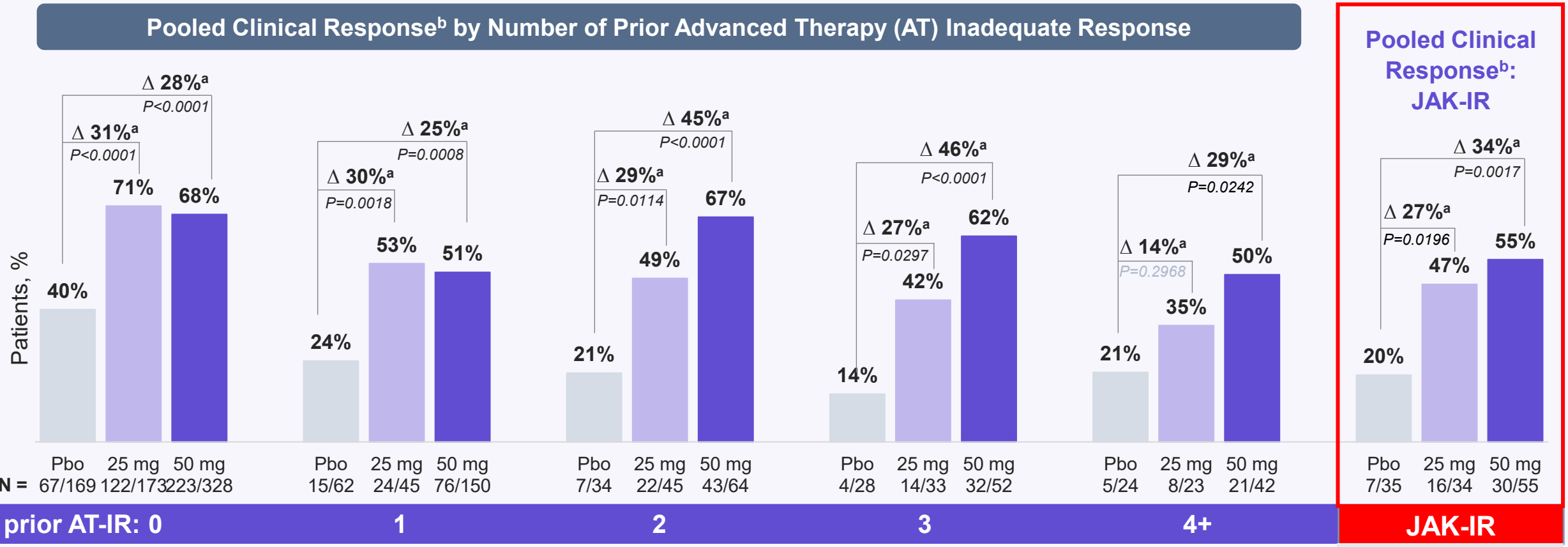
- 50 mg outperformed 25 mg in subjects with prior AT-IR; 25 mg and 50 mg performed similarly with no prior AT-IR



All *P* values are nominal.
[a]Endoscopic improvement is defined as MES=0 or 1 (MES of 1 modified to exclude friability). HEMI is defined as MES=0 or 1 and Geboes Index score ≦3.1
[b]% Difference is for ABX464 minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: inadequate response to advanced therapies (yes/no), baseline oral corticosteroids usage (yes/no). *P* values are 2-sided. NRI is used for subjects with missing outcome at week 8 and subjects reporting any IE prior to week 8.
Danese S, et al. Oral presentation. United European Gastroenterology Week; October 4-7, 2025; Berlin, Germany.

Clinical Response at Week 8 by Number of Prior AT Inadequate Responses and Prior JAK Inhibitor

50 mg clinical response was consistent in subgroups with no prior AT-IR through ≥4 AT-IR or JAK-IR



≈21% of AT-IR population had JAK-IR

All *P* values are nominal.
[a]% Difference is for ABX464 minus placebo and is based on estimated common risk difference using the Mantel-Haenszel weights adjusting for the randomization stratification factors: inadequate response to advanced therapies (yes/no), Baseline oral corticosteroids usage (yes/no). *P* values are 2-sided. NRI is used for subjects with missing outcome at week 8 and subjects reporting any IE prior to week 8.
[b]Clinical response is defined as a reduction from baseline in MMS ≥2 points and a relative reduction from baseline in MMS ≥30%, and a reduction from baseline in RBS ≥1 point and/or RBS=0 or 1.
Danese S, et al. Oral presentation. United European Gastroenterology Week; October 4-7, 2025; Berlin, Germany.

Safety Summary—ABTECT 1 and 2: Pooled Full Data Set

	ABTECT 1 and 2: Pooled Full Data Set		
Treatment-Emergent Adverse Events (TEAE), n (%)	**Placebo (n=317)**	**Obefazimod 25 mg (n=319)**	**Obefazimod 50 mg (n=636)**
Any TEAE	161 (50.8)	156 (48.9)	383 (60.2)
TEAE leading to study drug discontinuation	15 (4.7)	8 (2.5)	32 (5.0)
Serious TEAE	10 (3.2)	7 (2.2)	20 (3.1)
Death	0	0	0
Malignancy	0	0	1 (0.2)[a]
Serious/severe (grade ≥3) infections and opportunistic infections	1 (0.3)[b]	1 (0.3)[c]	4 (0.6)[d]

Sands BE et al. Oral presentation presented at: United European Gastroenterology Week, October 4–7 2025, Berlin, Germany.
[a]Prostate cancer stage I. [b]Bronchopulmonary aspergillosis. [c]Appendicitis. [d]Pneumonia (2), anal abscess, COVID-19.

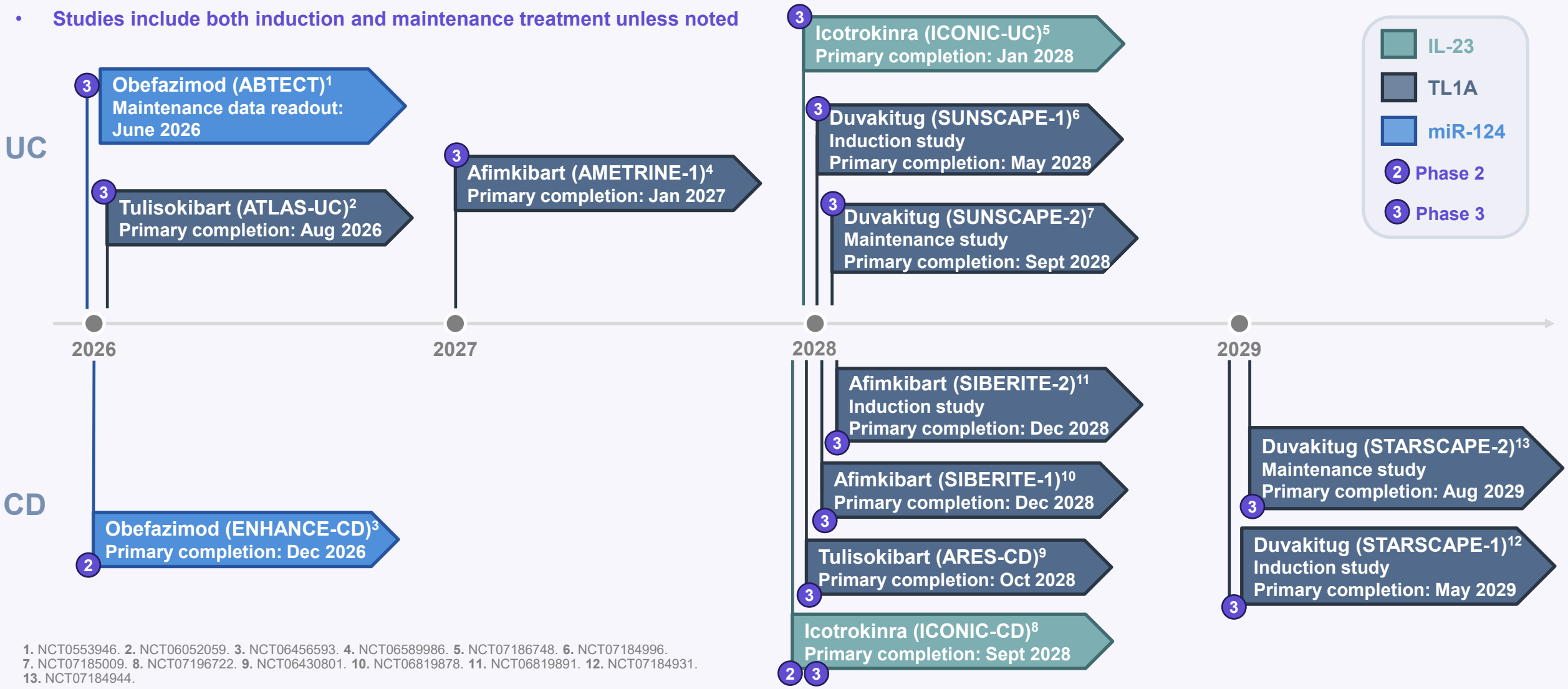
Treatment-Emergent Adverse Events (≥1% and Greater Than Placebo)

