Visualizing the Future

Advances in IL-23-Targeted Therapies in the Treatment of IBD

This activity is supported by an educational grant from Janssen Biotech, Inc., administered by Janssen Scientific Affairs, LLC.- both are Johnson & Johnson companies.

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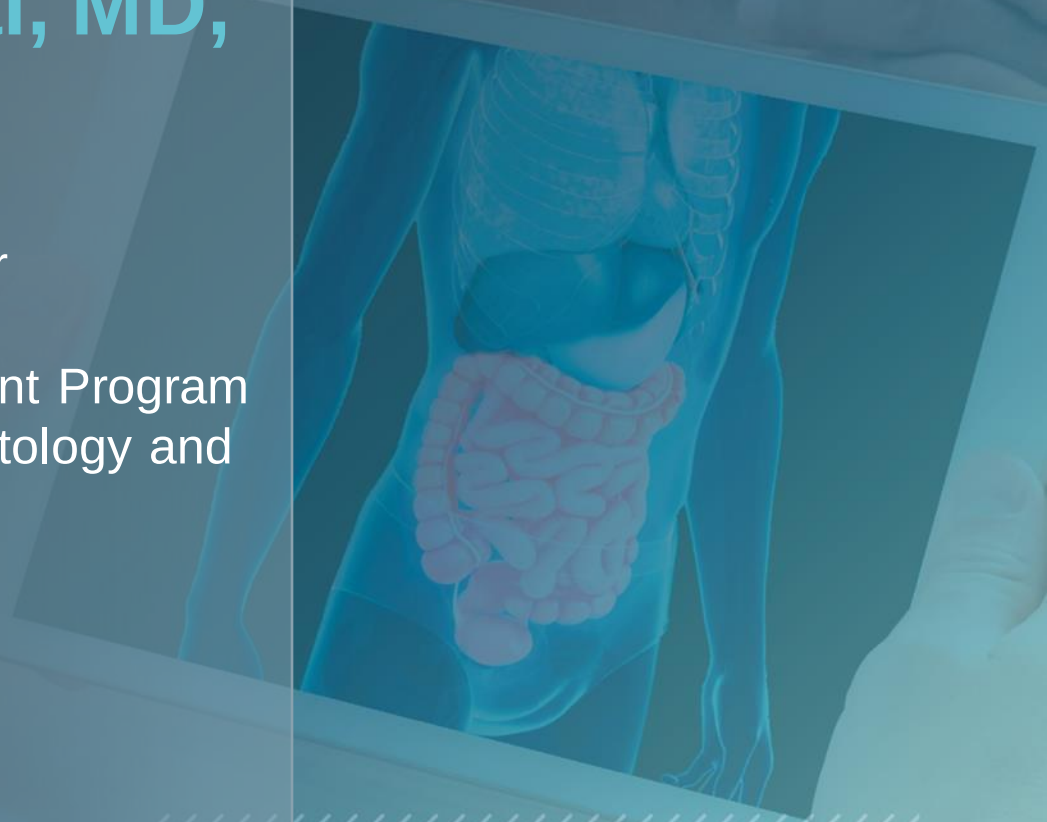

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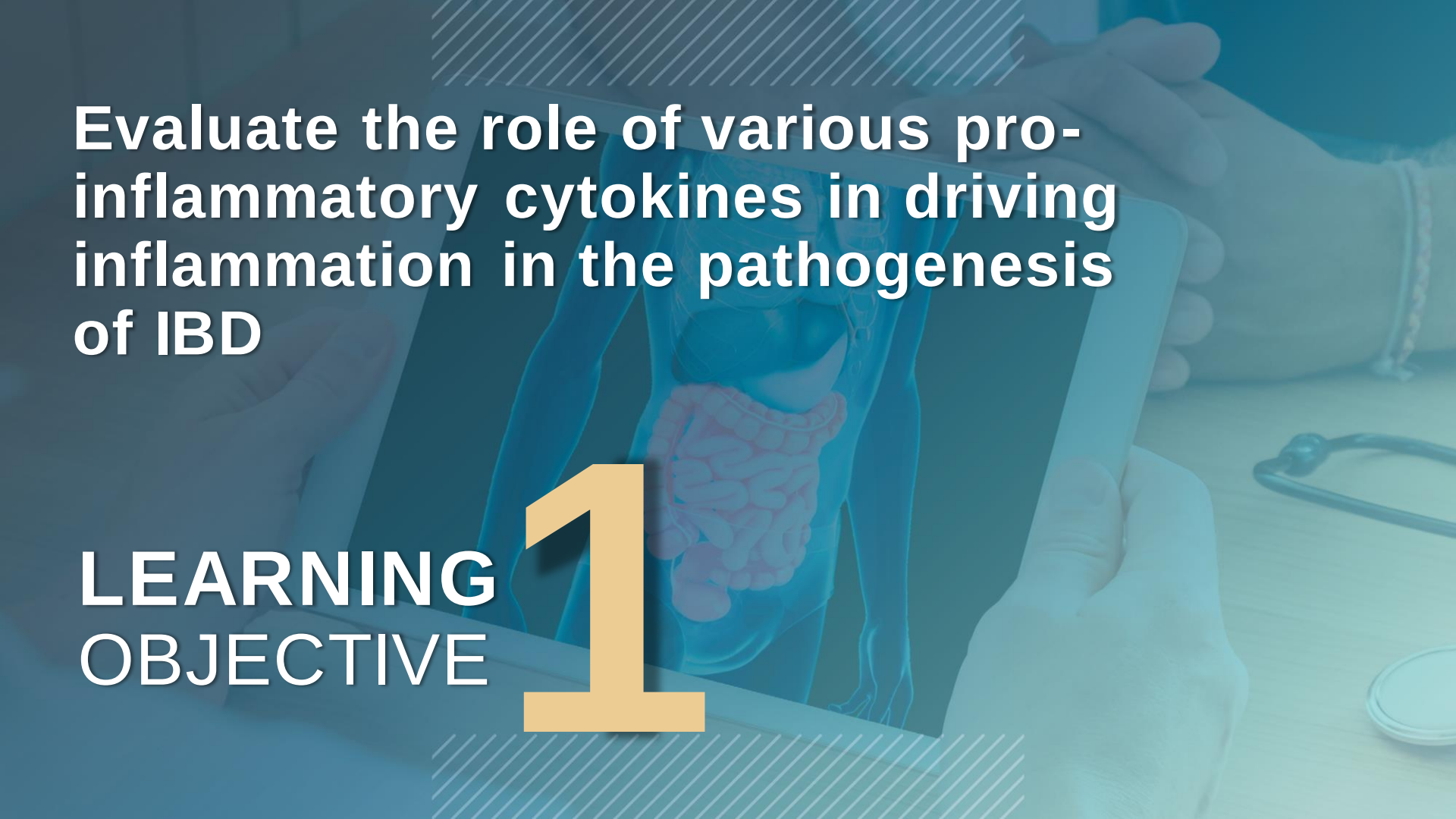
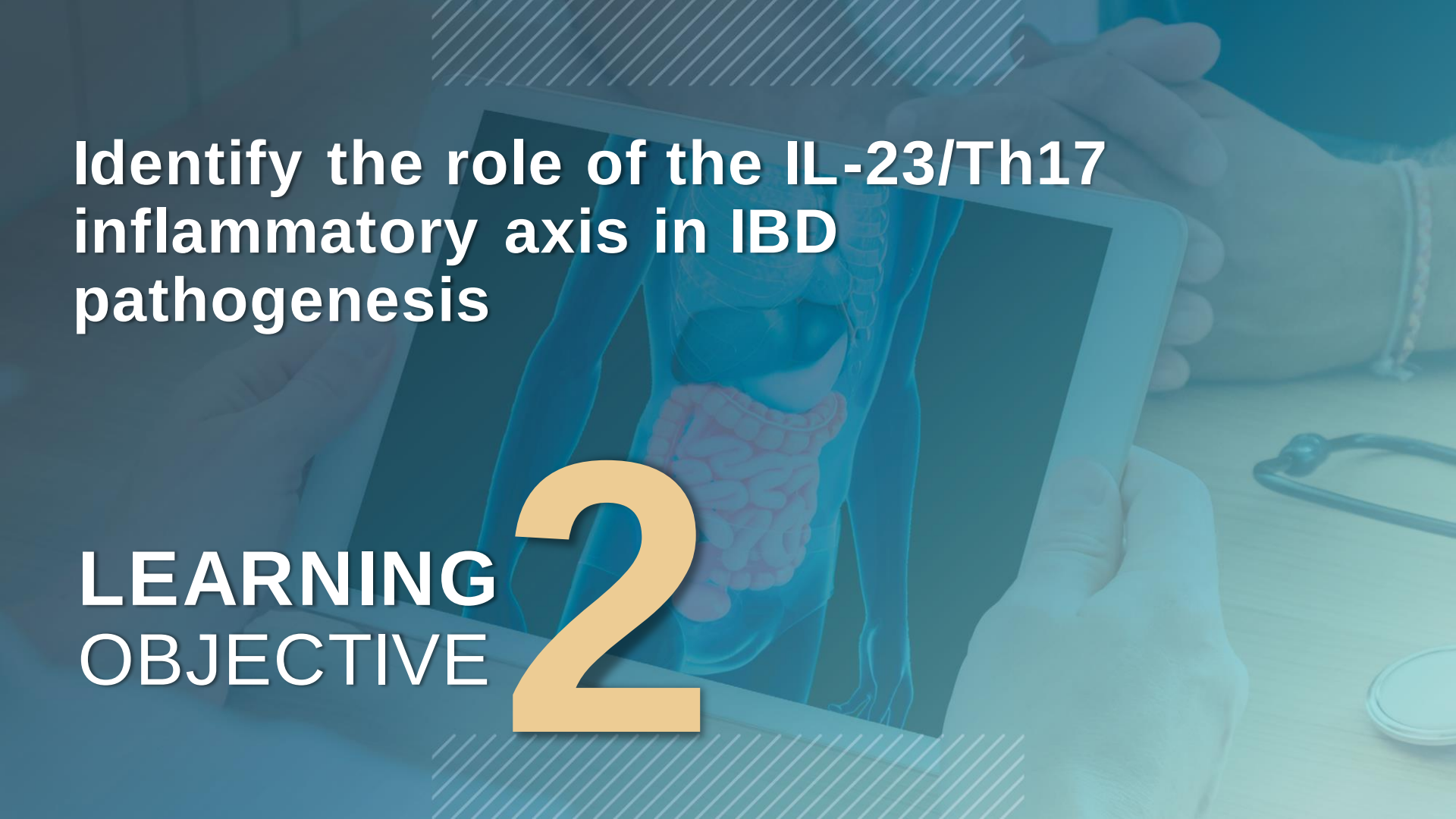


