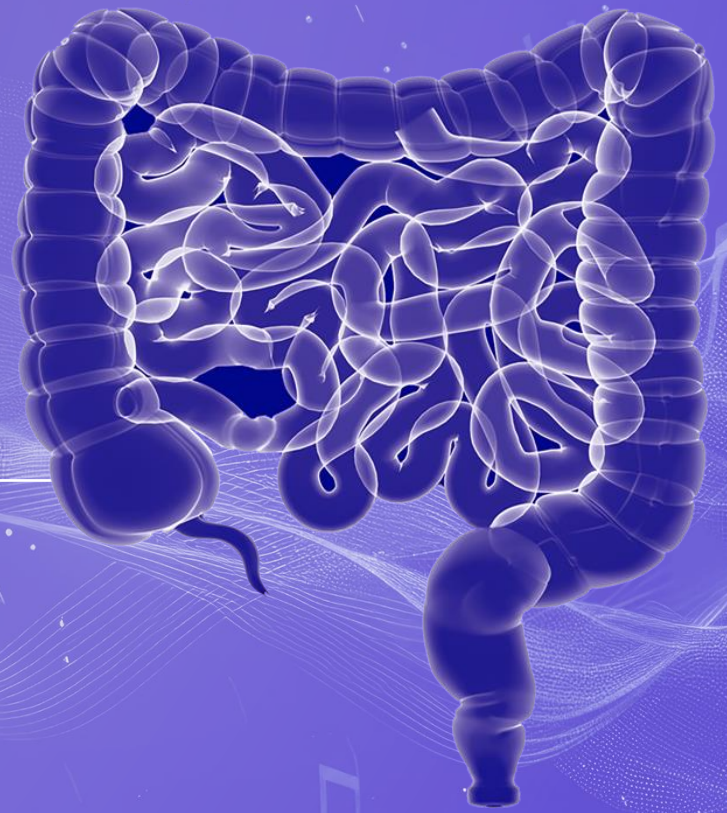
ABIVAX

Oral Advanced Therapies in Ulcerative Colitis: Are More Options Needed?



13 October 2024 | 10:00–11:00 AM CEST

Scan to view speaker bios, presentation slides and recording, and post-symposium evaluation

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Faculty

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Disclosures

Marla C. Dubinsky serves as a consultant and advisor to: AbbVie, Abivax, Arena Pharmaceuticals, Astra Zeneca, Boehringer Ingelheim International GmbH, Bristol-Meyer Squibb, Celltrion, Eli Lilly and Company, F. Hoffmann-La Roche Ltd, Genentech Inc, Gilead, Janssen Pharmaceuticals, Johnson & Johnson, Merck, Pfizer Inc, Prometheus Biosciences, Spyre, and Takeda Pharmaceuticals

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Agenda

Advent of Oral Advanced Therapies in Ulcerative Colitis

Séverine Vermeire, MD, PhD

10:00–10:10 AM

Current Oral Advanced Therapies in Ulcerative Colitis: Opportunities for Innovation

Marla C. Dubinsky, MD

10:10–10:30 AM

Exploring New Oral Advanced Therapies for Ulcerative Colitis in the Pipeline

Séverine Vermeire, MD, PhD

10:30–10:50 AM

Q&A

Marla C. Dubinsky, MD
Séverine Vermeire, MD, PhD

10:50–11:00 AM

Objectives

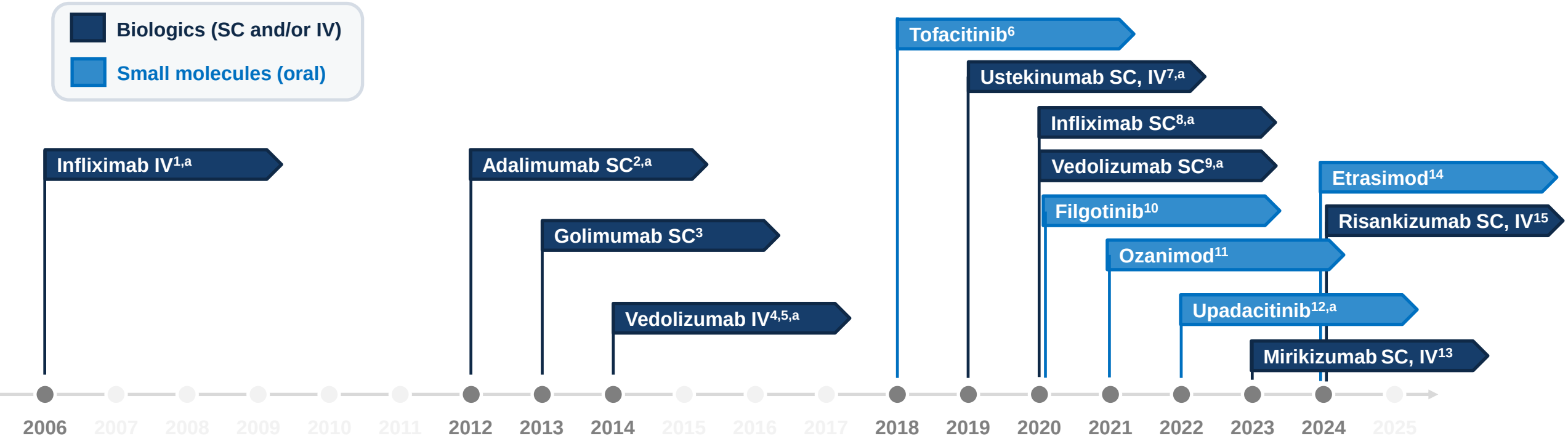
- Our symposium will provide an overview of existing oral advanced therapies in ulcerative colitis (UC), including how these medications are utilized, considerations for use, and unmet needs that remain
- We will also review oral advanced therapies in late-stage clinical development for UC, with an emphasis on mechanism of action and available clinical data for these potential future therapies

Advent of Oral Advanced Therapies in Ulcerative Colitis

Séverine Vermeire, MD, PhD

KU Leuven, Leuven, Belgium

The Number of Advanced Therapies in UC Is Expanding Rapidly



Most advanced therapies are biologics designed to be injected or infused

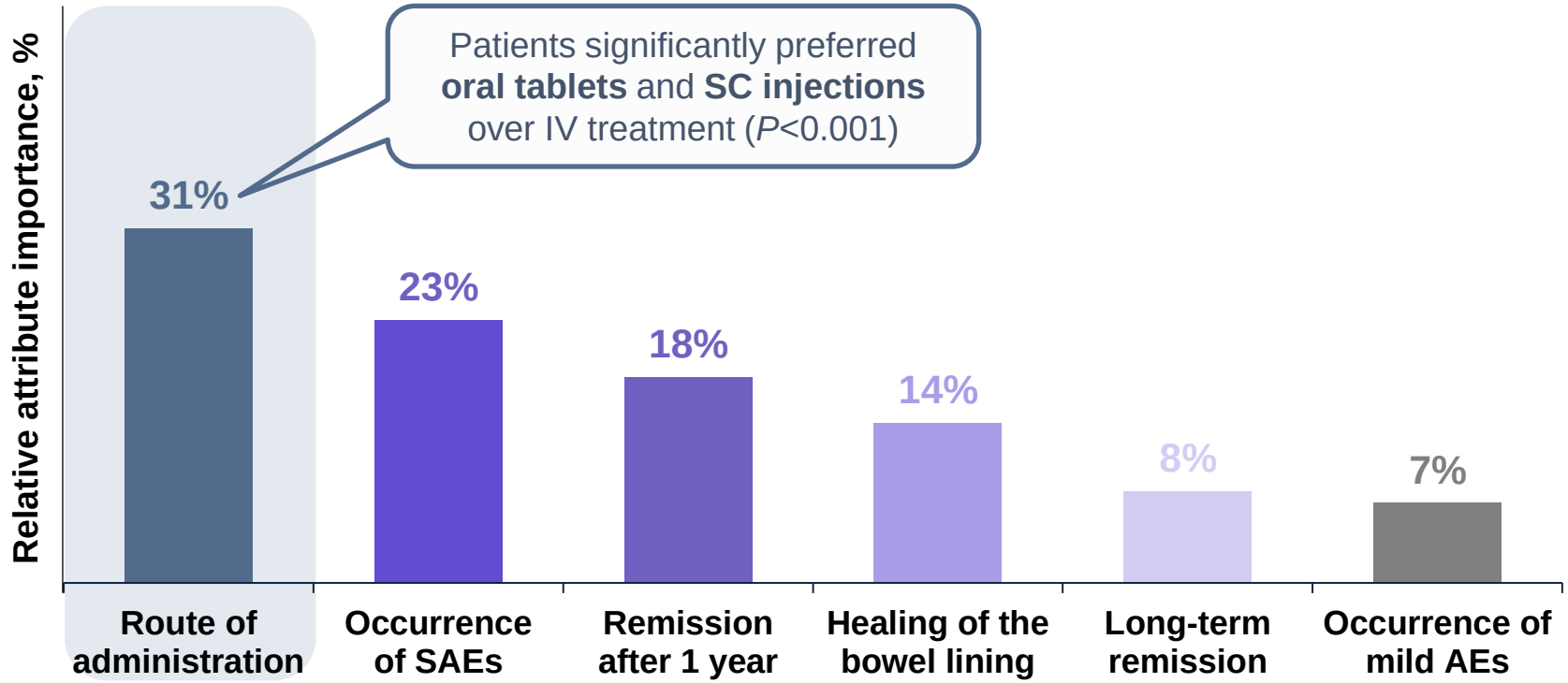
[a]Approved for Crohn's disease as well (EMA 1999/infliximab IV[16]; 2007/adalimumab[17]; 2014/vedolizumab IV[4]; 2016/ustekinumab[18]; 2020/infliximab subQ[8]; 2020/vedolizumab subQ[10]; 2023/upadacitinib[19]). EMA, European Medicines Agency; IV, intravenous; SC, subcutaneous; UC, ulcerative colitis.

1. Hisa EC, et al. *APLAR J Rheumatol.* 2006;9:107-118. **2.** Abbott. Press release. April 11, 2012. **3.** Johnson & Johnson. Press release. September 23, 2013. **4.** Takeda. News release. May 28, 2014. **5.** EPAR. Entyvio. **6.** Pfizer. Press release. August 1, 2018. **7.** BusinessWire. September 4, 2019. **8.** European Pharmaceutical Review. News article. July 29, 2020. **9.** Takeda. Press release. May 8, 2020. **10.** EPAR. Jyseleca. **11.** BMS. Press release. November 23, 2021. **12.** AbbVie. Press release. July 26, 2022. **13.** EPAR. Omvoh. **14.** Pfizer. Press release. February 19, 2024. **15.** AbbVie. Press release. June 18, 2024. **16.** Melsheimer R, et al. *Biologics*. 2019;13:139-178. **17.** PharmaTimes. June 8, 2007. **18.** Johnson & Johnson. Press release. November 11, 2016. **19.** AbbVie. Press release. April 17, 2023.