	ABTECT 1 and 2: Pooled Full Data Set		
	Placebo (n=317)	**Obefazimod 25 mg (n=319)**	**Obefazimod 50 mg (n=636)**
Headache[a]	19 (6.0)	51 (16.0)	153 (24.1)
Headache leading to study **discontinuation** (per subject), n (%)	0	1 (0.3)	7 (1.1)
Time to onset of first TE headache per subject (days), median	7.0	1.0	1.0
Duration of headache for all TE headaches, days, median	2.0	3.0	2.0
Nausea	4 (1.3)	16 (5.0)	46 (7.2)
Lipase increased	7 (2.2)	9 (2.8)	27 (4.2)
Abdominal pain	2 (0.6)	2 (0.6)	24 (3.8)
Vomiting	1 (0.3)	7 (2.2)	18 (2.8)
Upper abdominal pain	2 (0.6)	5 (1.6)	18 (2.8)
Back pain	0	4 (1.3)	13 (2.0)
Alanine aminotransferase increased	2 (0.6)	5 (1.6)	10 (1.6)
Hypertriglyceridemia	0	3 (0.9)	12 (1.9)
Dyslipidemia	2 (0.6)	1 (0.3)	9 (1.4)
Pyrexia	1 (0.3)	3 (0.9)	8 (1.3)
Amylase increased	1 (0.3)	4 (1.3)	7 (1.1)
Hyperlipidemia	1 (0.3)	0	7 (1.1)
Hypertension	2 (0.6)	1 (0.3)	7 (1.1)

Sands BE et al. Oral presentation presented at: United European Gastroenterology Week, October 4–7 2025, Berlin, Germany.
[a]Headache Custom MedDRA Query includes the following preferred terms: headache, tension headache, procedural headache, cluster headache, cervicogenic headache, and migraine. All other TEAEs are shown by individual preferred term.
Data on File: ABX464-105 and ABX464-106.

Phase 2 and 3 Trials Are Underway

- Studies include both induction and maintenance treatment unless noted



1. NCT0553946. **2.** NCT06052059. **3.** NCT06456593. **4.** NCT06589986. **5.** NCT07186748. **6.** NCT07184996. **7.** NCT07185009. **8.** NCT07196722. **9.** NCT06430801. **10.** NCT06819878. **11.** NCT06819891. **12.** NCT07184931. **13.** NCT07184944.

Based on the data presented, which upcoming data are you most excited about?

Thank you!

Q&A

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Program evaluation

BACK-UP

Phase 2 & 3 Trials are Underway

		Population	Design	Primary Endpoints
Tulisokibart	**ATLAS-UC[1]**	Moderately to severely active UC	• Study 1: 12-week induction + 40-week maintenance • Study 2: 12-week induction	• Clinical remission at week 12 and 52[a]
	ARES-CD[2]	Moderately to severely active CD	• Study 1: 12-week induction + 40-week maintenance • Study 2: 12-week induction	• Clinical remission at week 12 and 52[a] • Endoscopic response at week 12 and 52[a]
Afimkibart	**AMETRINE-1[3]**	Moderately to severely active UC	• 12-week induction + OLE	• Clinical remission at week 12 and 52
	SIBERITE-1[4]	Moderately to severely active CD	• 12-week induction + 40-week maintenance	• Clinical remission at week 52 • Endoscopic response at week 52
	SIBERITE-2[5]	Moderately to severely active CD	• 12-week induction	• Clinical remission at week 12 • Endoscopic response at week 12
Duvakitug	**SUNSCAPE-1[6]**	Moderately to severely active UC	• 12-week induction	• Clinical remission at week 12
	SUNSCAPE-2[7]	Moderately to severely active UC	• 40-week maintenance	• Clinical remission at week 40
	STARSCAPE-1[8]	Moderately to severely active CD	• 12-week induction	• Clinical remission at week 12 • Endoscopic response at week 12
	STARSCAPE-2[9]	Moderately to severely active CD	• 40-week maintenance	• Clinical remission at week 40 • Endoscopic response at week 40
Icotrokinra	**ICONIC-UC[10]**	Moderately to severely active UC	• 12-week induction + 40-week maintenance	• Clinical remission at week 12 and 52
	ICONIC-CD[11]	Moderately to severely active CD	• Induction study 1: 12-week induction • Induction study 2: 12-week induction • 40-week maintenance	• Induction study 1: clinical response at week 12 • Induction study 2: clinical remission and endoscopic response at week 12 • Maintenance study: clinical remission and endoscopic response at week 40
Obefazimod	**ENHANCE-CD[12]**	Moderately to severely active CD	• 12-week induction + 40-week maintenance	• Change from baseline in CDAI score at week 12 and 52
	ABTECT-M[13]	Moderately to severely active UC	• 44-week maintenance	• Clinical remission at week 44

[a]Study 1 only.

1. NCT06052059. 2. NCT06430801. 3. NCT06589986. 4. NCT06819878. 5. NCT06819891. 6. NCT07184996. 7. NCT07185009. 8. NCT07184931. 9. NCT07184944. 10. NCT07196748. 11. NCT07196722. 12. NCT06456593. 13. NCT05535946.

TL1A inhibitors

Tulisokibart (MK7240, PRA023), Afimkibart (RVT-3101), Duvakitug (TEV-48574)

Tulisokibart: Phase 2 Study Design (ARTEMIS-UC)

Inclusion Criteria

- Adult patients with moderately to severely active UC
- MMS=4–9, with MES ≥2 and RB ≥1
- Inadequate response to, a loss of response to, or an intolerance to conventional or biologic therapy for UC[b]

Induction (12 weeks)

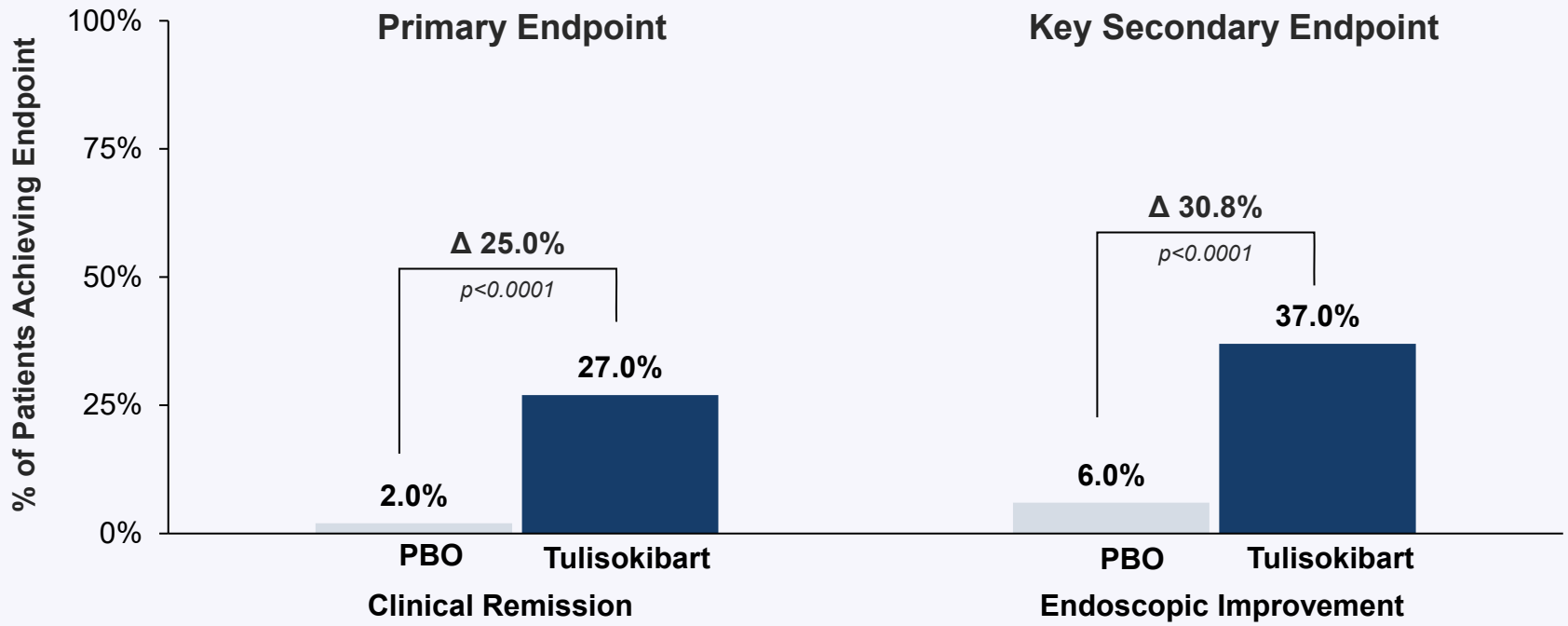
Primary Endpoint

- Clinical remission at week 12

CS, corticosteroid; MES, Mayo endoscopic subscore; MMS, modified Mayo score; RB, Mayo rectal bleeding subscore.
[a]1000 mg on day 1; 500 mg at weeks 2, 6, and 10. [b]≤4 advanced agents from ≤3 classes.
Sands BE, et al. *J Crohns Colitis*. 2023;17(Suppl 1):i56-i59.