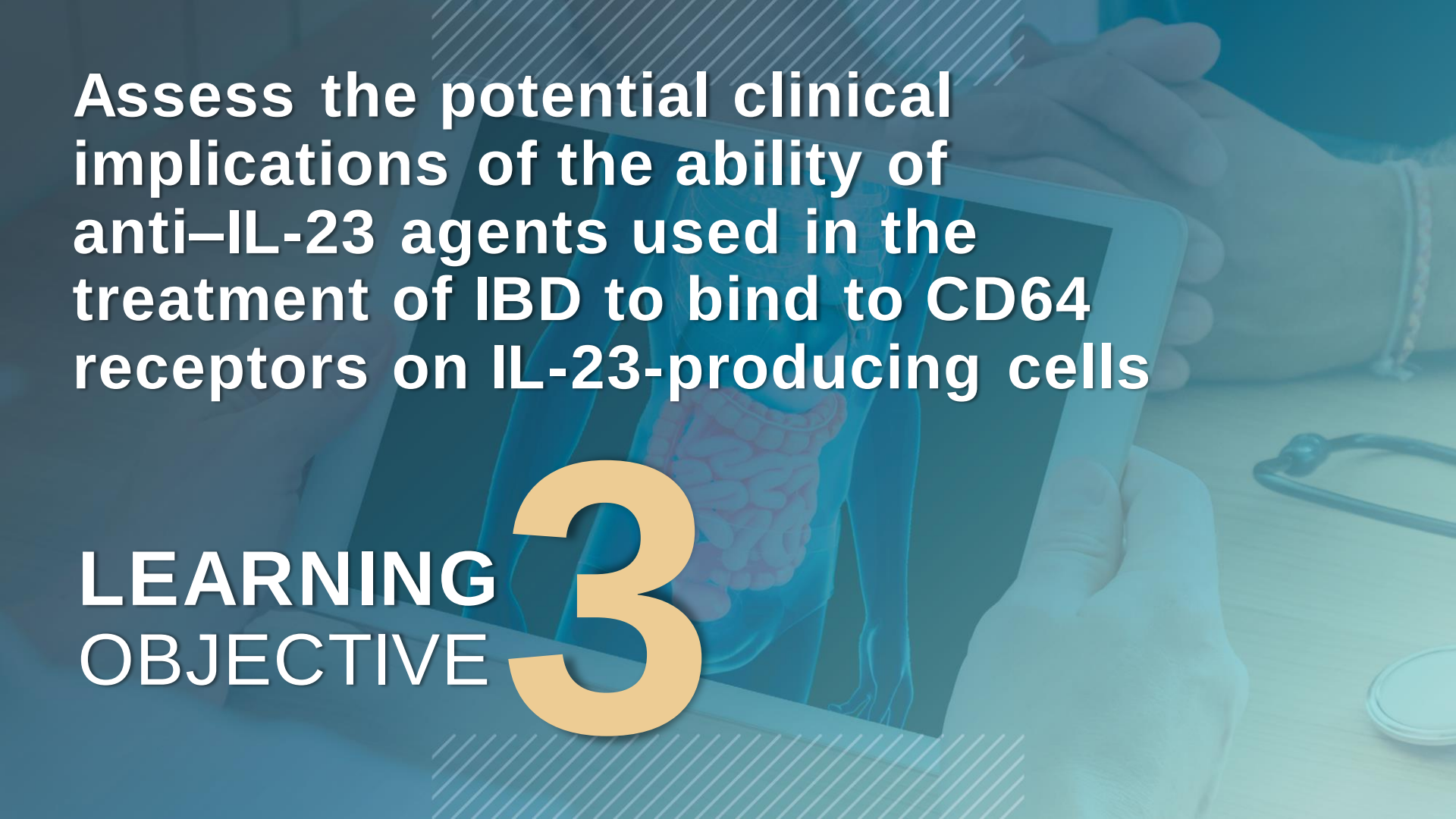
Evaluate the role of various pro-inflammatory cytokines in driving inflammation in the pathogenesis of IBD

LEARNING OBJECTIVE 1



Identify the role of the IL-23/Th17 inflammatory axis in IBD pathogenesis

LEARNING OBJECTIVE 2



Assess the potential clinical implications of the ability of anti–IL-23 agents used in the treatment of IBD to bind to CD64 receptors on IL-23-producing cells

LEARNING OBJECTIVE 3

Audience Response - Icebreaker

What is the most difficult aspect of patient care for IBD? (pick your top 3)

A. Knowledge of drugs
B. Prior authorizations
C. Drug positioning
D. Loss of response
E. Lack of time with patients
F. Staffing challenges

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What is the most difficult aspect of patient care for IBD?