Patients Identify Route of Administration as an Important Treatment Attribute

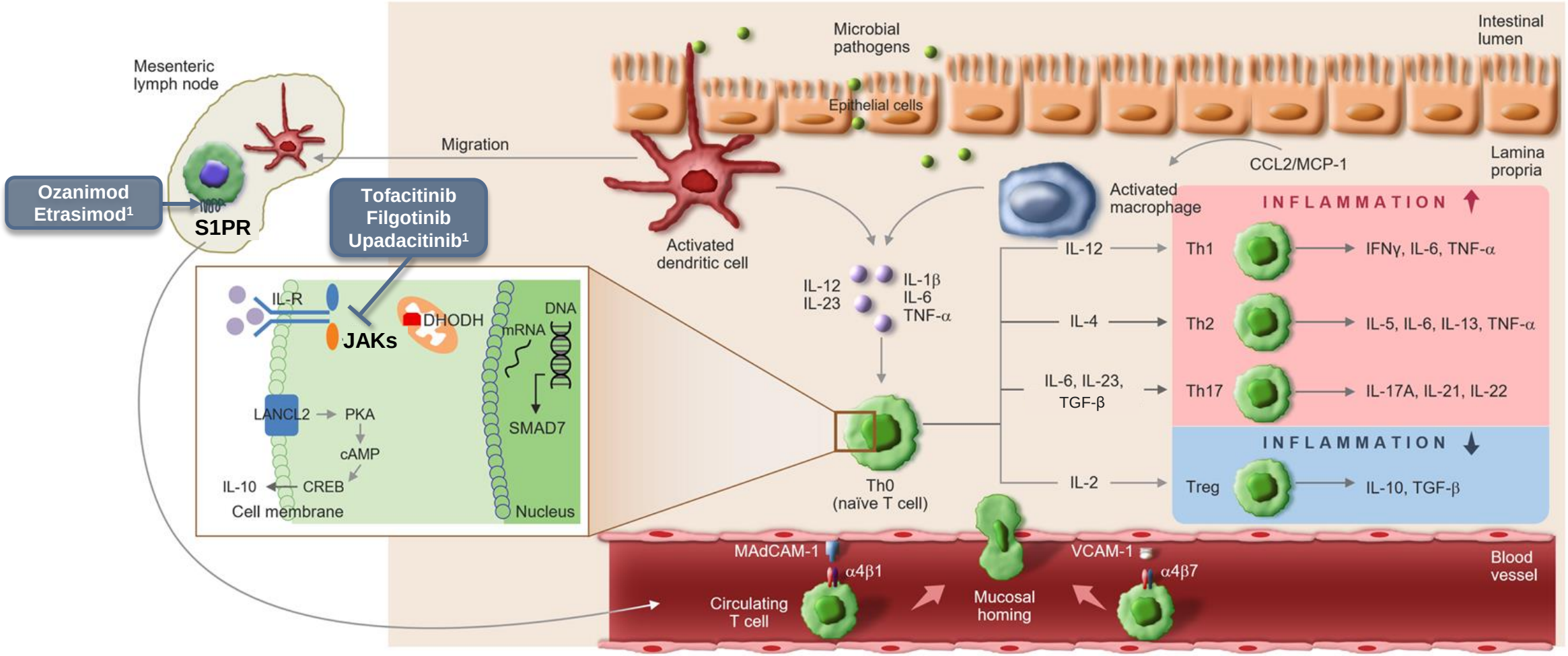
In a recent study on patient preferences, patients with UC (n=326) ranked **route of administration** as the most important attribute when selecting a treatment

Preference for treatment attributes in patients with UC



Descriptive, observational, noninterventional, stated-preference study of 326 patients with UC conducted across 7 European countries; data were collected through an online cross-sectional survey.
AE, adverse event; IV, intravenous; SAE, serious adverse event; SC, subcutaneous; UC, ulcerative colitis.
Fiorino G, et al. *Inflamm Bowel Dis*. 2024; Epub ahead of print.

Currently Approved Oral Advanced Therapies Target JAKs or S1PRs



cAMP, cyclic adenosine monophosphate; CREB, c-AMP 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; PKA, protein kinase; S1PR, sphingosine-1-phosphate receptor; 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; VCAM-1, vascular cell adhesion molecule. **1.** Shivaji UN, et al. *Lancet Gastroenterol Hepatol.* 2020;5(9):850-861.

Overview of Current JAK Inhibitors in Moderate to Severe UC

	Tofacitinib[1]	Filgotinib[2]	Upadacitinib[3,4]
Manufacturer (brand name)	Pfizer (Xeljanz®)	Alfasigma (Jyseleca®)	AbbVie (Rinvoq®)
Selectivity	JAK3 = JAK1 > JAK2	JAK1 > JAK2 > JAK3 *and* TYK2	JAK1 >>> JAK3
Proposed MoA	Inhibition of JAK signaling prevents downstream activation of STAT proteins and is thought to disrupt cytokine signaling, including pathways pivotal to intestinal homeostasis and inflammation[5]		
Indication (UC)	Adult patients with **inadequate response, loss of response, or intolerance** to conventional therapy or a biologic agent		
Induction dose	10 mg BID for 8–16 weeks	200 mg QD for 10–22 weeks	45 mg QD for 8–16 weeks
Maintenance dose	5–10 mg BID	100–200 mg QD	15–30 mg QD

BID, twice daily; JAK, Janus kinase; MoA, mechanism of action; QD, once daily; STAT, signal transducer and activator of transcription; TYK2, tyrosine kinase 2; UC, ulcerative colitis.

1. Xeljanz® Summary of Product Characteristics. **2.** Jyseleca® Summary of Product Characteristics. **3.** Rinvoq® Summary of Product Characteristics. **4.** Danese S, et al. *Lancet.* 2022;399:2113-2128. **5.** Honap S, et al. *Frontline Gastroenterol*. 2024;15:59-69.

Overview of Current S1PR Modulators in Moderate to Severe UC

	Ozanimod[1]	Etrasimod[2]
Manufacturer (brand name)	Bristol Myers Squibb (Zeposia®)	Pfizer (Velsipity®)
Selectivity	S1PR1 *and* S1PR5	S1PR1 *and* S1PR4 *and* S1PR5
Proposed MoA	Modulation of S1PRs sequesters specific lymphocyte subsets in lymph nodes, resulting in fewer peripheral immune cells available to traffic to sites of inflammation[3]	
Indication (UC)	Adult patients[a] with **inadequate response, loss of response, or intolerance** to conventional therapy or a biologic agent	
Dosing	Days 1−4: 0.23 mg QD Days 5−7: 0.46 mg QD Day 8 and after: 0.92 mg QD	2 mg QD

[a]Etrasimod is indicated for treatment of moderate to severe UC in patients ≥16 years of age.
BID, twice daily; MoA, mechanism of action; QD, once daily; S1PR, sphingosine-1-phosphate receptor; UC, ulcerative colitis.
1. Zeposia® Summary of Product Characteristics. **2.** Velsipity® Summary of Product Characteristics. **3.** Sandborn WJ, et al. *Lancet.* 2023;401:1159-1171.

Oral Advanced Therapies Are Gaining Momentum in UC

Most advanced therapies for patients with UC are **administered IV or SC,** which may be undesirable and a barrier to treatment for some patients[1]

The development of oral advanced therapies is gaining momentum with the **recent approval of a number of JAK inhibitors and S1PR modulators**[2-6]

IV, intravenous; JAK, Janus kinase; S1PR, sphingosine-1-phosphate receptor; SC, subcutaneous; UC, ulcerative colitis.

1. Imbrizi M, et al. *Pharmaceuticals (Basel).* 2023;16(9):1272. **2.** Pfizer. Press release. August 1, 2018. **3.** BMS. Press release. November 23, 2021. **4.** EPAR. Jyseleca. **5.** AbbVie. Press release. July 26, 2022. **6.** Pfizer. Press release. February 19, 2024.

Patient With UC: Treatment Timeline

Male patient with UC born in 1965

2004 Patient quits smoking

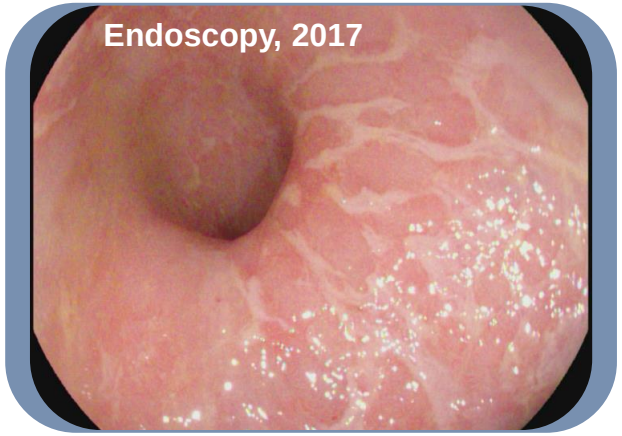
2005 **UC diagnosis**
Treatment with 5-ASA and azathioprine

2009 **Flare**
Steroids and infliximab

2014 LOR to infliximab
Switch to adalimumab
PNR to adalimumab
Start tofacitinib

2016 LOR to tofacitinib
Start vedolizumab
PNR to vedolizumab

2017 Start IL-23 p19 inhibitor clinical trial
PNR to IL-23 p19 inhibitor
Surgery proposed; patient refused



Where to go from here?

5-ASA, 5-aminosalicylic acid; IL, interleukin; LOR, loss of response; PNR, primary nonresponse; UC, ulcerative colitis.

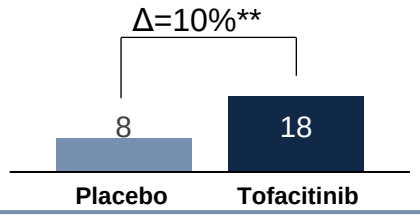
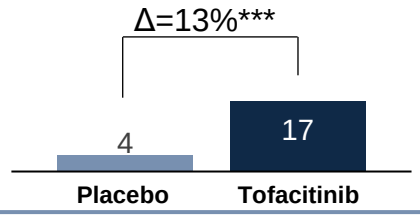
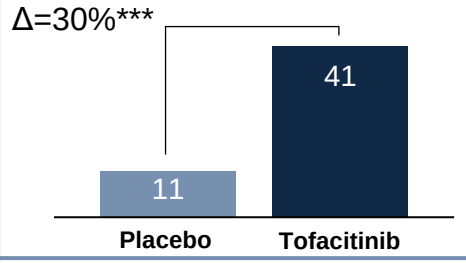
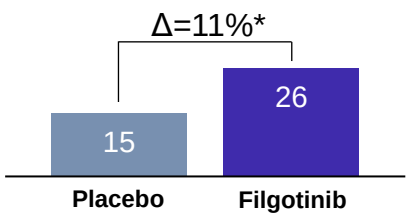
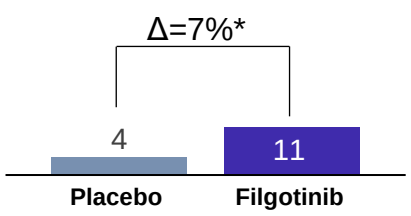
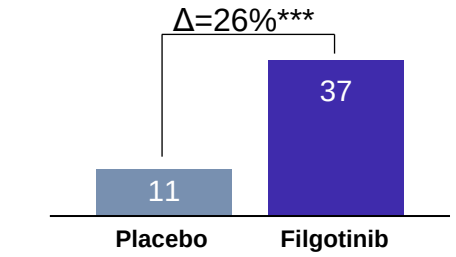
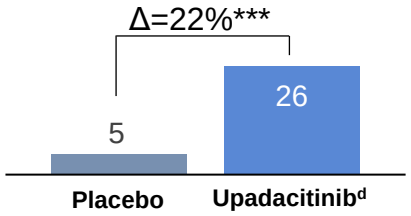
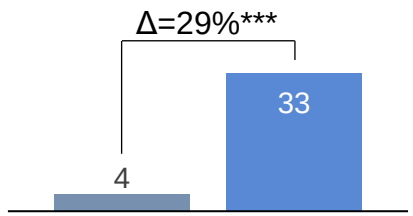
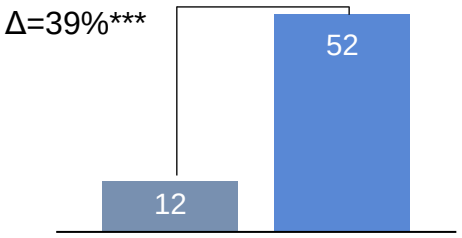
Current Oral Advanced Therapies in Ulcerative Colitis: Opportunities for Innovation