Tulisokibart: Efficacy

Clinical Outcomes at Week 12



All remaining ranked secondary endpoints were met[a]

FAS: N=135.
Clinical remission per modified Mayo Score ES ≤1, RB=0, and SF ≤1 and not greater than baseline. Endoscopic improvement is defined as ES ≤1 with no friability.
[a]Ranked secondary endpoints included endoscopic improvement, clinical response, symptomatic remission, mucosal healing, histologic improvement, histologic-endoscopic mucosal improvement, and IBDQ response. All ranked secondary endpoints were statistically significant according to multiplicity-controlled 2-sided alpha of 0.05.
Sands BE, et al. *J Crohns Colitis*. 2023;17(Suppl 1):i56-i59.

Tulisokibart Safety in ARTEMIS-UC and APOLLO-CD

ARTEMIS-UC				
Treatment-emergent adverse events (TEAEs), n (%)	**Placebo (n=88)**	**Induction (n=90)**	**100mg (n=30)**	**200mg (N=35)**
Any TEAE	38 (43)	41 (46)	23 (77)	22 (63)
TEAE leading to study drug discontinuation	3 (3)	1 (1)	2 (7)	1 (3)
Serious TEAE	7 (8)	1 (1)	0	0
Death	0	0	0	0
Infection	16 (18)	16 (18)	11 (37)	16 (46)
Most common TEAEs ≥5%				
Ulcerative colitis	9 (10)	1 (1)	-	-
COVID-19	4 (5)	5 (6)	-	-

APOLLO-CD	
Treatment-emergent adverse events (TEAEs), n (%)	**Induction (n=55)**
Any TEAE	43 (78)
TEAE leading to study drug discontinuation	2 (4)
Serious TEAE	8 (15)
Death	0
Infection	25 (45)
Most common TEAEs ≥5%	
COVID-19	6 (11)
Urinary tract infection	5 (9)
Crohn's disease	5 (9)
Anemia	4 (7)
Nasopharyngitis	3 (5)
Fatigue	3 (5)

Sands BE et al. N Engl J Med 2024. Feagan BG et al. Lancet Gastroenterol Hepatol 2025.

Tulisokibart: Next Steps

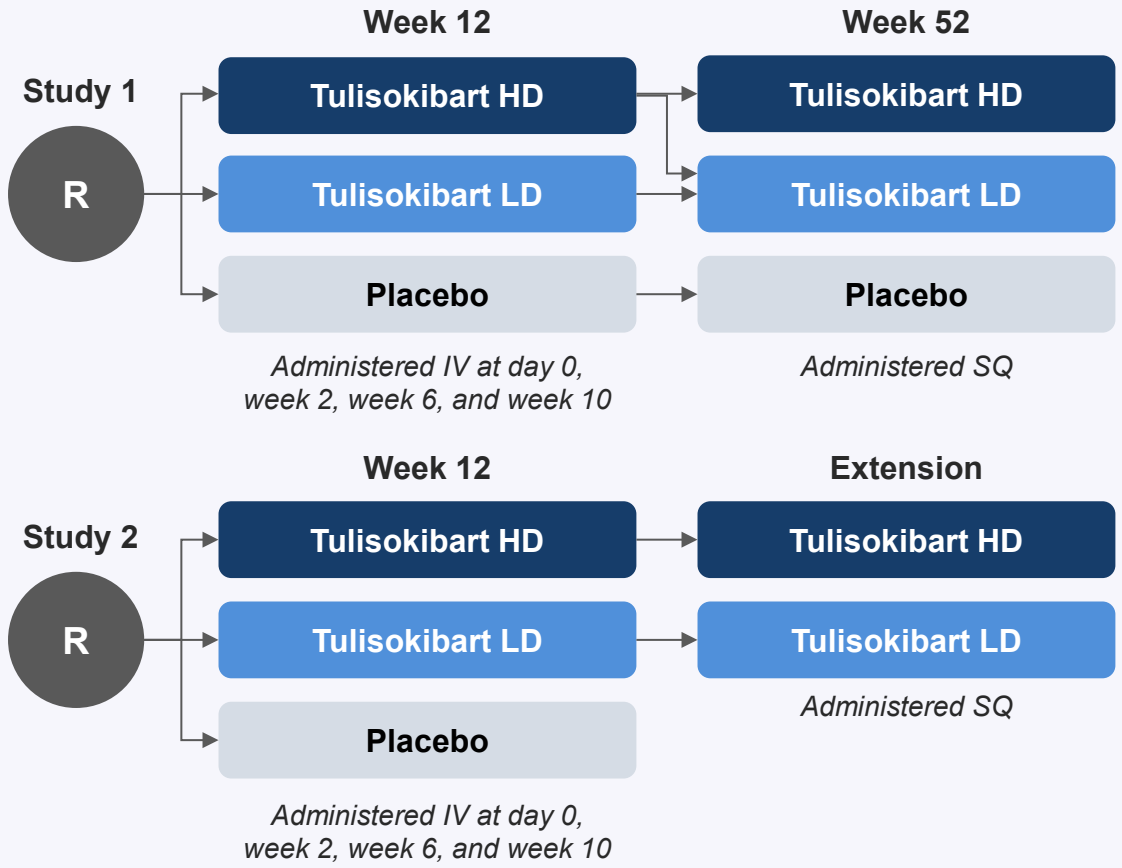
Randomized, Double-blind, Placebo-Controlled Study

A phase 3 study is underway to confirm these findings

N≈1020

Inclusion Criteria

- Moderately to severely active UC
- At least 1 of the following:
  - Inadequate response, loss of response, or intolerance to ≥1 protocol-specified UC treatment
  - CS dependent



Study 1 and Study 2 Primary Endpoints

- Clinical remission (MMS) at week 12
- Clinical remission (MMS) at week 52[a]
- Proportion of patients with ≥1 AE
- Proportion of patients who discontinue study intervention due to AEs

Key Secondary Efficacy Endpoints

- Clinical response (pMMS) at week 2
- Endoscopic improvement at week 12
- HEMI at week 12
- Endoscopic remission at week 12

AE, adverse effect; HEMI, histologic-endoscopic mucosal improvement; HD, high dose. LD, low dose; MMS, modified Mayo score.
[a]Only for study 1.
NCT06052059.