Faculty Icebreaker

Section 1

Overview of the IL-23/Th17 Pathway in the Pathogenesis of IBD

Jessica R. Allegretti, MD, MPH, FACG, AGAF

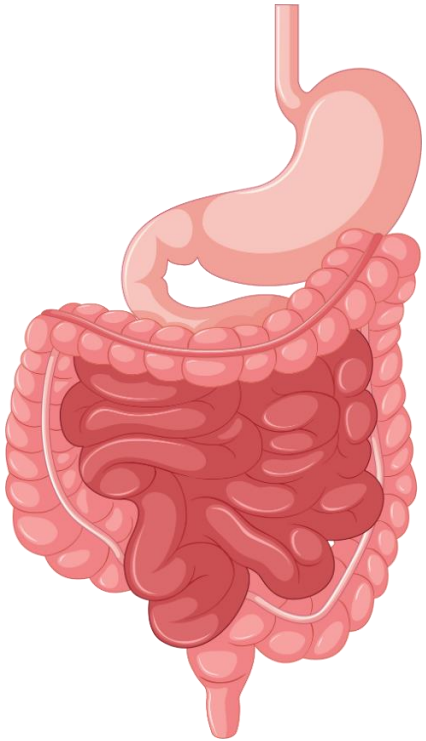
IBD Pathogenesis

Genetics

- IGRM
- NOD_2
- IL23R
- ATG16L1
- LRRK2
- IBD5
- others

Environment

- Diet
- Lifestyle
- Smoking
- Stress
- Drugs
- Antibiotics
- Infection
- Latitude
- Others



Immunology

- Immune dysregulation
- Impaired epithelial barrier function
- Defective autophagy
- Skewed lymphocyte populations
- Altered cytokine production

Gut Microbiome

- ↑ Enterobacteriaceae
- ↑ Pasteurellaceae
- ↑ Veillonellaceae
- ↑ Fusobacteriaceae
- ↓ Erysipelotrichales
- ↓ Bacteroidetes
- ↓ Clostridioides

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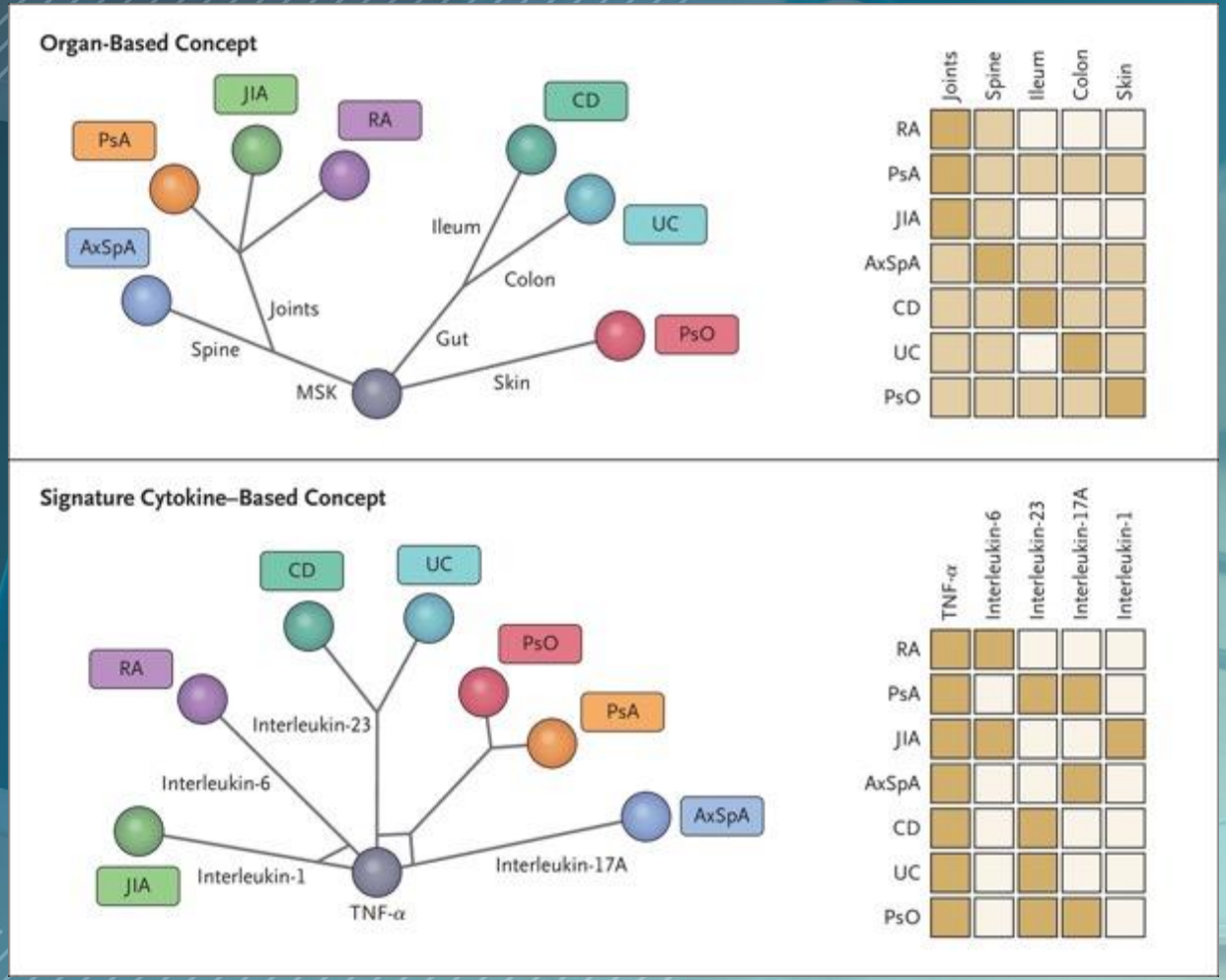
Oliveira SB, et al. *BMJ*. 2017;357:j2083. https://www.bmj.com/content/357/bmj.j2083.

Cytokine Connections in Immune-Mediated Inflammatory Diseases



Schett G, et al. *N Engl J Med*, 2021 Aug 12;385(7):628-639.

Why Target IL-23 in IBD?

- Inhibition of IL-23 decreases mucosal inflammation and improves epithelial barrier integrity
- Inhibiting IL-23 suppresses gut inflammation in T-cell-mediated colitis
- Anti-IL-23 therapy preserves protective IL-17 gut functions
  - Animal models of IL-17 blockade in colitis had mixed results
  - Trials of anti-IL-17A/IL-17A receptor antagonists in IBD resulted in worse outcomes vs placebo

Hohenberger M, et al. *J Dermatolog Treat.* 2018;29(1):13-18. Vuyuru SK, et al. *Drugs.* 2023;83(10)873-891. Wallace KL, et al. *World J. Gastroenterol.* 2014;20(1):6-21.