Marla C. Dubinsky, MD

Mount Sinai, New York, NY, USA

JAK Inhibitors Are Effective in Moderate to Severely Active UC

Primary Efficacy Endpoint: Clinical Remission

Proportion of patients, %	Induction Study 1	Induction Study 2	Maintenance Study[a]
OCTAVE program (tofacitinib)[1,b]			
SELECTION program (filgotinib)[2,c]	*Biologic naive* 	*Biologic experienced* 	
U-ACHIEVE and U-ACCOMPLISH program (upadacitinib)[3]			

In a post hoc analysis of OCTAVE data, rates of clinical remission based on MMS[4] were:

	Placebo	Tofa
Induction 1	8%	25%
Induction 2	6%	18%
Maintenance[a]	12%	42%

Induction: 8 weeks
Maintenance: 52 weeks

Induction: 10 weeks
Maintenance: 58 weeks

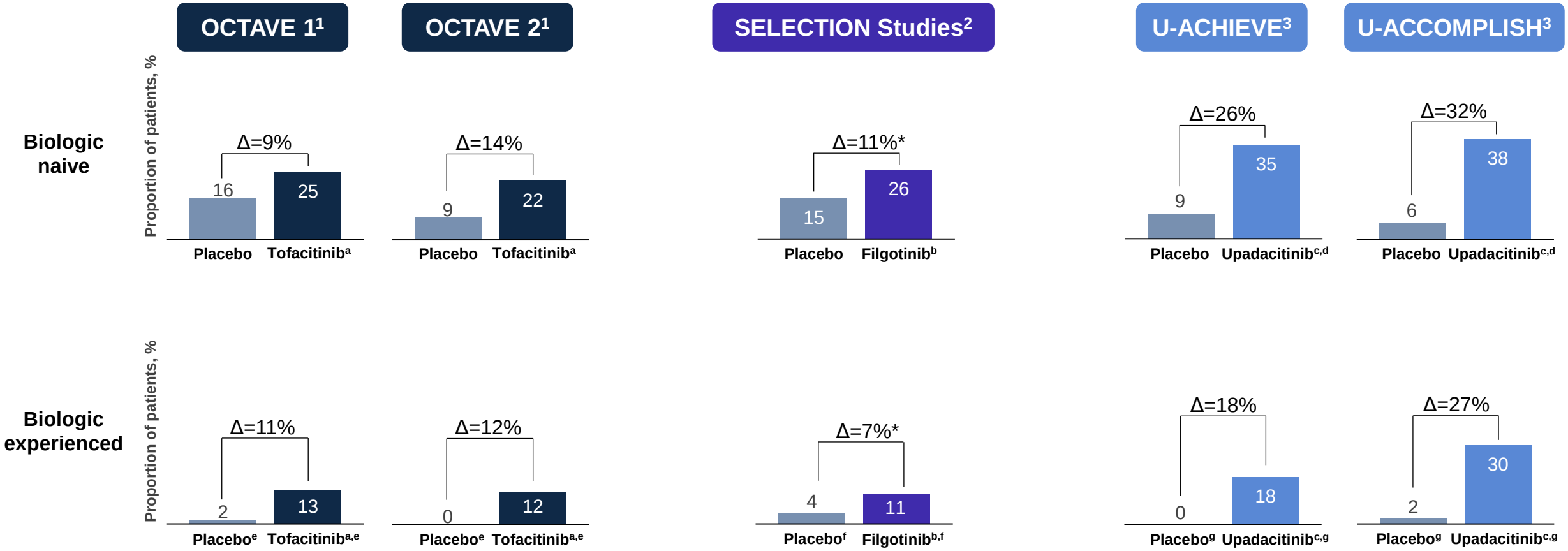
Induction: 8 weeks
Maintenance: 52 weeks

For illustrative purposes only; not a head-to-head comparison. Differences exist between trial designs and patient characteristics, and caution should be exercised when comparing data across trials. *P<0.05. **P<0.01. ***P<0.001. [a]Maintenance data shown here are among induction responders who entered the maintenance study. [b]Tofacitinib 10 mg BID. [c]Filgotinib 200 mg QD. [d]Upadacitinib 45 mg QD. [e]Upadacitinib 30 mg QD. BID, twice daily; JAK, Janus kinase; MMS, modified Mayo score; QD, once daily; tofa, tofacitinib.

1. Sandborn WJ, et al. *N Engl J Med.* 2017;376:1723-1736. **2.** Feagan BG, et al. *Lancet.* 2021;397:2372-2384. **3.** Danese S, et al. *Lancet.* 2022;399:2113-2128. **4.** Sandborn WJ, et al. *Therap Adv Gastroenterol.* 2022;15:1–13.

JAK Inhibitors Are Effective in Biologic-Naive and Biologic-Experienced Patients

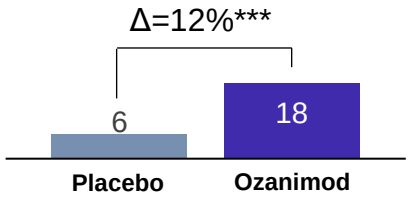
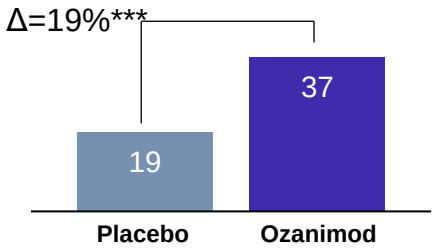
Clinical Remission at the End of Induction



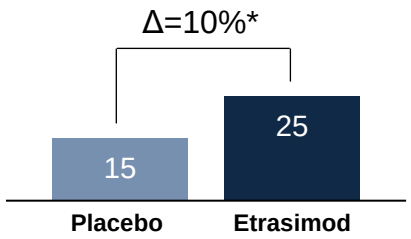
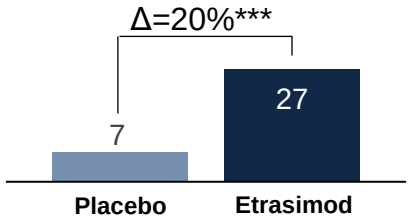
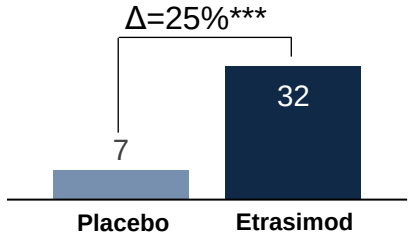
For illustrative purposes only; not a head-to-head comparison. Differences exist between trial designs and patient characteristics, and caution should be exercised when comparing data across trials. *$P<0.05$.
[a]Tofacitinib 10 mg BID. [b]Filgotinib 200 mg QD. [c]Upadacitinib 45 mg QD. [d]No prior biologic failure. [e]Prior TNF inhibitor treatment. [f]Prior TNF inhibitor and/or vedolizumab treatment. [g]Prior failure of TNF inhibitor, vedolizumab, or ustekinumab. Adv, advanced; JAK, Janus kinase; NA, not applicable; NR, not reported; TNF, tumor necrosis factor.
1. Sandborn WJ, et al. *N Engl J Med*. 2017;377(5):496-497. **2.** Feagan BG, et al. *Lancet.* 2021;397:2372-2384. **3.** Danese S, et al. *Lancet.* 2022;399:2113-2128.

S1PR Modulators Are Effective in Moderate to Severely Active UC

Primary Efficacy Endpoint: Clinical Remission

Proportion of patients, %	Induction Study	Maintenance Study[a]
TRUE NORTH program (ozanimod)[1,b] ***Design:*** *Re-randomization at maintenance*		

Induction: 10 weeks
Maintenance: 52 weeks

Proportion of patients, %	UC 12 Induction Study	ELEVATE UC 52 Induction and Maintenance[c] Study *(treat-through)*	
ELEVATE program (etrasimod)[2,d]			

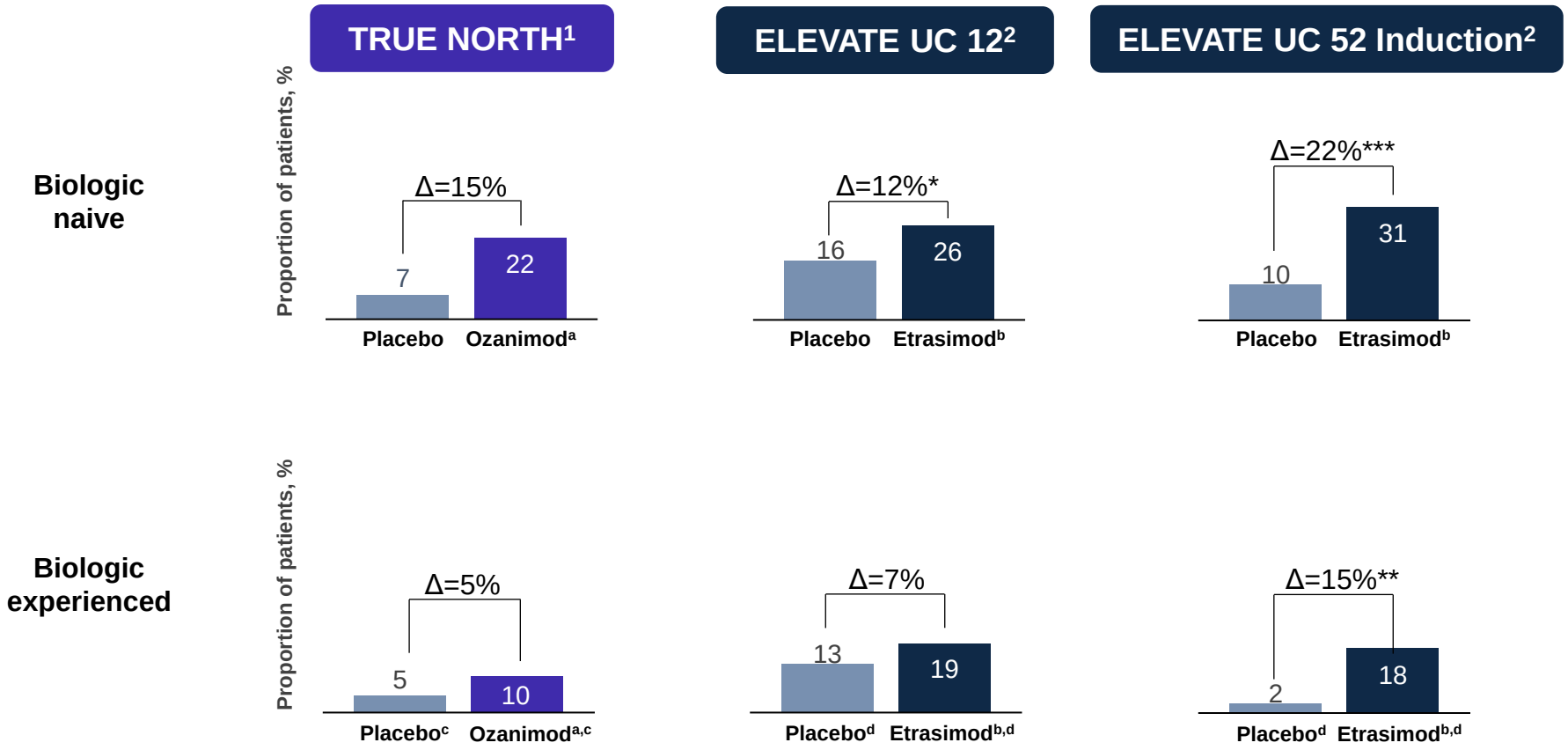
Induction: 12 weeks
Maintenance: 52 weeks

For illustrative purposes only; not a head-to-head comparison. Differences exist between trial designs and patient characteristics, and caution should be exercised when comparing data across trials. [a]Maintenance data shown here are among induction responders who entered the maintenance study. [b]Ozanimod 0.92 mg QD. [c]Maintenance data are among all patients randomized at baseline of induction. [d]Etrasimod 2 mg QD. *P<0.05. ***P<0.001. QD, once daily; S1PR, sphingosine-1-phosphate receptor; UC, ulcerative colitis.