Afimkibart (RVT-3101): Phase 2b Study Design (TUSCANY-2)

Randomized, Double-blind, Placebo-Controlled study[1-3]

Inclusion Criteria

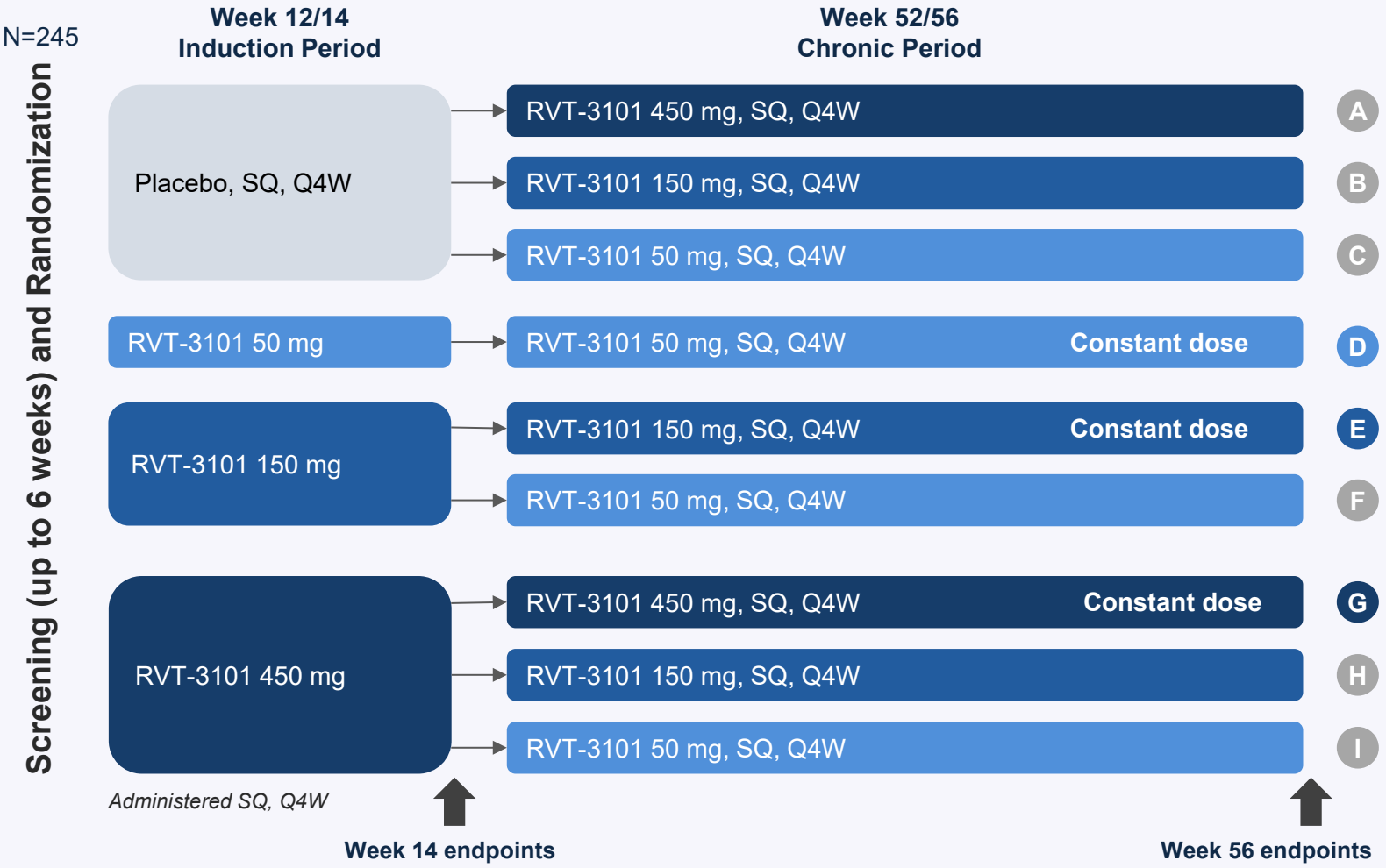
- Active UC
- Total Mayo Score ≥6
- ES ≥2
- Inadequate response to conventional and/or advanced therapy

Primary Endpoint

- Clinical remission at week 14
- Safety

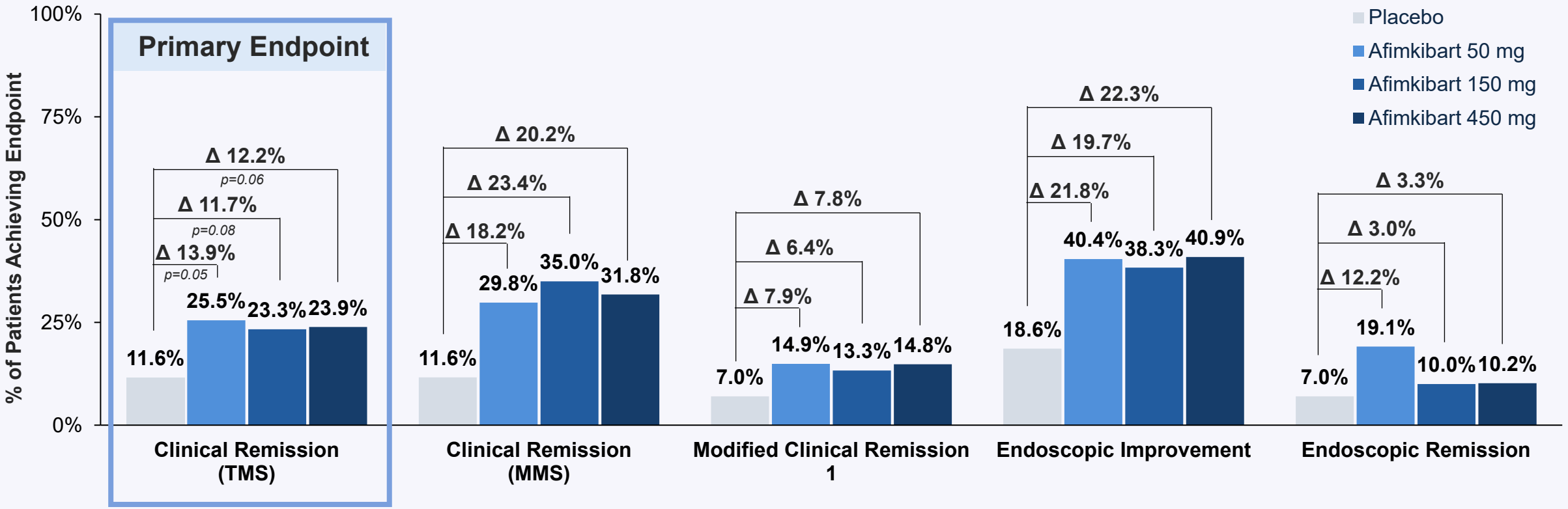
Key Secondary Efficacy Endpoints

- Endoscopic improvement at week 14
- Endoscopic remission at week 14
- Clinical remission at week 56
- Sustained clinical remission



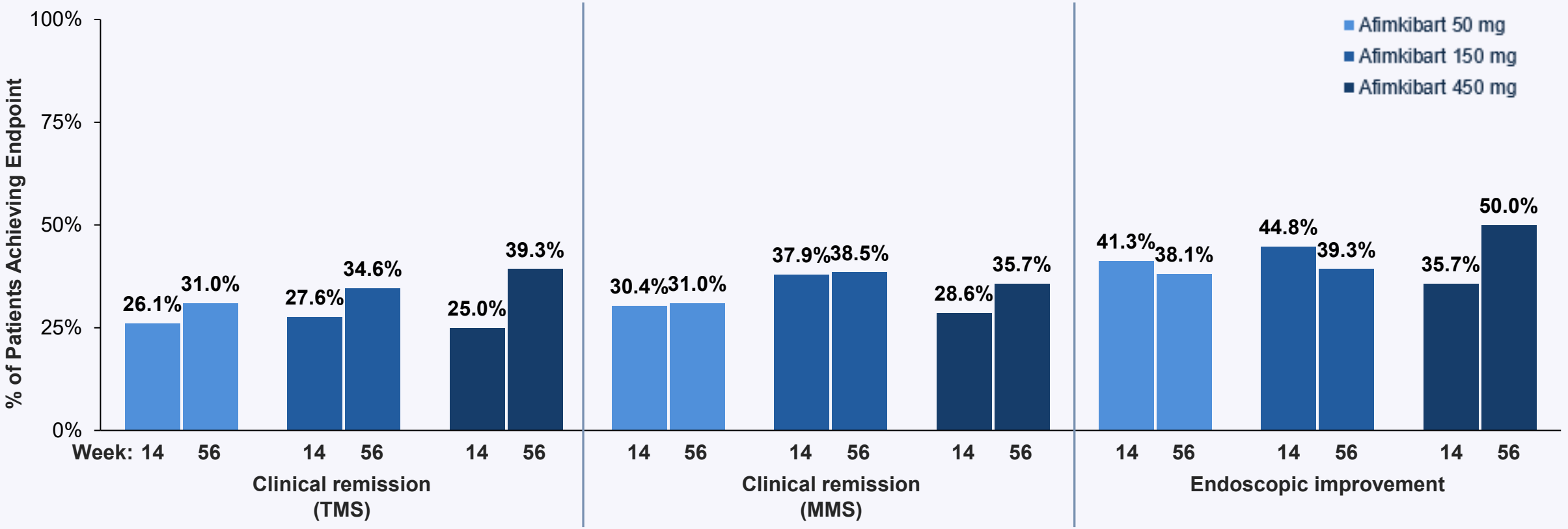
Danese S, et al. *Lancet Gastroenterol Hepatol.* 2025;10(10):882-895.