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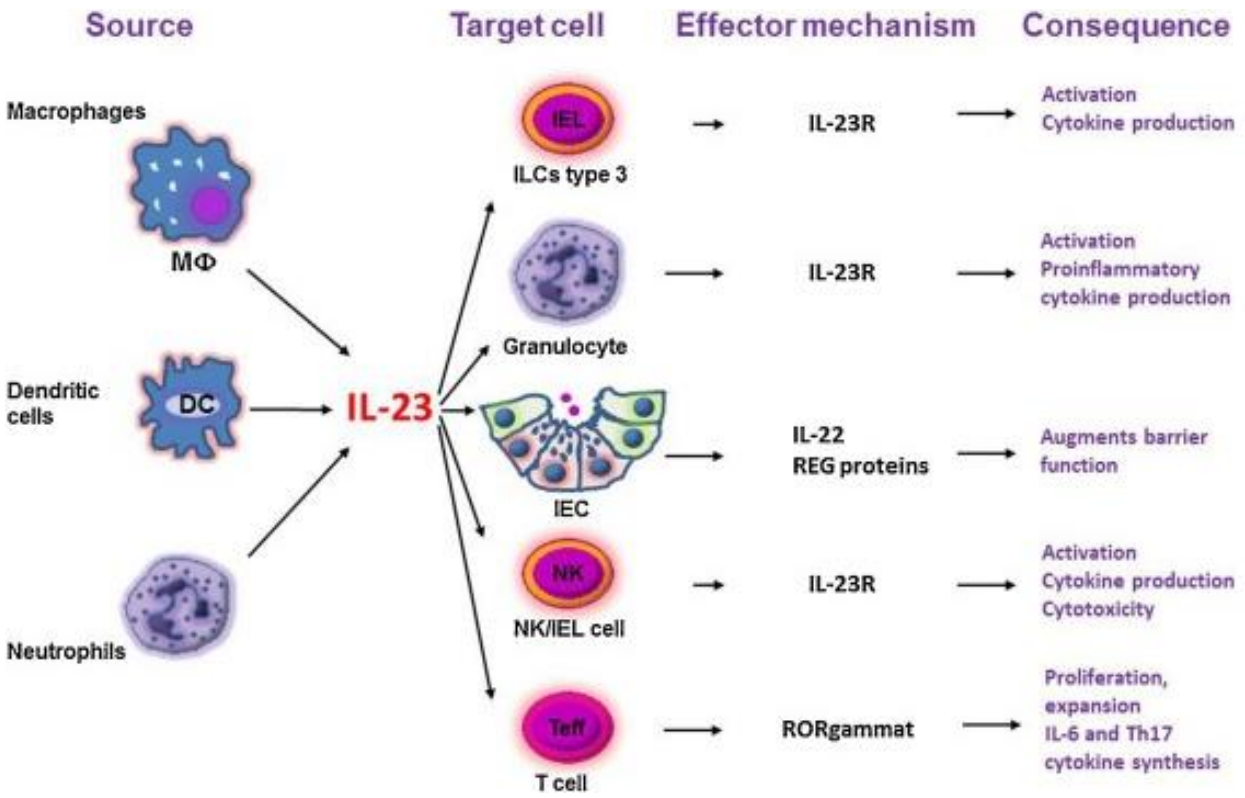
Sources of IL-23 in IBD



Neurath MF. *Cytokine Growth Factor Rev.* 2019;45:1-8.

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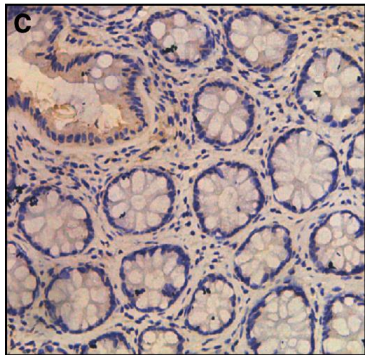
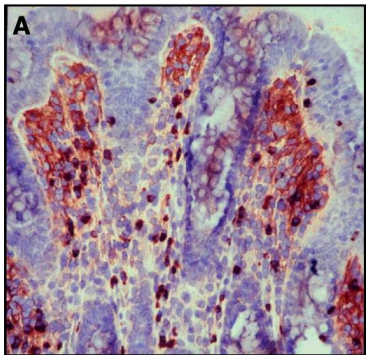
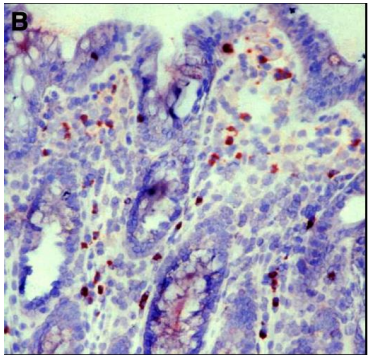
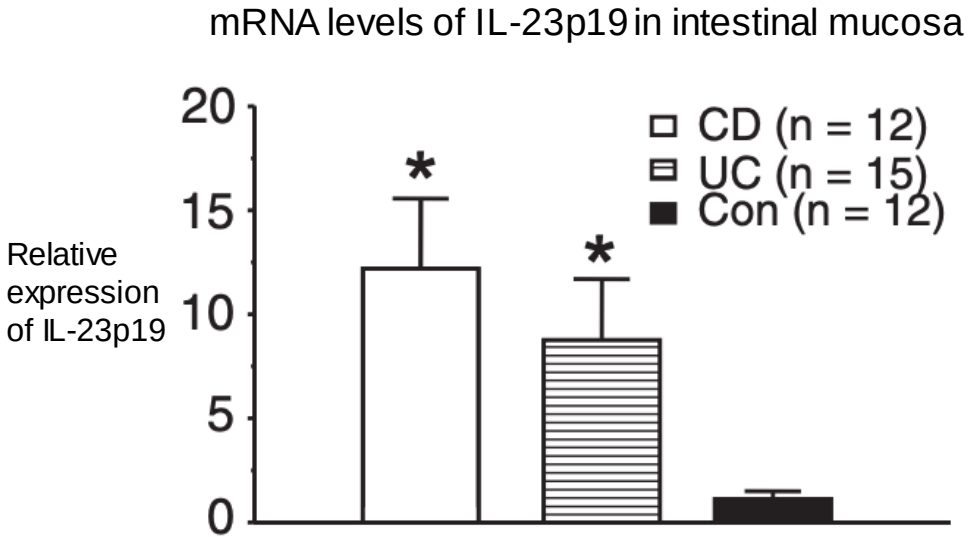
IL-23p19 is Highly Expressed in Inflamed Mucosa of IBD









*P < 0.05 versus control; Con = control

Liu Z, et al. *J Leukoc Biol*. 2011;89(4):597-606.