1. Sandborn WJ, et al. *N Engl J Med*. 2021;385:1280-1291. **2.** Sandborn WJ, et al. *Lancet.* 2023;401:1159-1171.

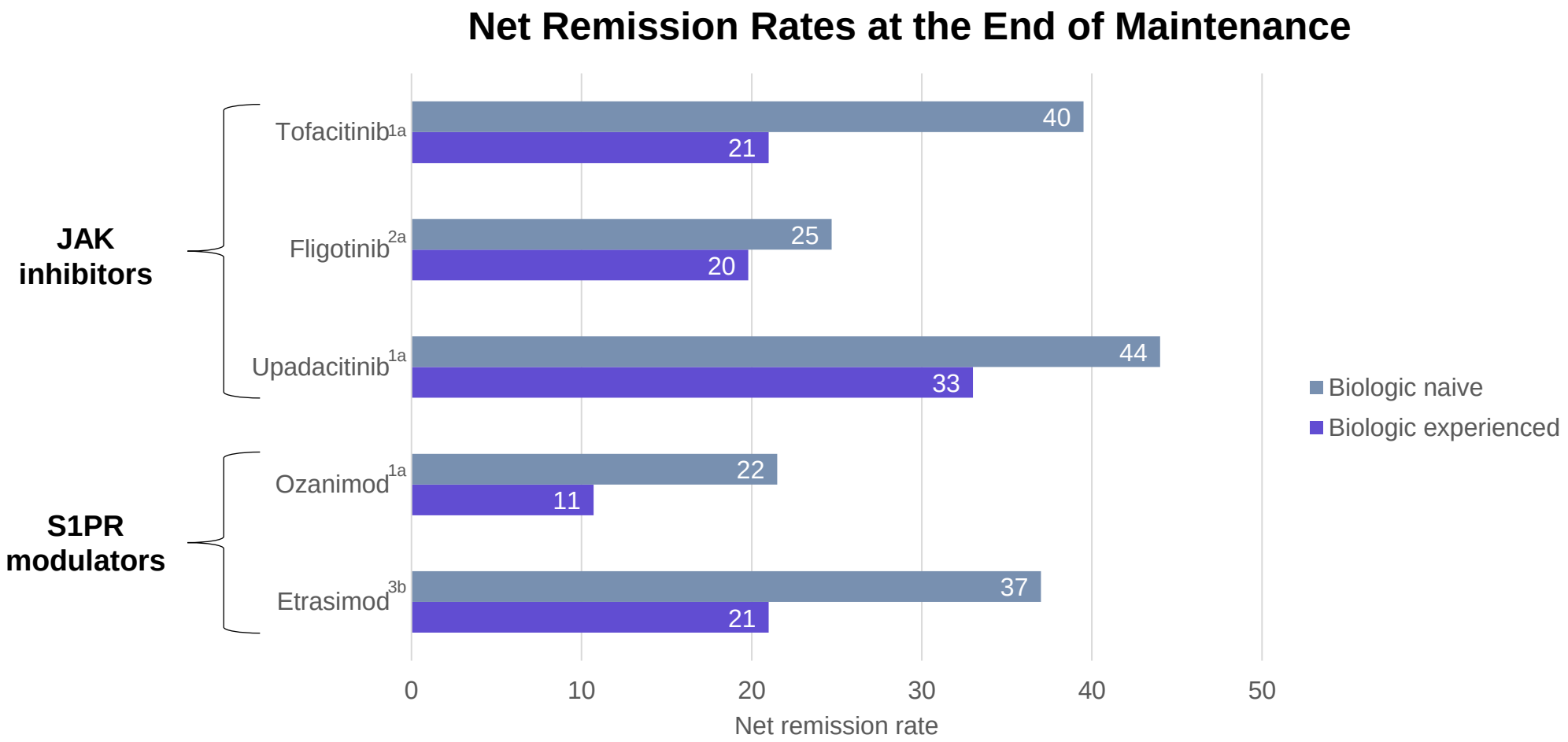
S1PR Modulators Are Effective in Biologic-Naive and Biologic-Experienced Patients

Clinical Remission at the End of Induction



For illustrative purposes only; not a head-to-head comparison. Differences exist between trial designs and patient characteristics, and caution should be exercised when comparing data across trials. [a]Ozanimod 0.92 mg QD. [b]Etrasimod 2 mg QD. [c]Prior TNF inhibitor use. [d]Prior exposure to biologics or JAK inhibitors. *P<0.05. **P<0.01. ***P<0.001. Adv, advanced; JAK, Janus kinase; S1PR, sphingosine-1-phosphate receptor; TNF, tumor necrosis factor; UC, ulcerative colitis. **1.** Sandborn WJ, et al. *N Engl J Med.* 2021;385:1280-1291. **2.** Vermeire S, et al. *J Crohns Colitis.* 2024:jjae079.

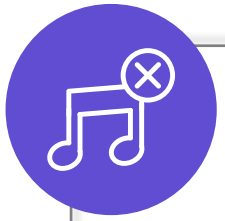
Therapeutic Ceilings, as Shown by Net Remission Rates With Available Oral Advanced Therapies, Suggest There Is Room for Improvement



[a]Net remission rate at the end of maintenance was calculated by multiplying the induction response rate by the maintenance remission rate for each study. [b]ELEVATE UC 52 utilized a treat-through design comprising a 12-week induction period followed by a 40-week maintenance period; patients did not have to have a clinical response to enter the maintenance period. JAK, Janus kinase; S1PR, sphingosine-1-phosphate receptor. **1.** Kayal M, et al. *Clin Gastroenterol Hepatol*. 2023;21:3433-3436. **2.** Feagan BG, et al. *Lancet.* 2021;397:2372-2384. **3.** Sandborn WJ, et al. *Lancet.* 2023;401:1159-1171.

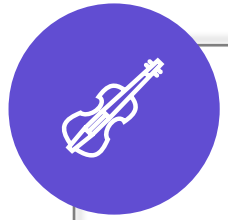
Many Factors May Influence Treatment Decisions and Determination of Patient Suitability for a Given Treatment

- Careful patient selection and informed discussions of risks and benefits of oral advanced therapies, including consulting experts as needed, are important[1-4]
- Treatment decisions may also be influenced by the need for pre-initiation testing and considerations for potential adverse events during therapy[1-4]



Patient Selection

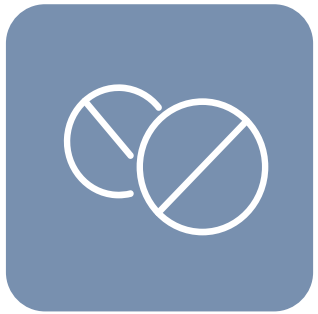
Pre-initiation Testing



Safety Monitoring

1. Jairath V, et al. *J Can Assoc Gastroenterol*. 2024;7(4):282-289. **2.** Honap S, et al. *Frontline Gastroenterol*. 2024;15:59-69. **3.** Sands BE, et al. *J Crohns Colitis.* 2023;17:2012-2025. **4.** Clinician's Guide to Using Ozanimod for the Treatment of Ulcerative Colitis. Available at: https://pfizermedical.pfizerpro.com/api/vc/en/medical/assets/cc5eb625-6170-40fc-876c-f80336b5df5f/Etrasimod%20Initiation%20Guide.pdf.

New Oral Therapies That Are Well Tolerated and Effective in a Broader Range of Patients Would Meet Several Critical Needs in UC



There is a need for more effective oral advanced therapies that work in **biologic-naive** and **biologic-experienced** patients

Oral therapies with fewer **pre-initiation requirements** and **simplified monitoring** procedures would be valuable

Patients with UC need oral therapies that promote long-term **disease control** and have a **well-tolerated safety profile**

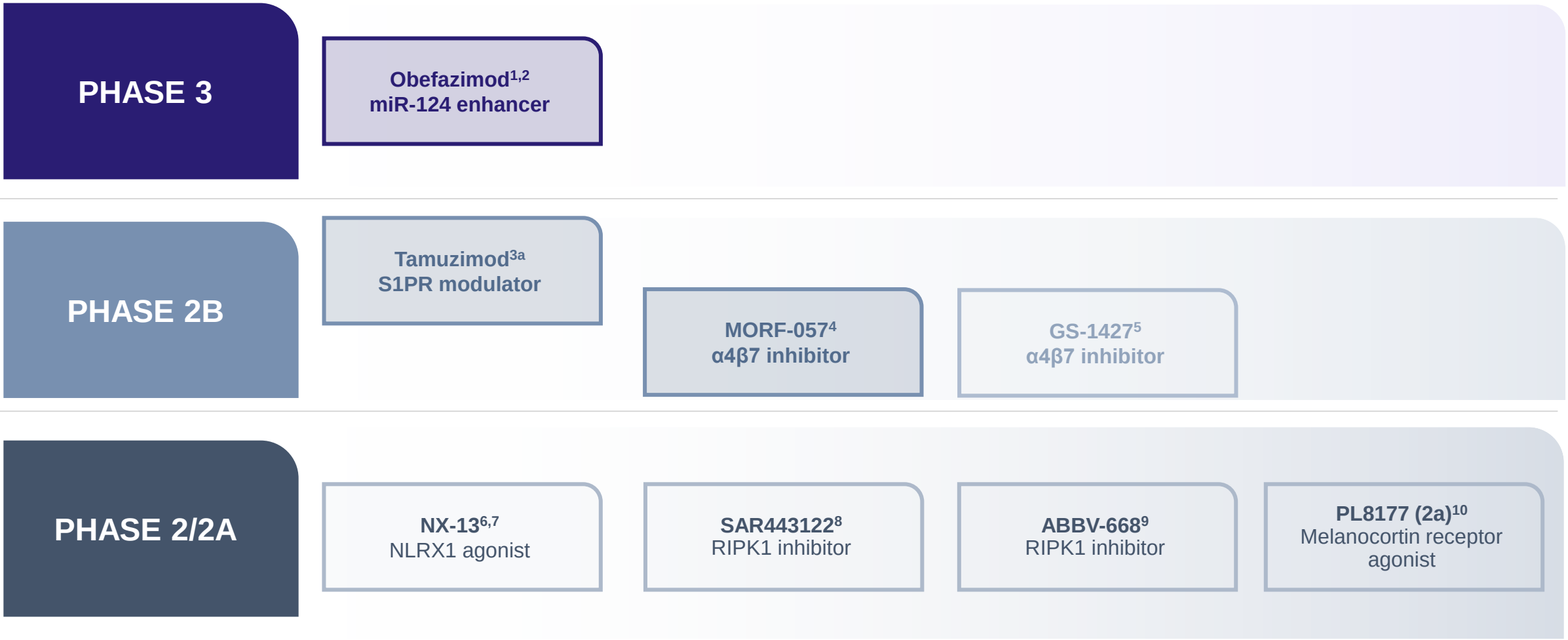
UC, ulcerative colitis.