Afimkibart (RVT-3101): Efficacy at Week 14



Data for endoscopic remission excluded 7 patients with missing data due to medical or operational complications resulting from COVID-19. Clinical remission by TMS was defined as TMS ≤2, with no individual subscore of >1. Clinical remission by MMS was defined as an endoscopic subscore of 0 or 1, a ≥1-point decrease from baseline to reach a stool frequency subscore of 0 or 1, and a rectal bleeding subscore of 0. Modified clinical remission 1 was defined as an endoscopic subscore of 0 or 1, a stool frequency subscore of 0, and a rectal bleeding subscore of 0. Endoscopic improvement was defined as an endoscopic subscore of 0 or 1. Endoscopic remission was defined as an endoscopic subscore of 0.
MMS, modified Mayo score; TMS, total Mayo score.
Danese S, et al. *Lancet Gastroenterol Hepatol.* 2025;10(10):882-895.

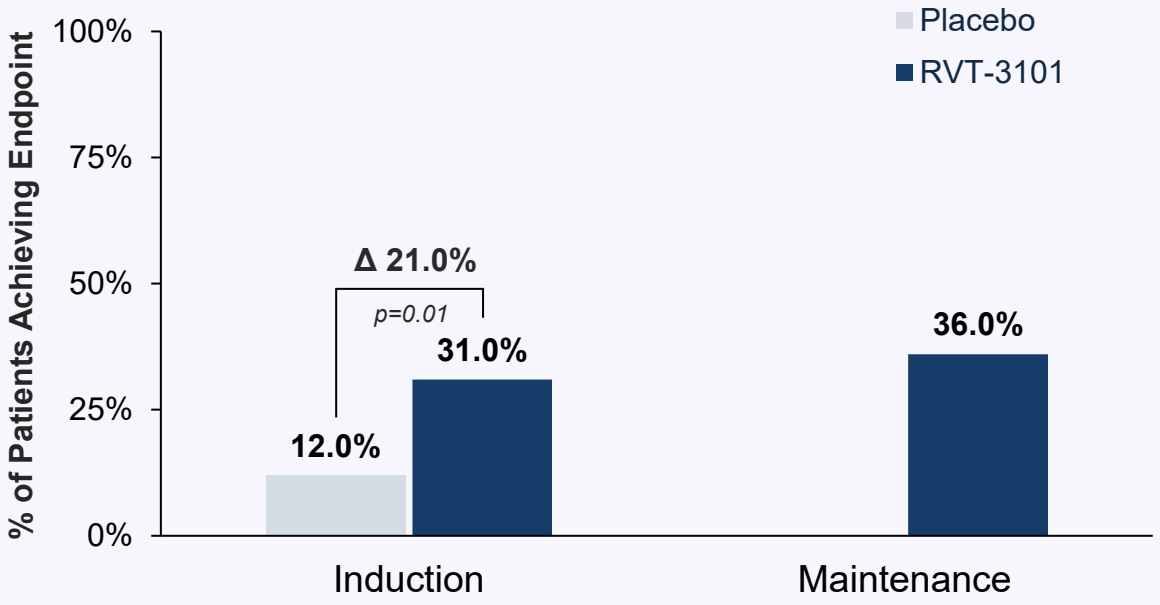
Afimkibart (RVT-3101): Efficacy at Weeks 14 and 56



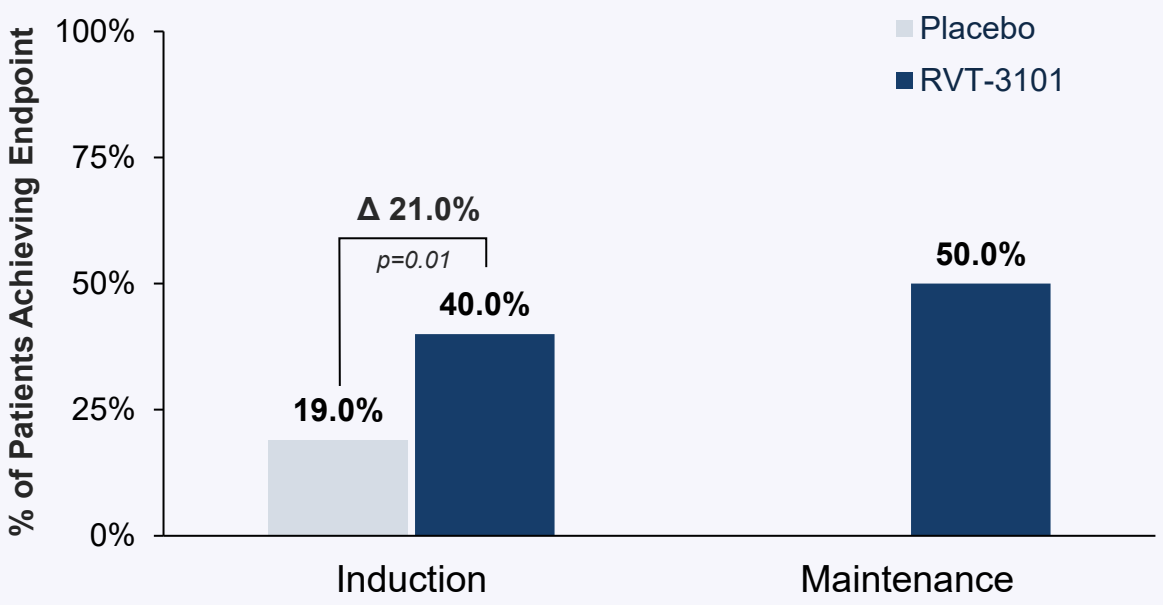
Includes patients in treatment sequences in which the doses were the same in the induction and maintenance periods. Clinical remission by TMS was defined as TMS ≤2, with no individual subscore of >1. Clinical remission by MMS was defined as an endoscopic subscore of 0 or 1, a ≥1-point decrease from baseline to reach a stool frequency subscore of 0 or 1, and a rectal bleeding subscore of 0. Modified clinical remission 1 was defined as an endoscopic subscore of 0 or 1, a stool frequency subscore of 0, and a rectal bleeding subscore of 0. Endoscopic improvement was defined as an endoscopic subscore of 0 or 1. Endoscopic remission was defined as an endoscopic subscore of 0.
MMS, modified Mayo score; TMS, total Mayo score.
Danese S, et al. *Lancet Gastroenterol Hepatol.* 2025;10(10):882-895.

Afimkibart (RVT-3101): Efficacy (Expected Phase 3 Dose)

Primary Endpoint: Clinical Remission[1,2]
(Week 14 and Week 56)



Key Secondary Endpoint: Endoscopic Improvement[1,2]
(Week 14 and Week 56)



All data for patients treated with the expected phase 3 dose in induction and maintenance.[1-3] Clinical remission (MMS) is defined as ES ≤1, a ≥1-point decrease from baseline to achieve SF ≤1, and RB=0. Endoscopic improvement is defined as ES ≤1.3.

1. Roivant. Investor presentation. January 2023. 2. Roivant. Investor presentation. June 2023. 3. NCT04090411.

Afimkibart Safety in TUSCANY-2

TUSCANY-2 Induction				
Treatment-emergent adverse events (TEAEs), n (%)	**Placebo (n=45)**	**50mg (n=47)**	**150mg (n=62)**	**450mg (N=91)**
Any TEAE	25 (56)	16 (34)	28 (45)	48 (53)
TEAE leading to study drug discontinuation	3 (7)	1 (2)	1 (2)	1 (1)
Serious TEAE	4 (9)	3 (6)	0	3 (3)
Death	0	0	0	0
Most common TEAEs ≥5%				
Anemia	4 (9)	2 (4)	5 (8)	2 (2)
Headache	1 (2)	2 (4)	1 (2)	9 (10)
Ulcerative colitis	1 (2)	3 (6)	1 (2)	4 (4)
Nausea	1 (2)	3 (6)	2 (3)	2 (2)
Pyrexia	1 (2)	0	1 (2)	5 (6)
Fatigue	0	0	1 (2)	5 (6)
Urinary tract infection	0	3 (6)	0	2 (2)

TUSCANY-2 Maintenance			
Treatment-emergent adverse events (TEAEs), n (%)	**50mg (n=46)**	**150mg (n=30)**	**450mg (N=29)**
Any TEAE	28 (61)	15 (50)	19 (66)
TEAE leading to study drug discontinuation	3 (7)	0	1 (3)
Serious TEAE	4 (9)	0	14 (14)
Death	0	0	0
Most common TEAEs ≥10%			
Anemia	4 (9)	0	3 (10)
Ulcerative colitis	7 (15)	2 (7)	1 (3)
Nausea	1 (2)	3 (10)	0
Pyrexia	2 (4)	2 (7)	1 (3)
SARS-CoV-2 test positive	0	3 (10)	2 (7)
Blood creatine phosphatase increased	3 (7)	0	3 (10)
Injection site reaction	1 (2)	0	0
Oropharyngeal pain	0	3 (10)	0

Danese S, et al. Lancet Gastroenterol Hepatol. 2025;10(10):882-895.