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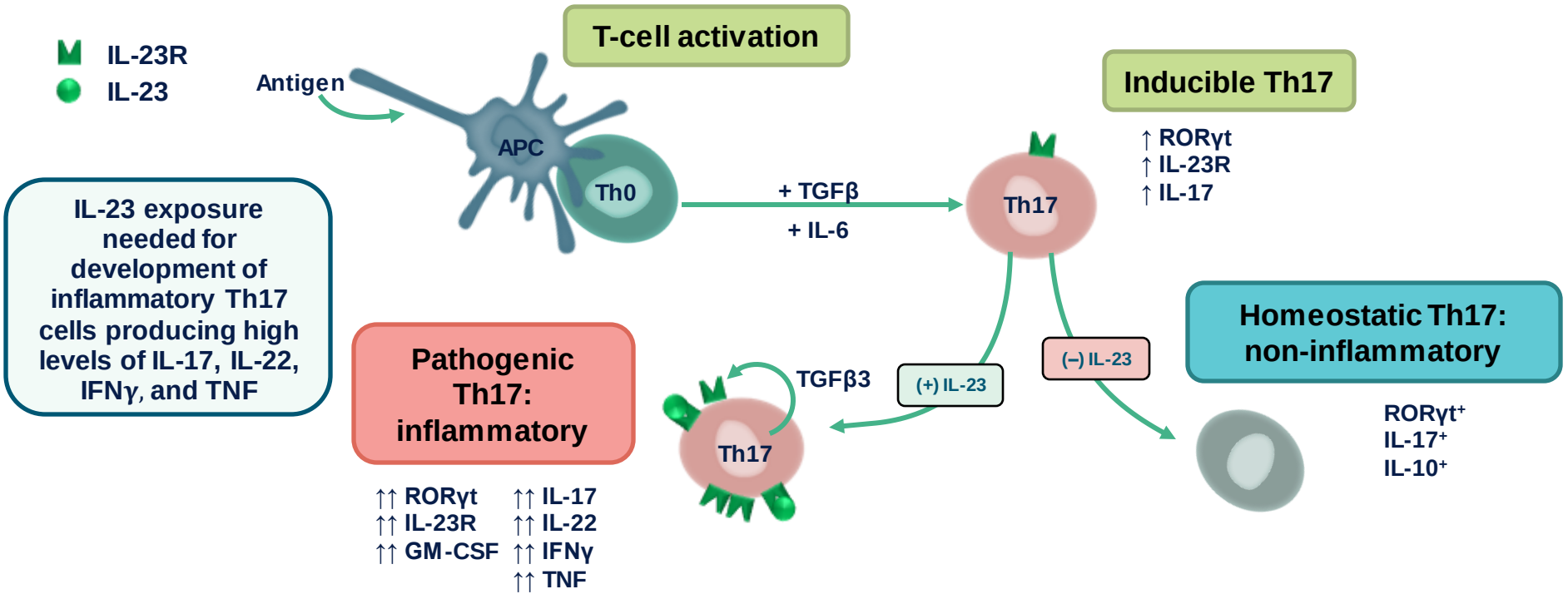
IL-23 Drives Development of Inflammatory Pathogenic Th17 Cells



APC = antigen-presenting cell; GM-CSF = granulocyte-macrophage colony-stimulating factor; IFN = interferon; RORγt = retinoic acid receptor-related orphan receptor γt; TGF = transforming growth factor.

Adapted from Zúñiga LA, et al. *Immunol Rev.* 2013;252(1):78–88. Gaffen SL, et al. *Nat Rev Immunol.* 2014;14(9):585–600. Schmitt H, et al. *Front Immunol.* 2021;12:622934.

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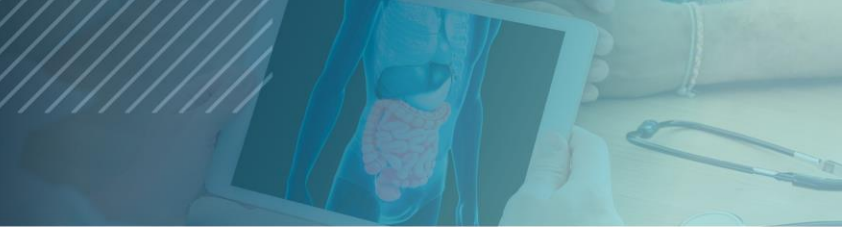
Audience Response



Which of the following is a potential cause of anti-TNF non-response in patients with IBD?

A. Drug interactions between anti-TNF agents and immunomodulators

B. Heightened production of IL-23 and development of apoptosis resistant T-cells

C. Down regulation of TNF-α receptors on monocytes

D. I don’t know

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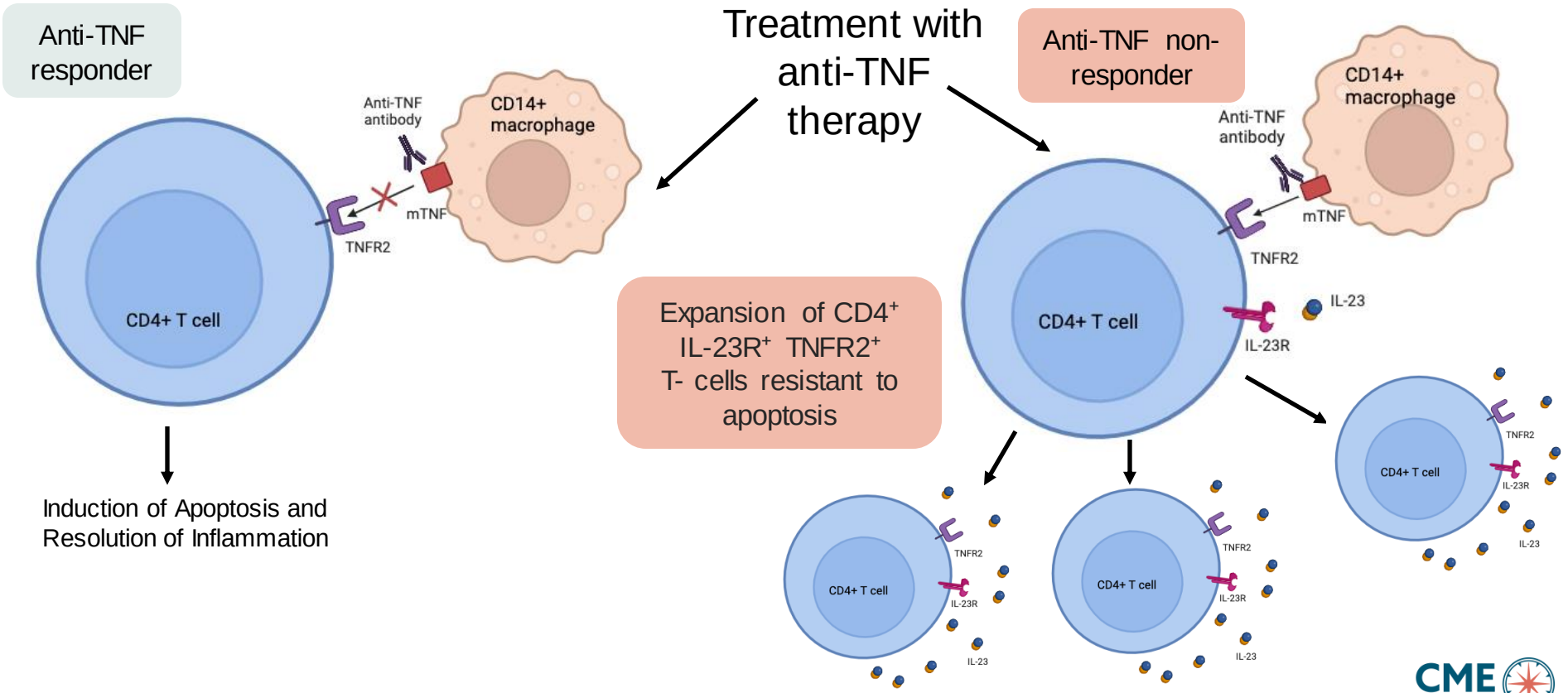
IL-23 Mediated Resistance to Anti-TNF



Adapted from Schmitt H, et al. *Semin Immunopathol*. 2019 Nov;41(6):737-746. Schmitt H, et al. *Gut*. 2019;68(5):814-828.