Exploring New Oral Advanced Therapies for Ulcerative Colitis in the Pipeline

Séverine Vermeire, MD, PhD

KU Leuven, Leuven, Belgium

A Range of Oral Therapies With Novel MoAs Are in Development

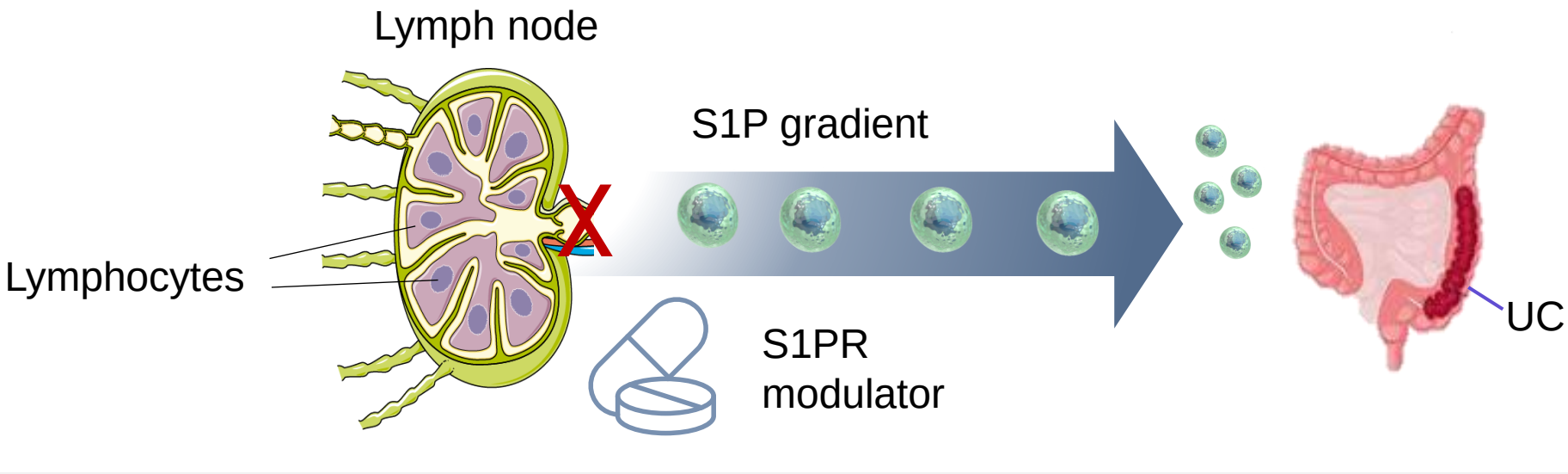


[a]Clinical data published in patients with ulcerative colitis. miR, microRNA; MoA, mechanism of action; NLRX1, nucleotide-binding oligomerization domain, leucine-rich repeat containing X1; RIPK1, receptor-interacting serine/threonine-protein kinase 1; S1PR, sphingosine-1-phosphate receptor.

1. Vermeire L, et al. *J Crohns Colitis*. 2023;17(10):1689-1697. **2.** NCT05507203. **3.** Sands BE, et al. ECCO 2024. Oral Presentation. **4.** NCT05611671. **5.** NCT06290934. **6.** Verstockt B, et al. *J Crohns Colitis*. 2024;18:762-772. **7.** NCT05785715. **8.** NCT05588843. **9.** NCT05570006. **10.** NCT05466890.

Tamuzimod Is a Novel Oral Selective S1PR Modulator

- S1PR modulators bind S1PRs on lymphocyte surfaces, leading to receptor internalization and sequestration of lymphocytes within lymph nodes
- Tamuzimod has selectivity for S1PR1 and is in development for the treatment of UC
  - Two S1PR modulators (ozanimod, etrasimod) have already been approved for the treatment of UC

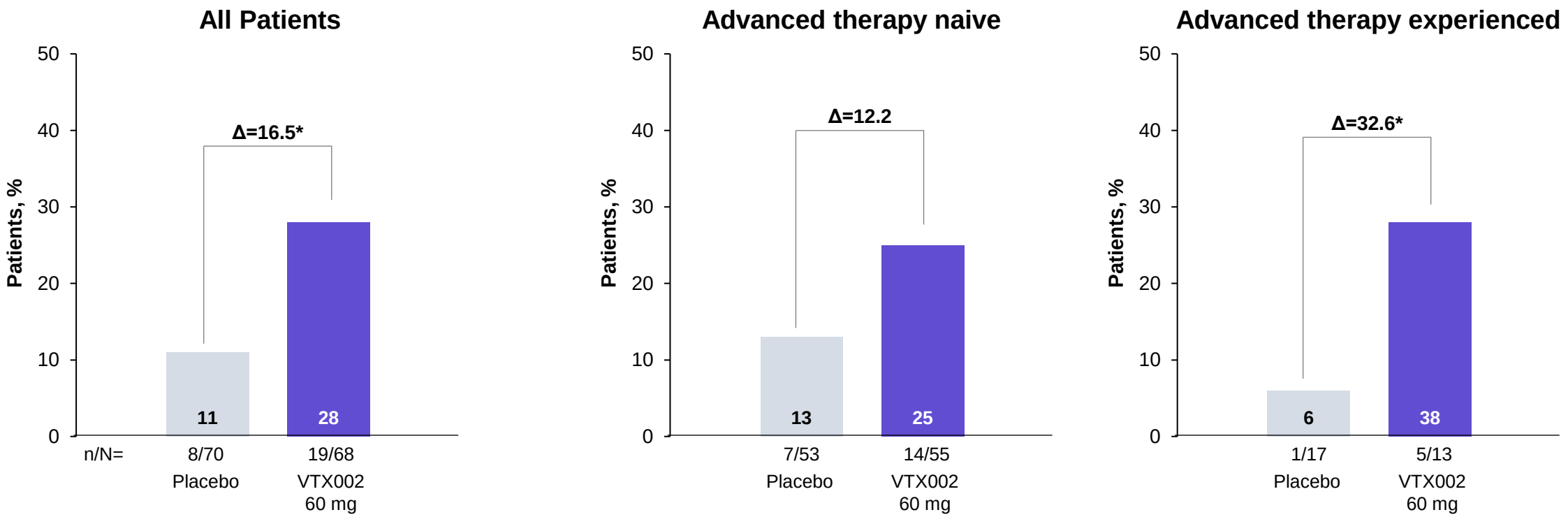


S1PR, sphingosine-1-phosphate receptor; UC, ulcerative colitis.
Sands BE, et al. ECCO 2024. Oral Presentation.

Tamuzimod: Results From a Phase 2 Randomized Double-Blind Study

Study Objective: To assess the efficacy and safety of tamuzimod (VTX002) in patients with UC

Clinical Remission at Week 13 (Primary Endpoint)



VTX002 was superior to placebo for induction of clinical remission at Week 13, which seemed to be driven by efficacy in advanced-therapy−experienced patients

*P<0.05. n/N, number of patients who acheived clinical remission divided by number of patients in group. Clinical remission defined as modified Mayo stool frequency subscore of ≤1, rectal bleeding subscore of 0, and endoscopic subscore of ≤1. UC, ulcerative colitis.

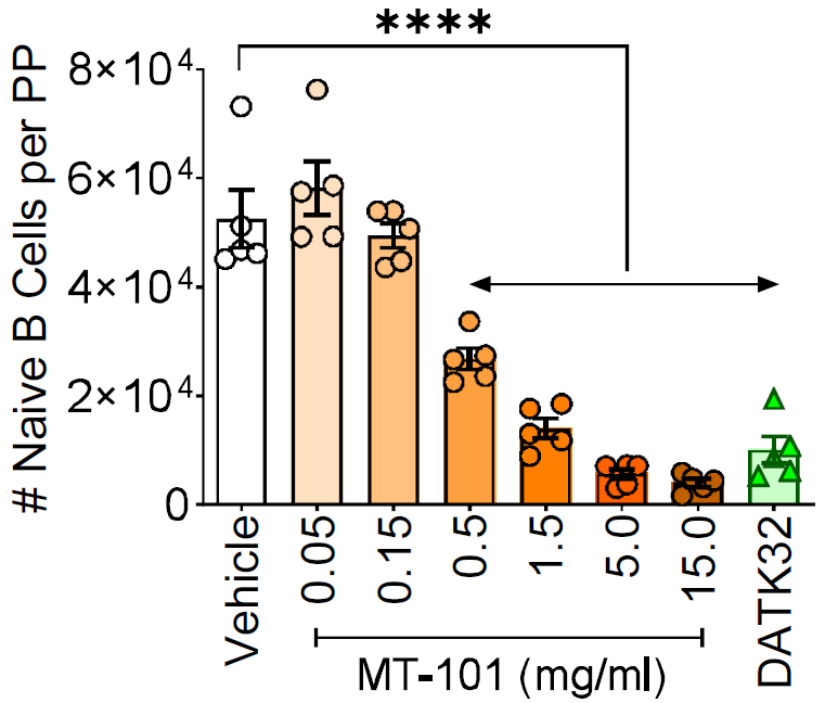
Sands BE, et al. ECCO 2024. Oral Presentation.

MORF-057 Selectively Inhibits Integrin α4β7

- Vedolizumab is an α4β7-targeting antibody (administered IV or SC) that is widely used and considered safe[1,2]; creating an orally administered molecule with the same target is of interest to drug developers

- In a mouse model, MORF-057 (MT-101)-related α4β7 blockade inhibited:
  - Lymphocyte trafficking to gut-associated lymphoid tissues and colonic lamina propria and attenuated gut secondary lymphoid tissue architecture[3]
  - Naive and T3 B lymphocyte trafficking to PPs and naive B, naive T, and CD4 Th lymphocytes in the colonic lamina propria[3]

Dose-Dependent α4β7 Inhibition by MORF-057 Potently Arrests Naive B Cell Trafficking to Mouse PPs[3]



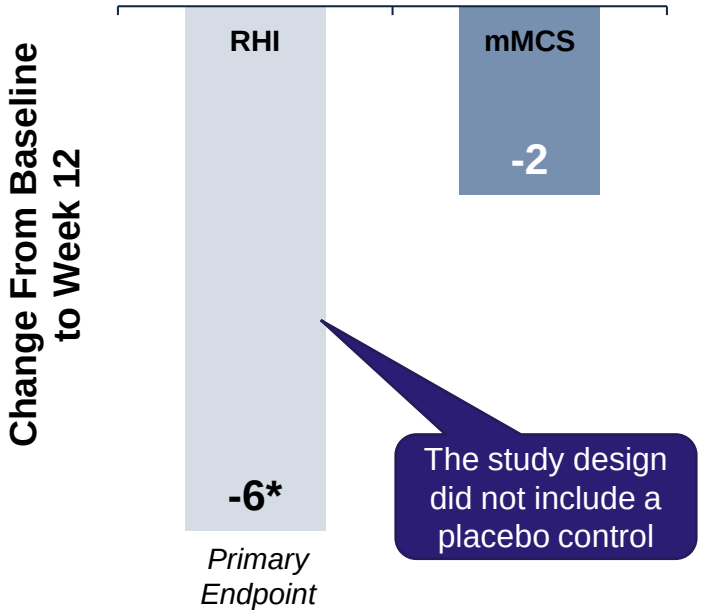
****P<0.0001. DATK32, anti-mouse α4β7-blocking antibody; IV, intravenous; PP, Peyer's patch; SC, subcutaneous; Th, T-helper cell.

1. Ashraf H, et al. *Cureus*. 2023;15(11):e48338. **2.** Entyvio [package insert]. Takeda, Inc. April 2024. **3.** Redhu NS, et al. DDW 2022. Poster Presentation.