Afimkibart: Next Steps

Phase 3, Randomized, Double-blind, Placebo-Controlled Study (Ametrine-1)

N≈400

Inclusion Criteria

- Confirmed diagnosis of moderately to severely active UC assessed by MMS
- Demonstrated inadequate response, loss of response, and/or intolerance to ≥1 protocol-specified conventional or advanced UC therapy
- Body weight ≥40 kg
- Up to date with colorectal cancer screening performed according to local standards

Primary Endpoints

- Clinical remission at week 12
- Clinical remission at week 52

Secondary Efficacy Endpoints

- Change in pMMS at week 2
- Endoscopic improvement at week 12
- Endoscopic remission at week 12
- Clinical response at week 12
- Histologic improvement at week 12
- Histologic remission at week 12
- HEMI at week 12
- HEMR at week 12

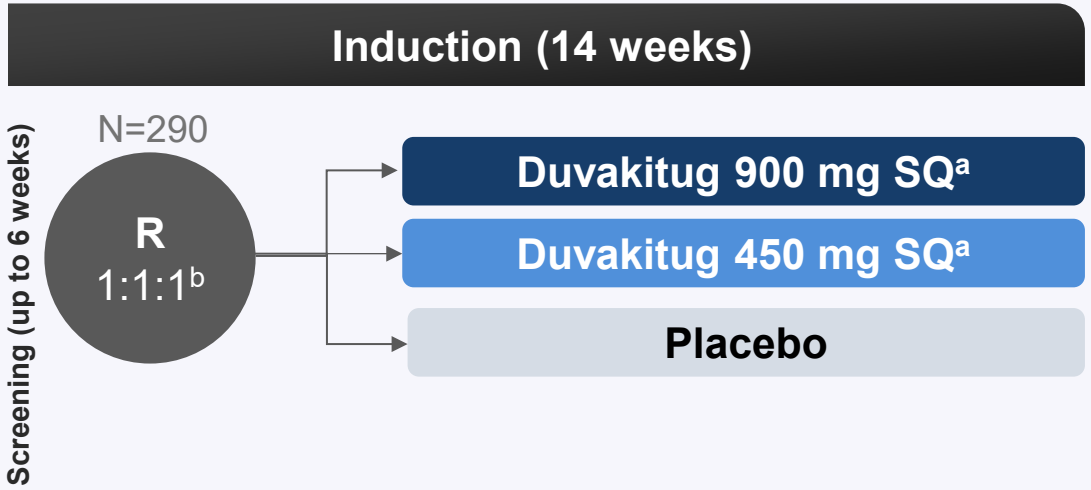
.
HEMI, histologic endoscopic mucosal improvement; HEMR, histologic endoscopic mucosal remission; MMS, Modified Mayo Score; pMMS, partial Modified Mayo Score.
NCT06589986.

Duvakitug: Phase 2b Study Design (RELIEVE UCCD)[1-3]

Randomized, Double-blind, Placebo-Controlled Study

Inclusion Criteria

- Adults 18–75 years old with diagnosis of moderately to severely active UC ≥3 months[1,2]
- UC: MMS=5–9, with MES ≥2[1,2]
- CD: SES-CD score of ≥6 (≥4 for isolated ileal disease)[3]
- Inadequate response, loss of response, or intolerance to previous conventional and/or advanced therapies



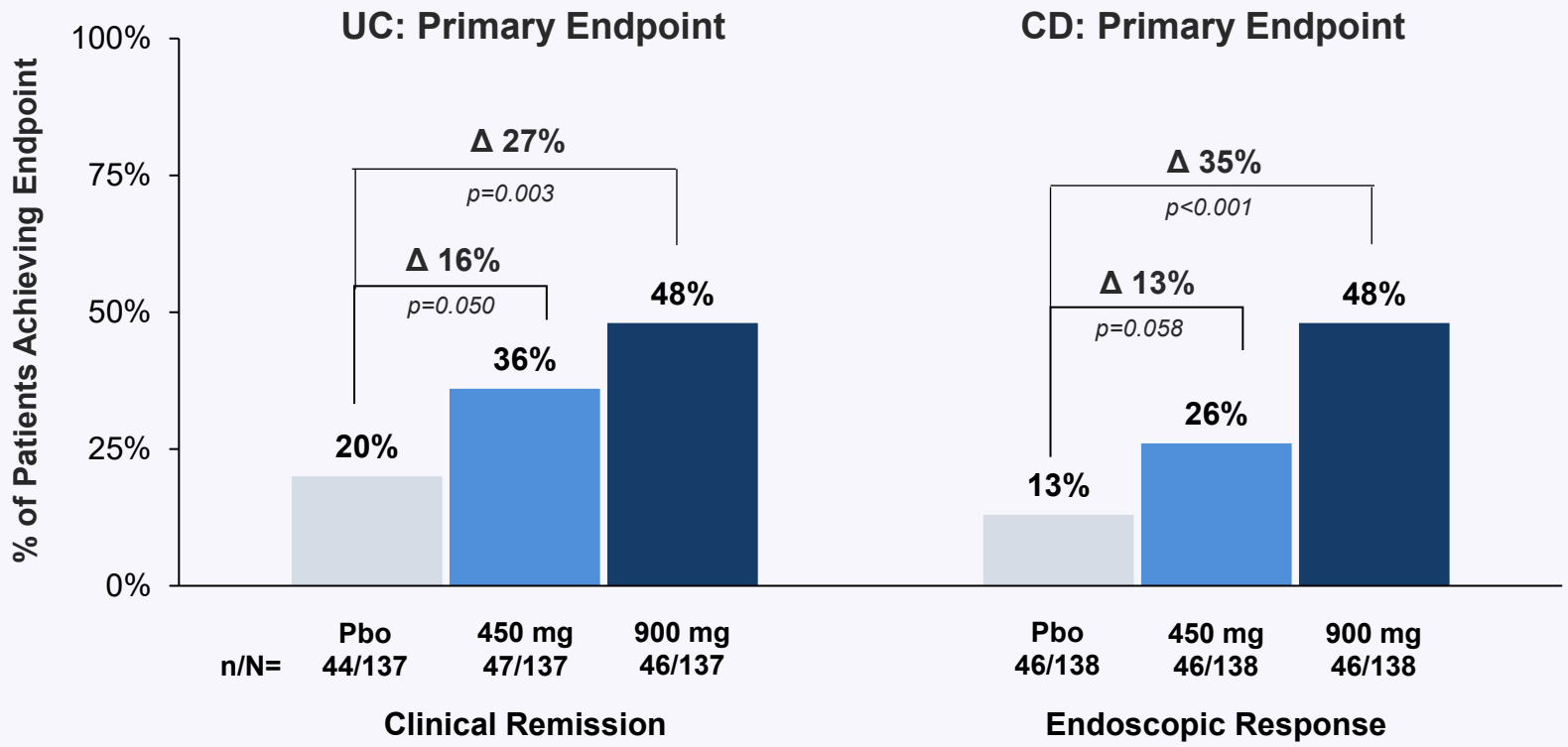
Primary Endpoint

- Clinical remission (MMS) at week 14 (UC)
- Endoscopic remission (SES-CD) at week 14 (CD)

AT, advanced therapy. CS, corticosteroid; MES, Mayo endoscopic subscore; MMS, modified Mayo score; SES-CD, simple endoscopic score for Crohn's disease.
[a]2250-mg loading dose on day 1; then placebo, 450 mg, or 900 mg every 2 weeks (6 doses). [b]Stratified by prior AT.
1. NCT05499130. 2. Reinisch W, et al. *J Crohns Colitis*. 2025;19(Suppl 1):i79-i80. 3. Jairath V et al. *Am J Gastroenterol*. 2025;120(Suppl):S1450.