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Audience Response

Which of the following is a potential cause of anti-TNF non-response in patients with IBD?

A. Drug interactions between anti-TNF agents and immunomodulators

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C. Down regulation of TNF-α receptors on monocytes

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Final Thoughts:
Cytokines and Pathogenesis

Faculty Discussion

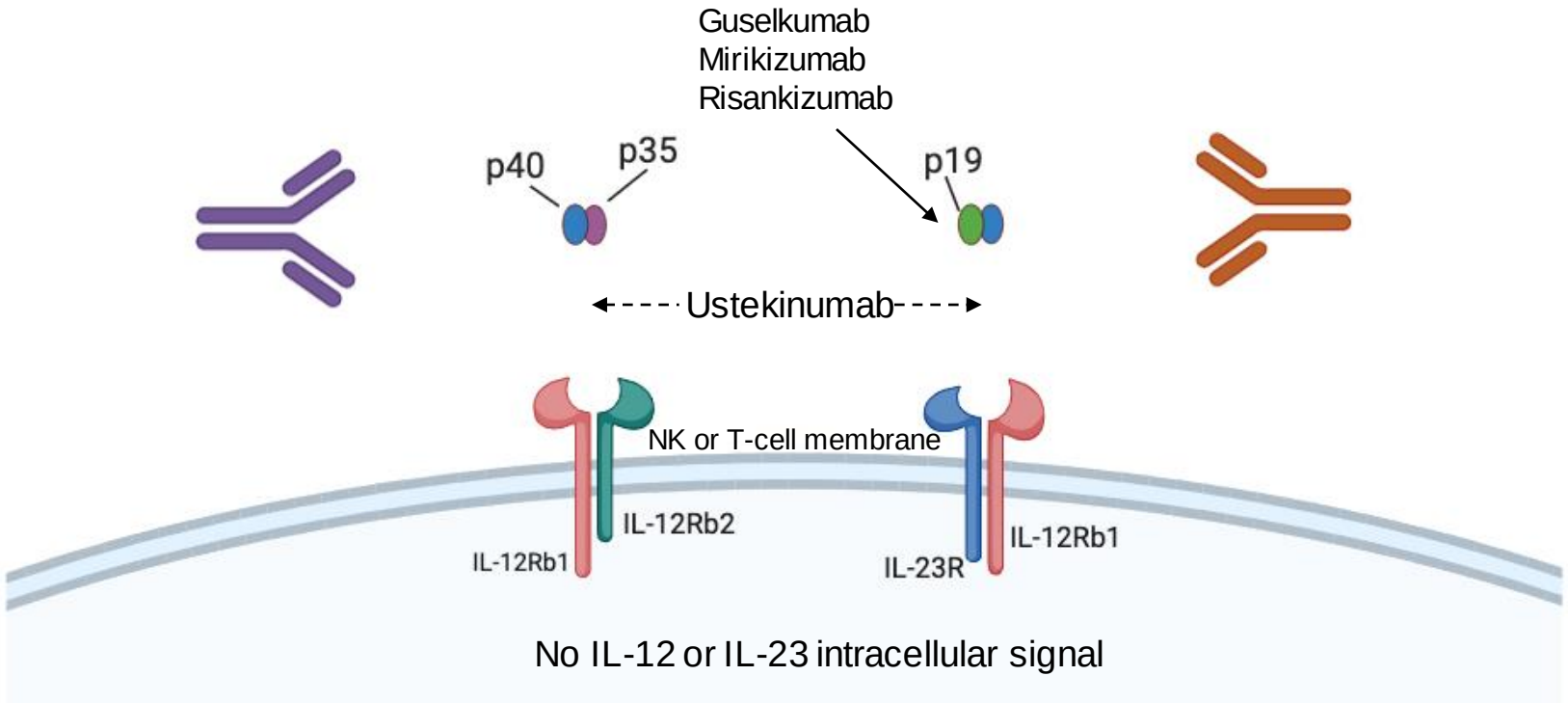
Section 2

Enhancing IL-23 Inhibition

Why is Targeting CD64+ Cells Important?

Jessica R. Allegretti, MD, MPH, FACG, AGAF

Anti-p40 (IL-12/23) and Anti-p19 (IL-23)



Adapted from Gately MK, et al. *Annu Rev Immunol.* 1998;16:495-521. Wilson NJ, et al. *Nat Immunol.* 2007;8(9):950-957. Nickoloff BJ, et al. *J Clin Invest.* 2004;113(12):1664-1675. Nestle FO, et al. *J Invest Dermatol.* 2004;123(6):xiv-xv. Created with Biorender.