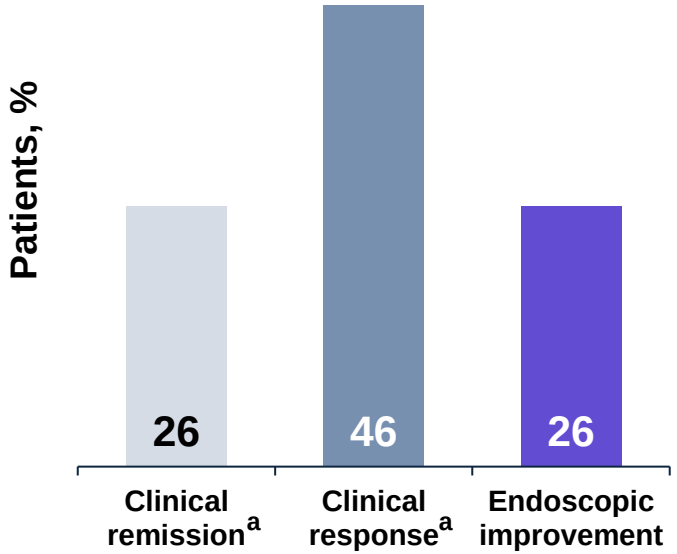
MORF-057: Results From the Phase 2a Open-Label 12-Week EMERALD-1 Study

Study Objective: To assess the safety, tolerability, pharmacokinetics, and efficacy of MORF-057 100 mg BID for induction treatment in adults with moderately to severely active UC

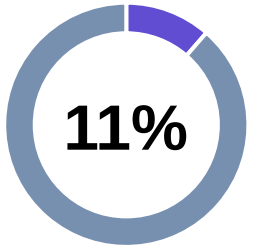
Change From Baseline to Week 12 in RHI and MMS



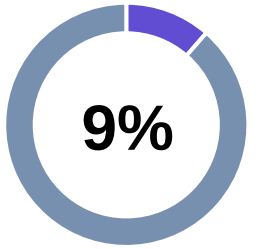
Secondary Efficacy Endpoints at Week 12



Safety Summary (Common TEAEs)



Exacerbation of UC was reported in 11% of patients

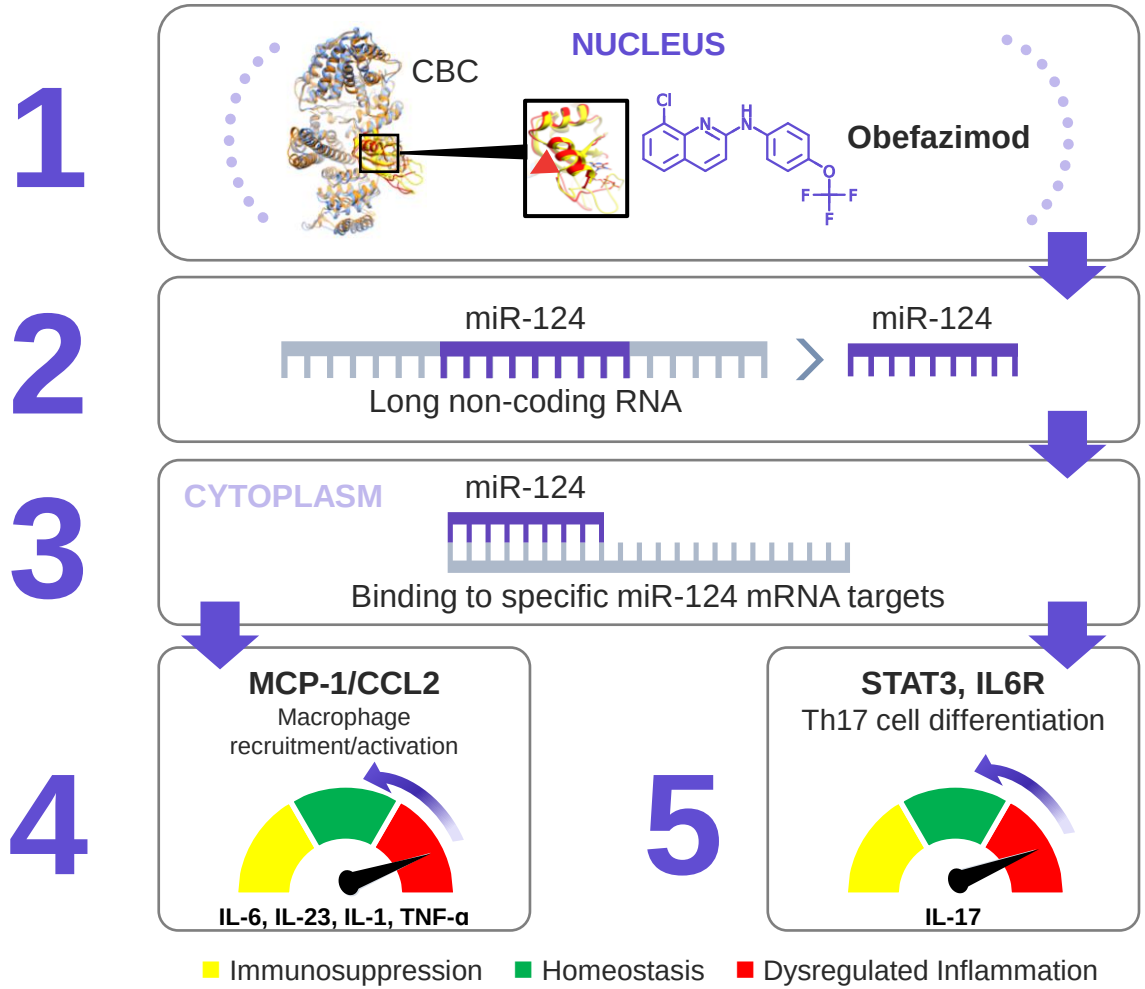


Anemia was reported in 9% of patients

*P<0.05 vs baseline. [a]Based on MMS. BID, twice daily; MMS, modified Mayo score; RHI, Robart's Histology Index; TEAE, treatment-emergent adverse event; UC, ulcerative colitis.

Sands BE, et al. *UEG J*. 2023;11(8):MP009.

Obefazimod Enhances Expression of miR-124, Resulting in Stabilization of the Dysregulated Inflammatory Response Present in UC[1-3]



1. Obefazimod binds to CBC within the nucleus (demonstrated by cryo-electron microscopy)[a]
2. Induces selective splicing of a single, long, non-coding RNA, leading to enhanced expression of miR-124
3. miR124 binds to its specific mRNA targets in the cytoplasm, reducing translation into their respective proteins
4. Reduced translation of MCP-1/CCL2 stabilizes macrophage activation and recruitment to the gut
5. Reduced translation of STAT3 and IL-6R stabilizes Th17 differentiation and related cytokines

[a]Cryo-electron microscopy is a technique for determining protein structure. CBC, cap binding complex; CCL2, C-C motif chemokine ligand 2; IL, interleukin; MCP-1, monocyte chemoattractant protein-1; miR, microRNA; R, receptor; STAT3, signal transducer and activator of transcription 3; Th, T-helper cell; TNF, tumor necrosis factor; UC, ulcerative colitis.

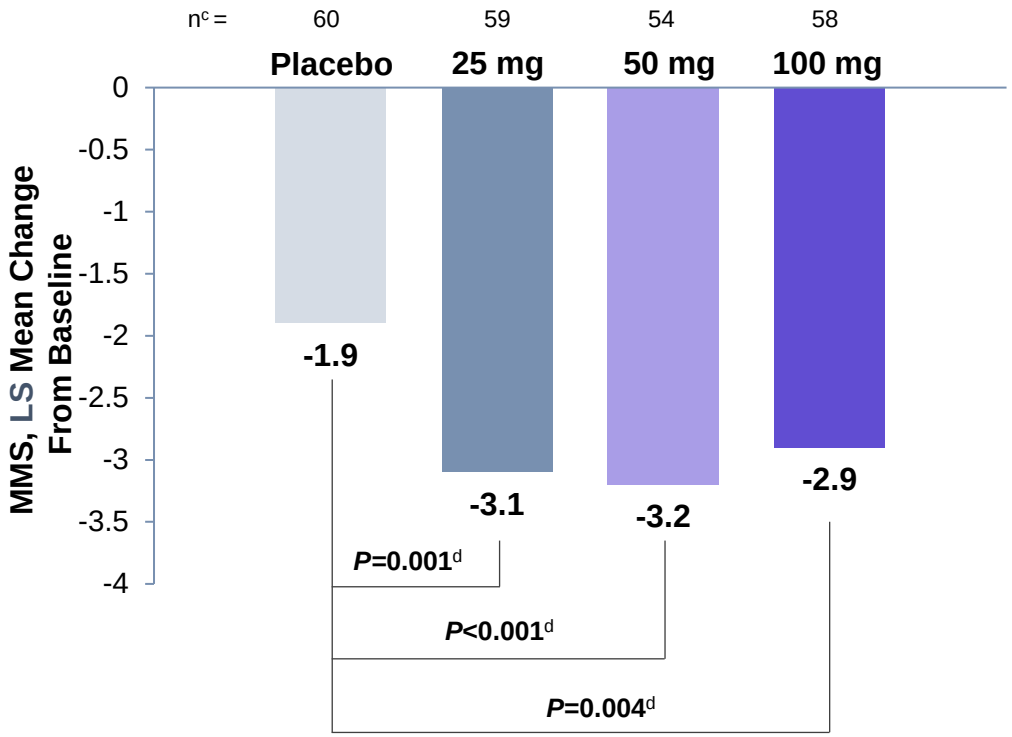
1. Vermeire S, et al. *Lancet Gastroenterol Hepatol*. 2022;7(11):1024-1034. **2.** Apolit C, et al. *Clin Transl Gastroenterol.* 2023;14:e00560. **3.** Data on file. Abivax.

Obefazimod: Results From a Phase 2 Randomized Double-Blind Study

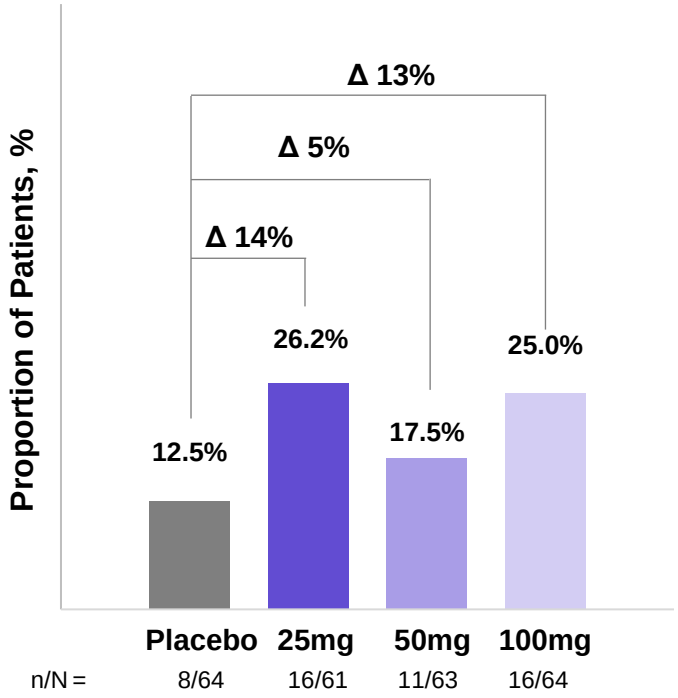
Statistically significant improvements were observed across all doses

- **49% of patients had prior advanced therapy use**
  - Among these patients, 93% had ≥2 prior advanced therapies

Change From Baseline[a] in MMS[b] at Week 8



Clinical Remission[e]



[a]ANCOVA model for change from baseline MMS at Week 8, which includes baseline MMS as a covariate, treatment and previous exposure to biological drugs or JAK inhibitors as fixed effects, and a random error term. [b]MMS is the sum of assessment scores (0−3) of mucosal appearance on endoscopy, stool frequency, and rectal bleeding. [c]n=number of patients in the category with data available for baseline and Week 8 visit. [d]*P* values are based on nonparametric ANCOVA using ranked data. [e]Clinical remission (per MMS) is defined as SFS of ≤1, RBS of 0, and endoscopic subscore of ≤1.