Duvakitug: Efficacy

Primary Outcome at Week 14[1-3]

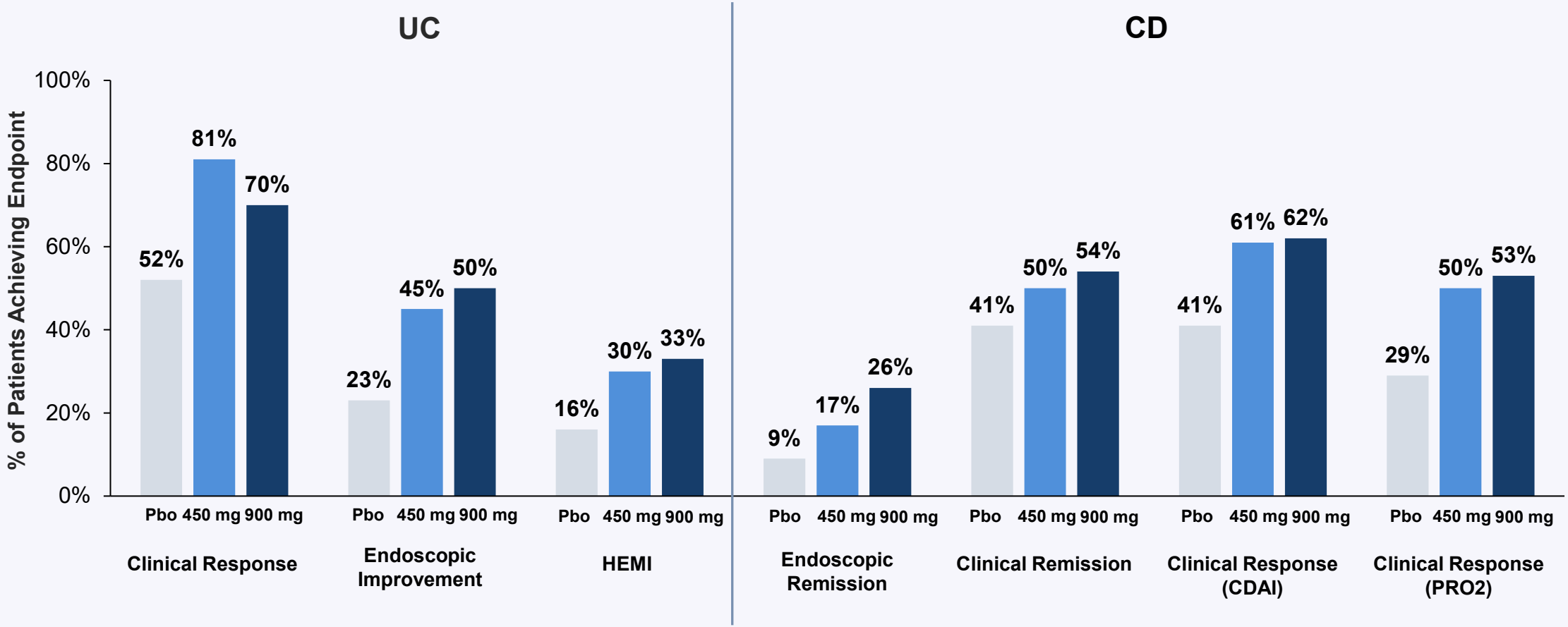


Pbo, placebo.

1. Reinisch W et al. *J Crohns Colitis*. 2025;19(Suppl 1):i79-i80. 2. Sanofi. Press release. February 22, 2025. 3. Jairath V et al. *Am J Gastroenterol*. 2025;120(Suppl):S1450.

Duvakitug: Efficacy

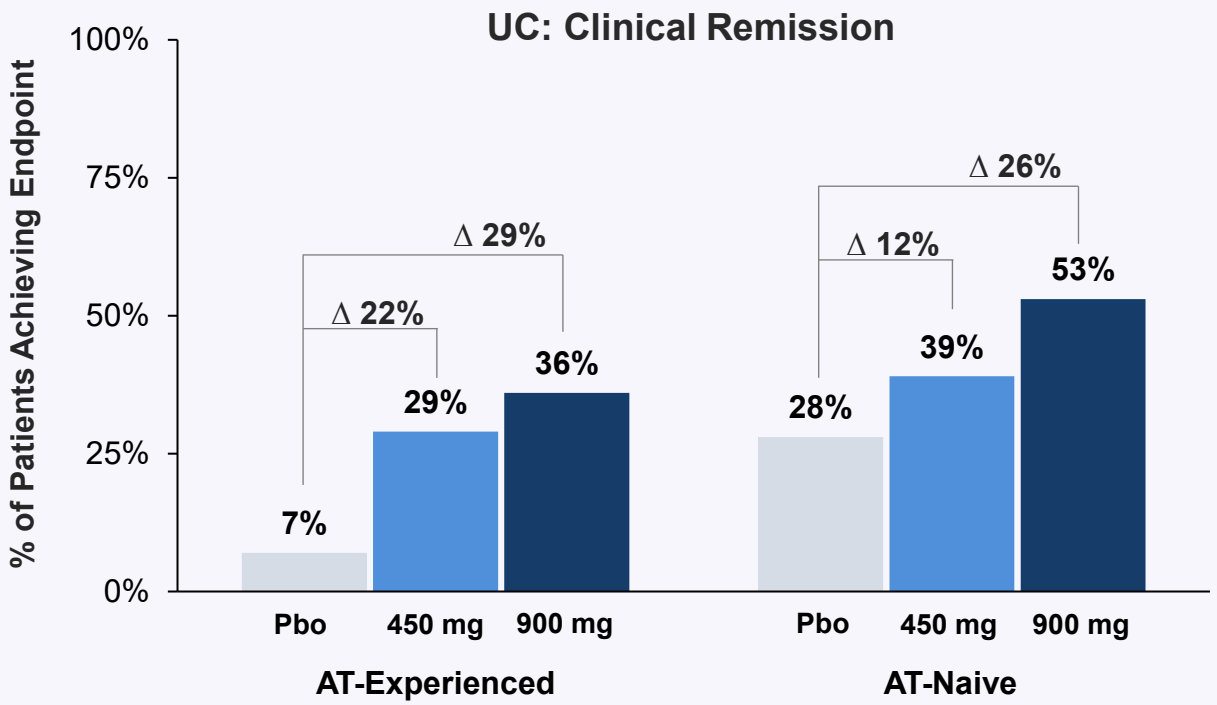
Additional Outcomes at Week 14

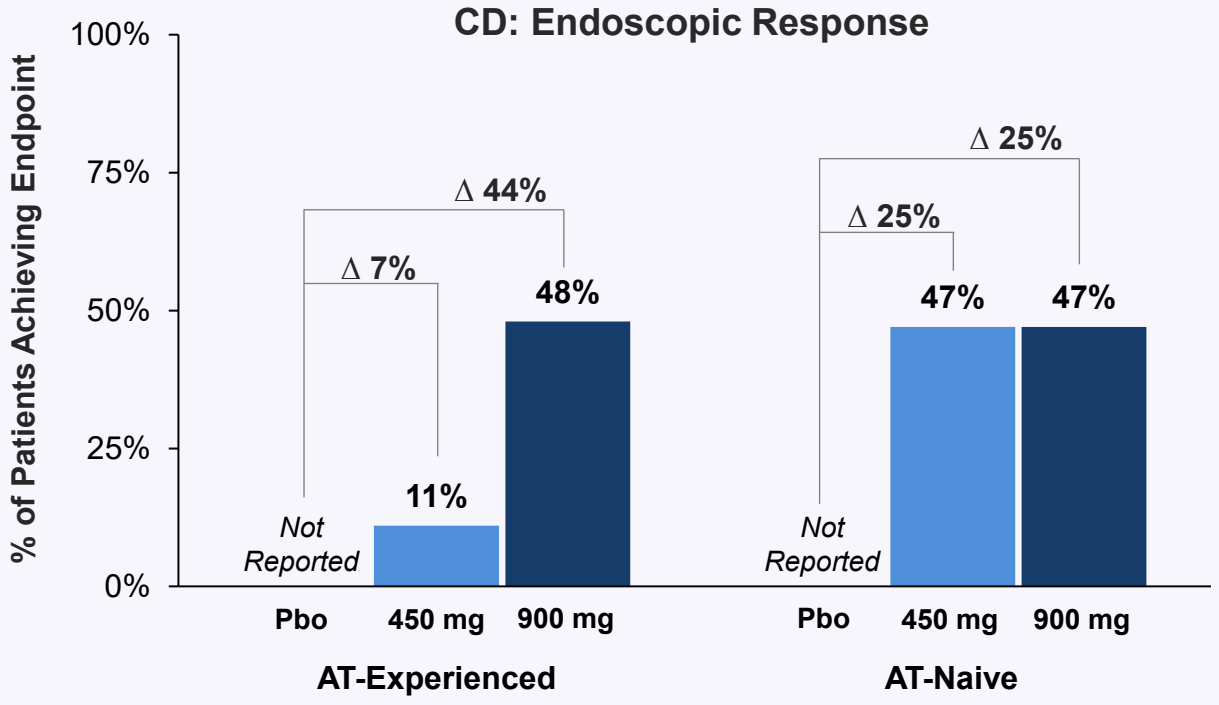


CDAI, Crohn's Disease Activity Index; HEMI, histologic-endoscopic mucosal improvement; Pbo, placebo; PRO2, 2-item patient-reported outcome.
Sanofi. Press release. February 22, 2025.