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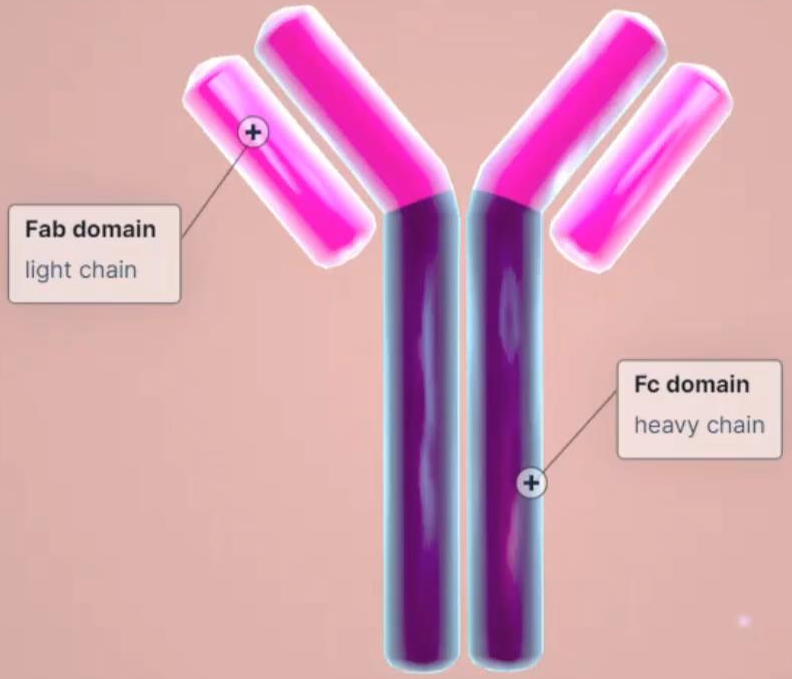
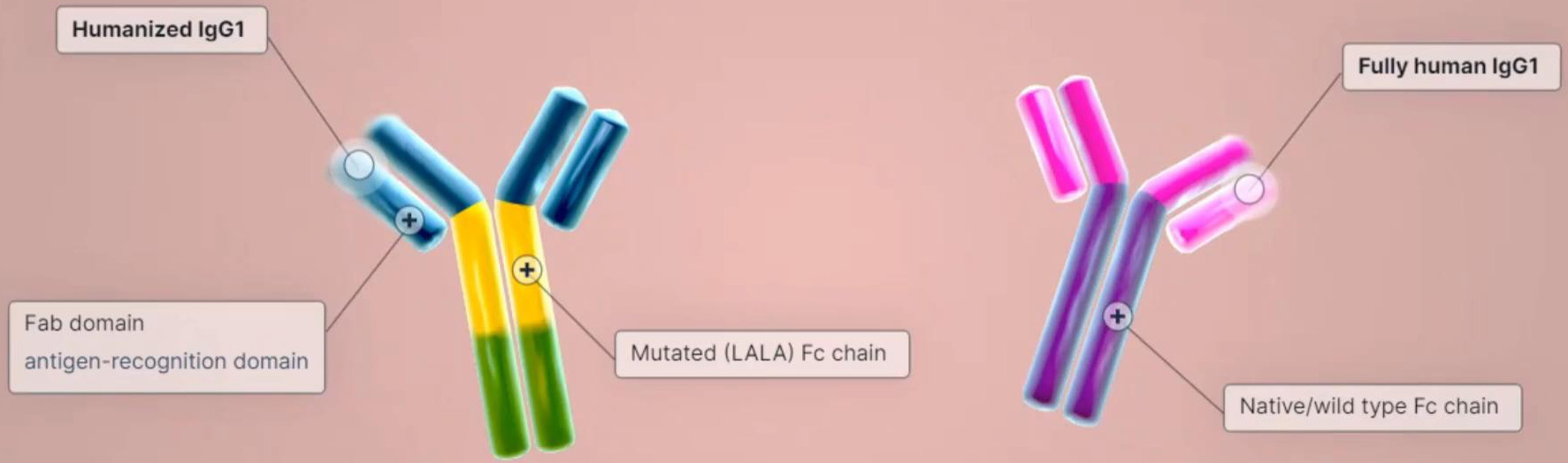
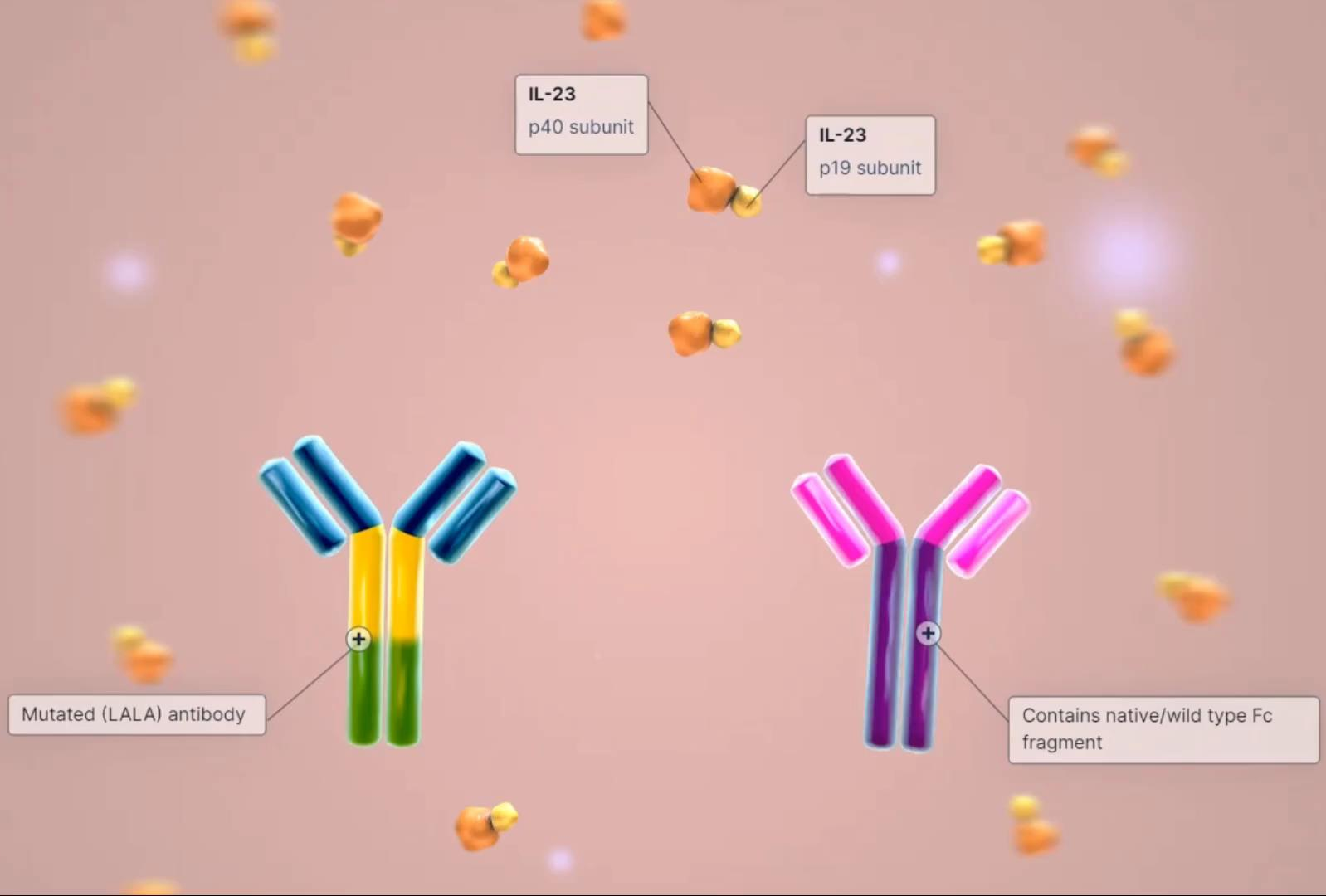
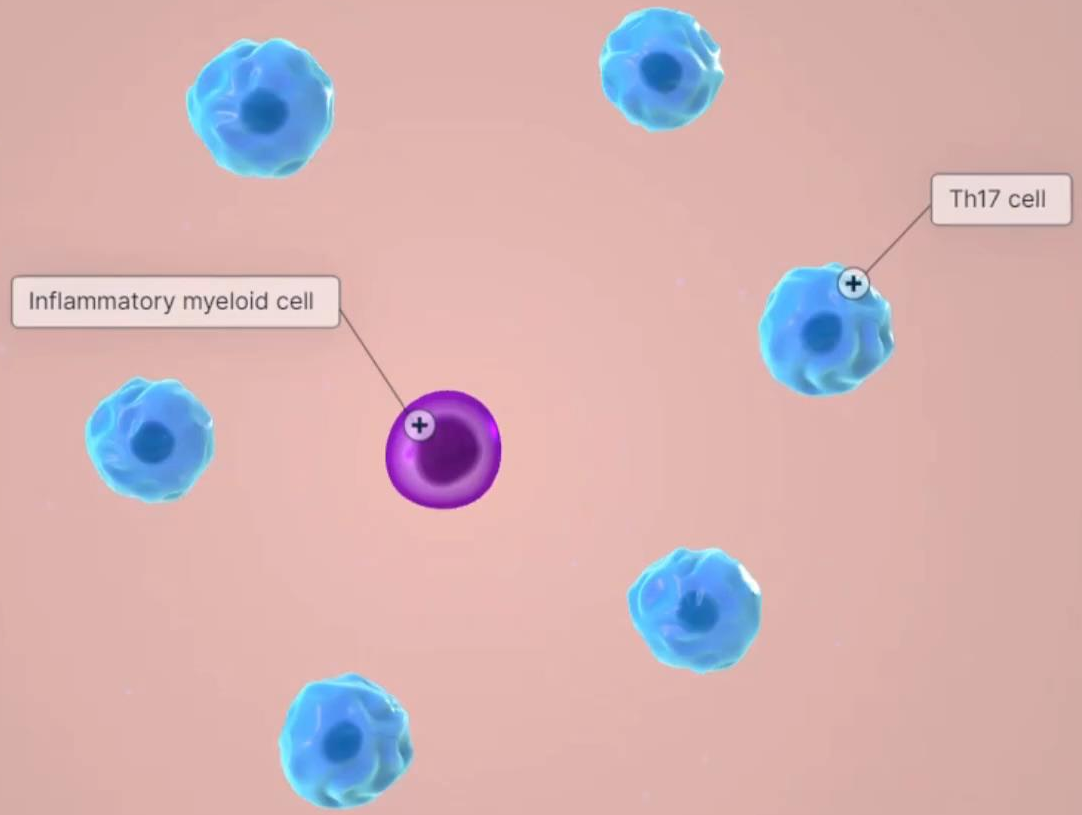