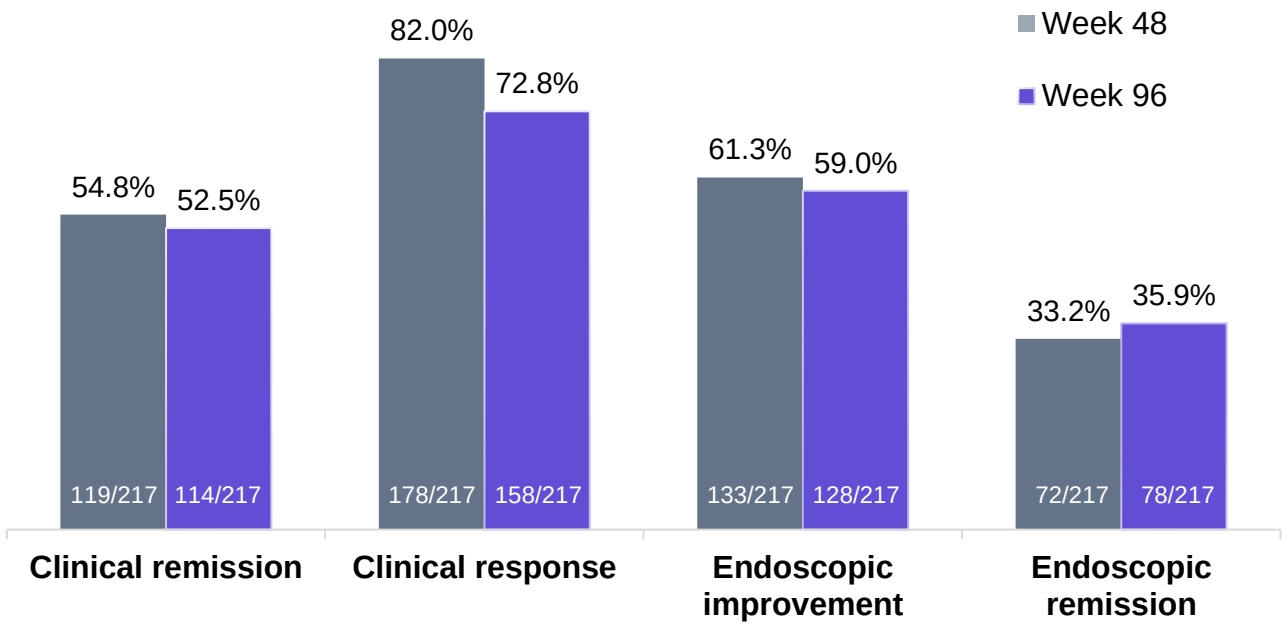
ANCOVA, analysis of covariance; JAK, Janus kinase; LS, least squares; MMS, modified Mayo score; RBC, rectal bleeding subscore; SFS, stool frequency subscore.

Vermeire S, et al. *Lancet Gastroenterol Hepatol*. 2022;7(11):1024-1034.

Obefazimod: Efficacy Results At Week 48 and Week 96

- Of 222 eligible patients, 217 entered the open-label maintenance study of obefazimod 50 mg QD[1]
  - 30 patients discontinued prior to Week 48[2]
  - 6 patients did not qualify for the second year of treatment (ie, were nonresponders)[2]
  - 17 patients discontinued between Weeks 48 and 96[2]
  - 164 patients completed the second year of treatment (cumulative dropout rate: 24%)[2]

Overall Efficacy Results at Weeks 48 and 96 (ITT analysis)[3]



All discontinuations were considered treatment failures for this analysis. Some discontinuations between Weeks 48 and 96 were a result of the Ukraine crisis.
ITT, intent-to-treat; QD, once daily.

1. Vermeire S, et al. *Lancet Gastroenterol Hepatol*. 2022;7(11):1024-1034. **2.** Data on file. Abivax. **3.** Vermeire S, et al. DDW 2024. Oral Presentation.

Obefazimod: Safety Summary

	Induction				Maintenance
	Placebo (n=64)	Obefazimod 25 mg (n=62)	Obefazimod 50 mg (n=63)	Obefazimod 100 mg (n=64)	Obefazimod 50 mg (N=217)
TEAEs Leading to Study Discontinuation	5 (7.8%)	4 (6.5%)	9 (14.3%)	8 (12.5%)	17 (7.8%)
Headache	5 (7.8%)	13 (21.0%)	19 (30.2%)	27 (42.2%)	25 (11.5)[a]
Discontinuation Due to Headache	0 (0%)	1 (1.6%)	3 (4.8%)	4 (6.3%)	1 (0.5%)
SAEs	4 (6.3%)	1 (1.6%)	4 (6.3%)	4 (6.3%)	18 (8.3%)
Serious Infections	0	0	1 (1.6%)	0	

Safety Summary

- TEAEs were reported in 58% of patients in the induction trial[1]
  - AEs reported in ≥5% of patients in any treatment group: headache, nausea, infections, UC
- In the maintenance study, 14% of subjects reported TEAEs[2]
  - The most common TEAEs up to 2 years: COVID-19, headache, UC, nasopharyngitis, back pain, and arthralgia
- The most common TEAE leading to study discontinuation was headache in induction and colitis ulcerative in maintenance[1,2]
- There was one malignancy reported (meningioma malignant) and no signal for serious infections[1,2,b]

Most headaches TEAEs[2]:

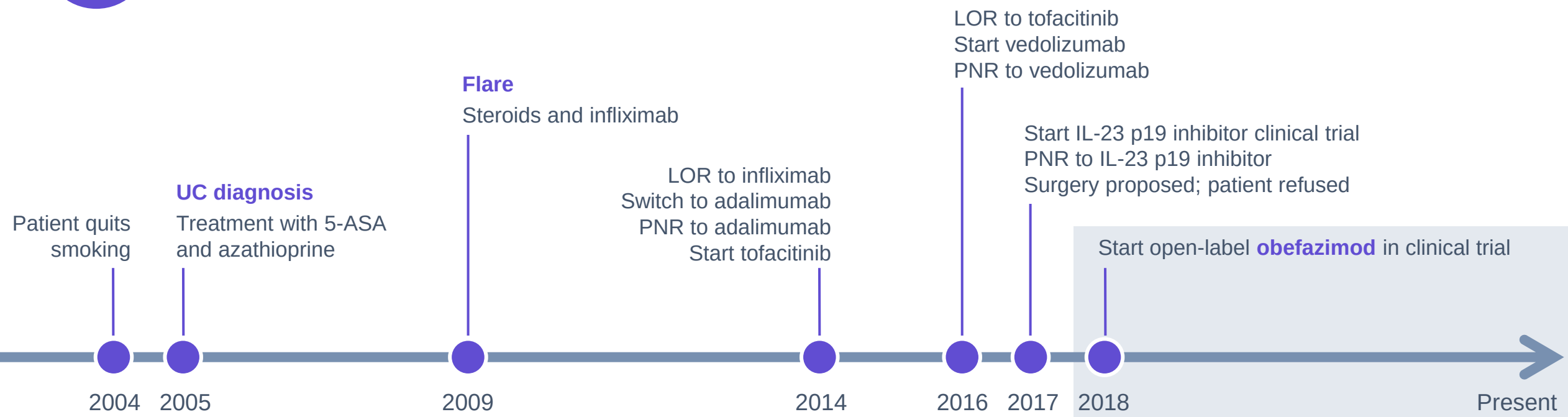
- Dose dependent
- Occurred at treatment initiation
- Resolved within 7 days and did not recur
- Mild to moderate in severity
- Managed with or without standard medications

[a]No headaches reported in second year of treatment. [b]One death was reported during the maintenance phase (car accident, not related to study treatment). SAE, serious adverse event; TEAE, treatment-emergent adverse event; UC, ulcerative colitis.

1. Vermeire S, et al. *Lancet Gastroenterol Hepatol*. 2022;7(11):1024-1034. **2.** Data on file. Abivax.

Patient With UC Treated With Obefazimod: Treatment Timeline

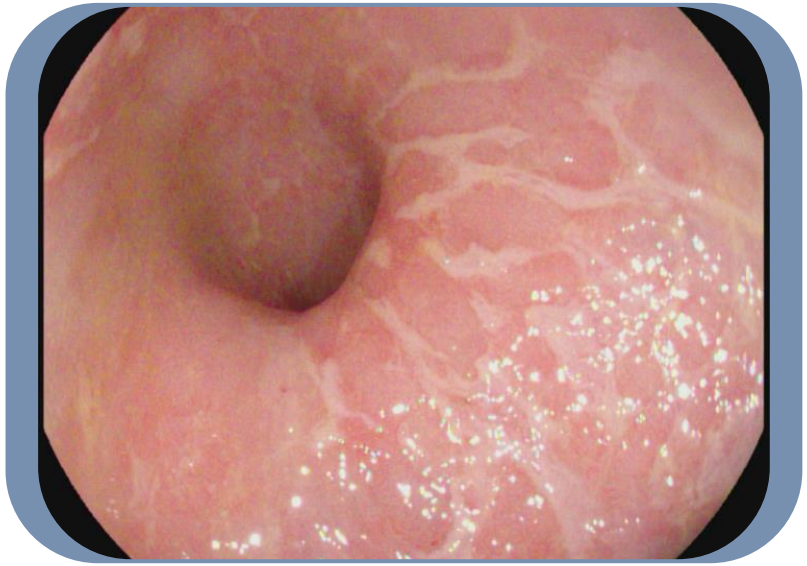
Male patient with UC born in 1965



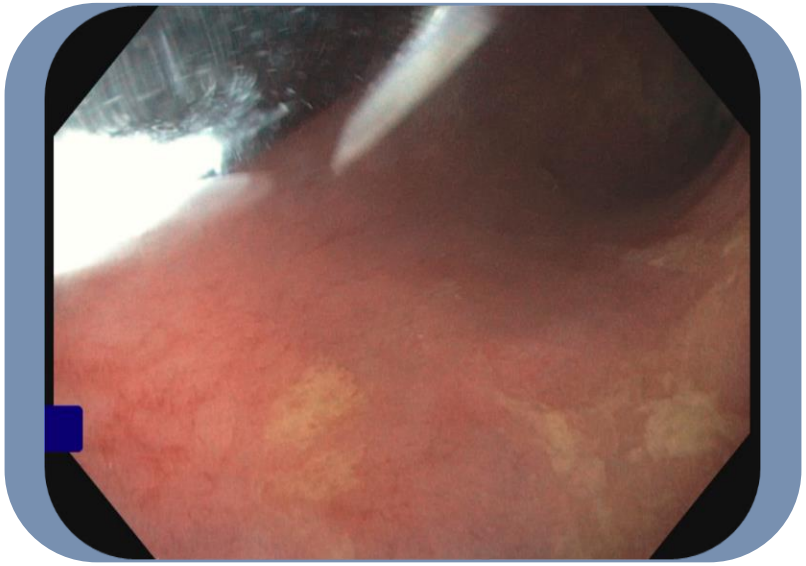
Evaluating clinical remission and endoscopic healing

5-ASA, 5-aminosalicylic acid; IL, interleukin; LOR, loss of response; PNR, primary nonresponse; UC, ulcerative colitis.