Duvakitug: Consistent Treatment Effect Regardless of Prior AT Experience

Primary Outcome at Week 14[1-3]



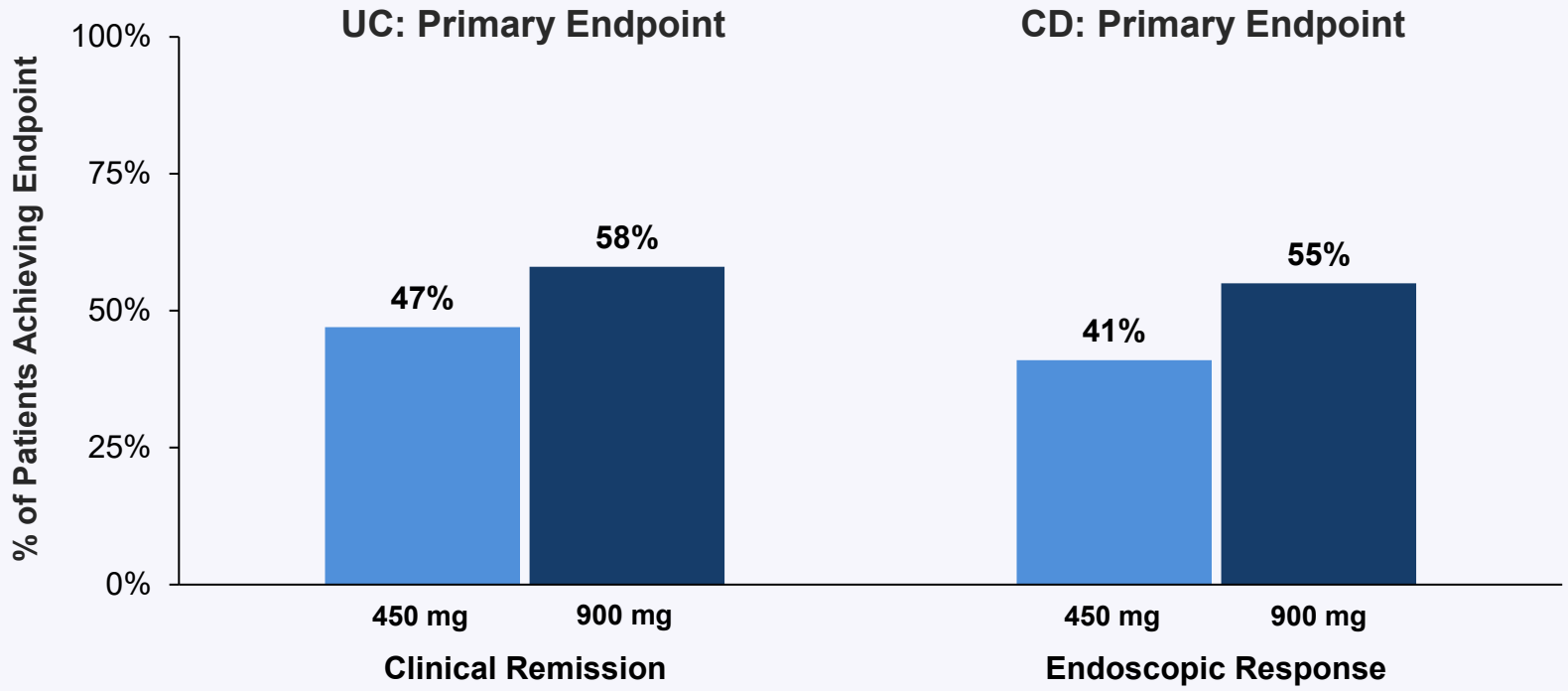


AT, advanced therapy; Pbo, placebo.

1. Reinisch W, et al. *J Crohns Colitis*. 2025;19(Suppl 1):i79-i80. 2. Sanofi. Press release. February 22, 2025. 3. Jairath V, et al. *Am J Gastroenterol*. 2025;120(Suppl):S1450.

Duvakitug: Maintenance of Efficacy in the RELIEVE UCCD LTE[a]

Primary Outcome at Week 44



For both UC and CD, consistent benefits were observed across additional efficacy endpoints

LTE, long-term extension.
[a]The RELIEVE UCCD LTE is an ongoing study to evaluate the long-term efficacy and safety of duvakitug. Patients who received duvakitug, completed the 14-week induction study, and were responders entered a 44-week double-blind maintenance period and were re-randomized to receive either 450 mg or 900 mg subcutaneous duvakitug every 4 weeks.
Sanofi. Press release. February 17, 2026.

Duvakitug Safety in RELIEVE UCCD Phase 2b

	UC Cohort			CD Cohort		
Treatment-emergent adverse events (TEAEs), n (%)	**Placebo (n=44)**	**450mg (n=47)**	**900mg (n=46)**	**Placebo (n=46)**	**450mg (n=46)**	**900mg (n=46)**
Any TEAE	23 (52)	23 (49)	20 (43)	22 (48)	31 (67)	20 (43)
TEAE leading to study drug discontinuation	2 (5)	0	1 (2)	1 (2)	4 (9)	1 (2)
Serious TEAE	1 (2)	0	1 (2)	5 (11)	6 (13)	1 (2)
Death	0	0	0	0	0	0
Most common TEAEs >2 participants in any treatment arm						
Anemia	3 (7)	1 (2)	1 (2)	1 (2)	3 (7)	0
Headache	NR	NR	NR	1 (2)	4 (9)	1 (2)
Nasopharyngitis	1 (2)	3 (6)	0	3 (7)	2 (4)	3 (7)
Upper respiratory tract infection	1 (2)	3 (6)	1 (2)			
Vomiting	0	3 (6)	0			

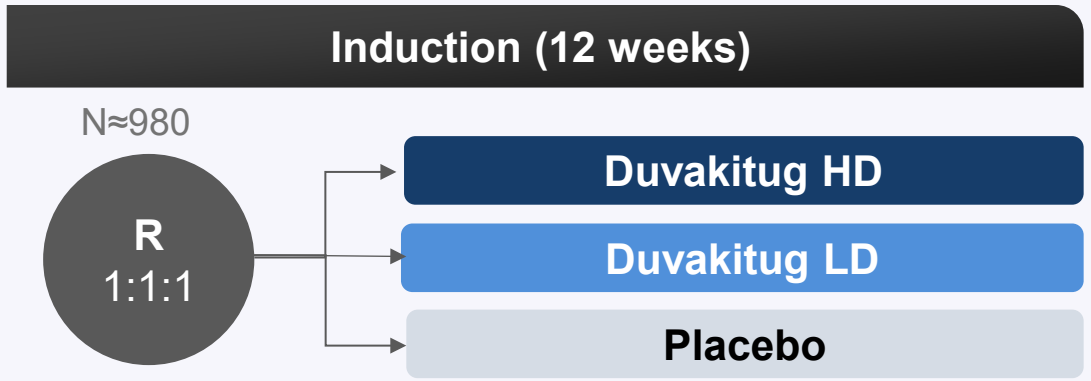
Reinisch W et al. ECCO 2025. Presentation OP40. Jairath V et al. ECCO 2025. Presentation OP41.

Duvakitug: Next Steps

Phase 3, Randomized, Double-blind, Placebo-Controlled Study (SUNSCAPE-1)

Inclusion Criteria

- Adults ≥18 and ≤80 years old with confirmed diagnosis of moderately to severely active UC ≥3 months prior to baseline
  - Where permitted locally, participants 16 to <18 years of age who meet the definition of Tanner stage 5 for development
- Inadequate response, loss of response, or intolerance to previous conventional and/or advanced therapies



Primary Endpoint

- Clinical remission (MMS) at week 12

Secondary Efficacy Endpoints

- Clinical response (MMS) at week 12
- Endoscopic improvement at week 12
- HEMI at week 12
- Endoscopic remission at week 12

HD, high dose; LD, low dose; HEMI, histologic-endoscopic mucosal improvement; MMS, modified Mayo score.
NCT07184996.