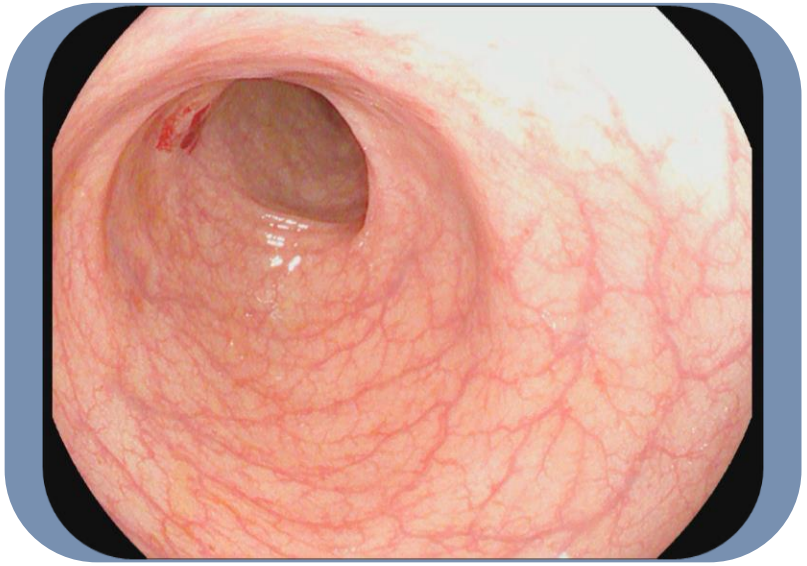
Patient With UC Treated With Obefazimod: Endoscopy Results



2017, Pre-obefazimod



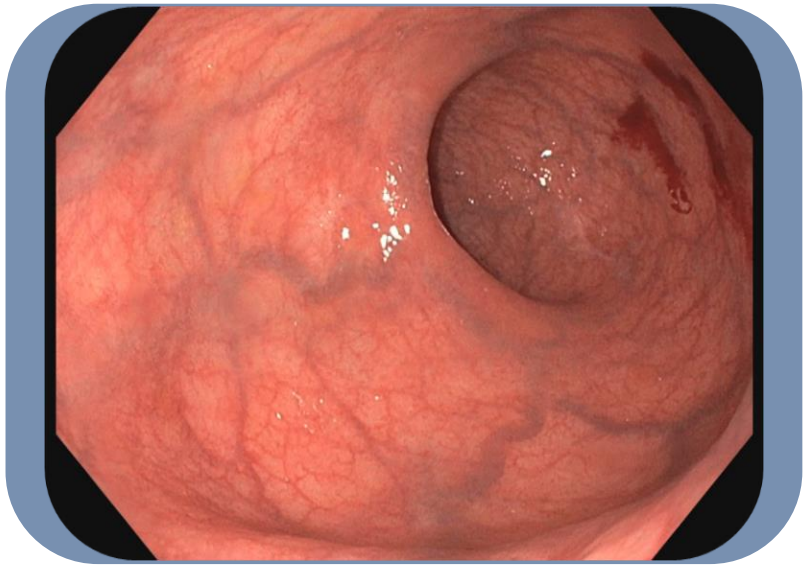
2018, 6 months



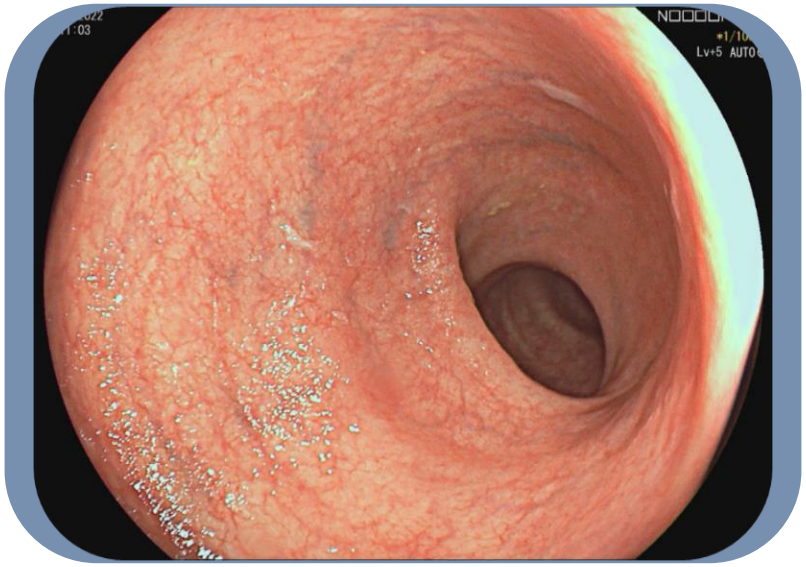
2020, ~1.5 years

Time on Obefazimod

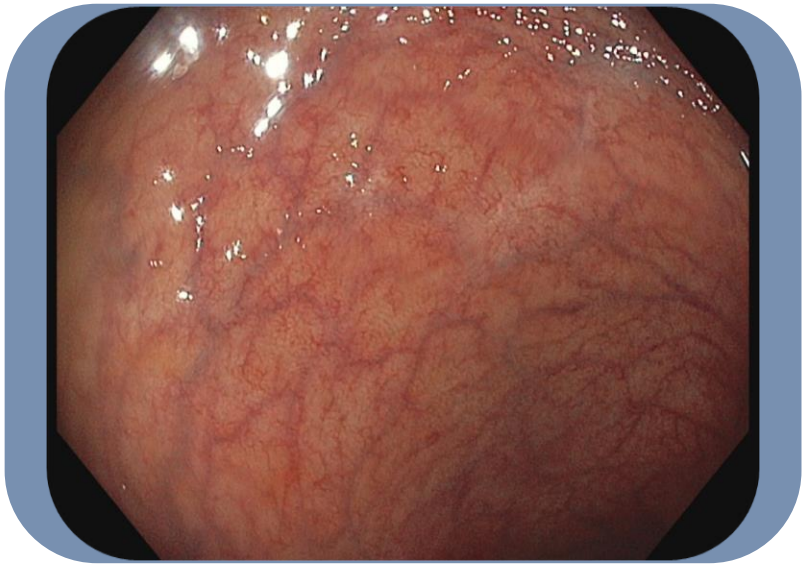
Patient With UC Treated With Obefazimod: Endoscopy and Safety Results



2021, ~2.5 years



2022, ~3.5 years

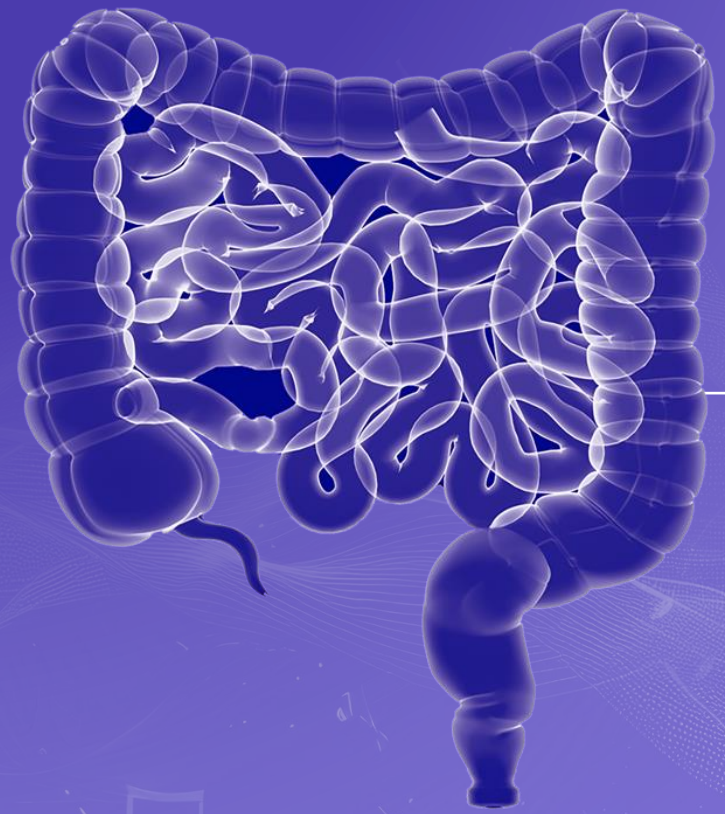


2023, ~5 years

Time on Obefazimod

During treatment with obefazimod, all adverse events were mild or moderate; none were considered related to treatment

Adverse event	Severity	Relatedness to treatment
Gastroesophageal reflux disease	Moderate	Not related
Concentric remodeling heart	Mild	Not related
Rosuvastatin intolerance	Moderate	Not related
Diabetes mellitus	Moderate	Not related
Obstructive sleep apnea syndrome	Moderate	Not related
Upper respiratory tract infection	Moderate	Not related



Conclusions

Conclusions

The number of oral advanced therapies for UC has increased in the past 10 years[1-5]

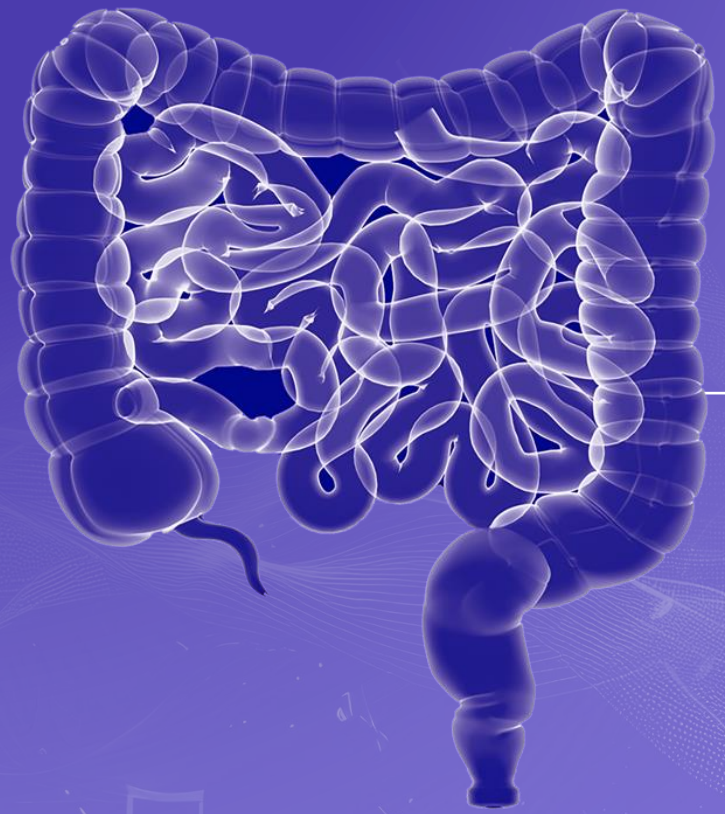
Although these new therapies have brought benefits to patients, unmet needs remain [6-7]

Novel advanced oral therapies such as tamuzimod, MORF-057, and obefazimod have shown encouraging results in clinical studies to date[8-10]

These emerging new therapies may strengthen the armamentarium for UC

UC, ulcerative colitis.

1. Pfizer. Press release. August 1, 2018. **2.** EPAR. Jyseleca. **3.** BMS. Press release. November 23, 2021. **4.** AbbVie. Press release. July 26, 2022. **5.** Pfizer. Press release. February 19, 2024. **6.** Imbrizi M, et al. *Pharmaceuticals (Basel).* 2023;16(9):1272. **7.** Jairath V, et al. *J Can Assoc Gastroenterol*. 2024;7(4):282-289. **8.** Sands BE, et al. ECCO 2024. Oral Presentation. **9.** Sands BE, et al. *UEG J*. 2023;11(8):MP009. **10.** Vermeire S, et al. *J Crohns Colitis.* 2023;17(10):1689-1697.



Questions?

Thank you!

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