Fab domain
light chain
Fc domain
heavy chain

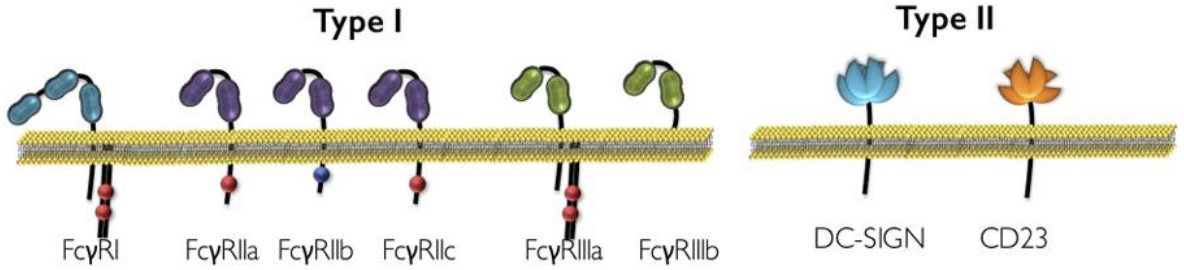

Humanized IgG1
Fab domain
antigen-recognition domain
Mutated (LALA) Fc chain
Fully human IgG1
Native/wild type Fc chain


IL-23
p40 subunit
IL-23
p19 subunit
Mutated (LALA) antibody
Contains native/wild type Fc fragment


Th17 cell
Inflammatory myeloid cell
IL-23

What are Fcγ receptors and CD64 receptors?

- Fcγ receptors: surface receptors on immune cells that recognize the Fc portion of IgG
- CD64 (FcγRI) is the only Fcγ receptor with high affinity for IgG1



	Type I						Type II	
	FcγRI	FcγRIIa	FcγRIIb	FcγRIIc	FcγRIIIa	FcγRIIIb	DC-SIGN	CD23
Neutrophils	#	+	+	-	-	+	-	#
Eosinophils	#	+	+	-	-	#	-	#
Basophils	#	+	+	-	-	+/-	-	#
Monocytes	+	+	+	-	+/-	-	-	#
Macrophages	+/-	+	+	-	+/-	-	+/-	#
Dendritic cells	-/#	+	+	-	-/#	-	+	-
Platelets	-	+	-	-	-	-	-	-

\+ Constitutive expression
\- No expression
\# Inducible expression

CD = cluster of differentiation; Ig = immunoglobulin.
Bournazos S, et al. *Microbiol Spectr*. 2016;4(6):10.

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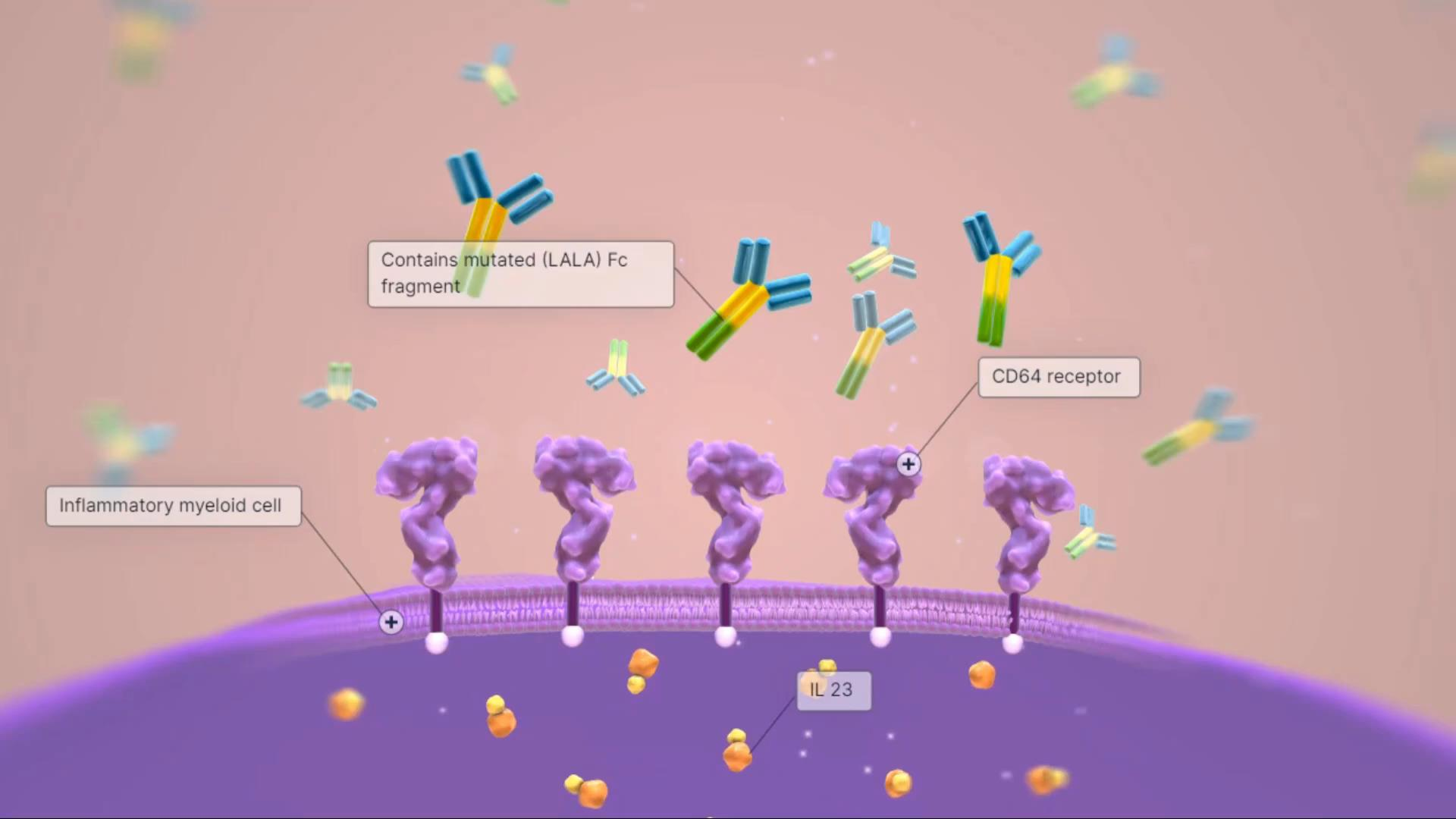
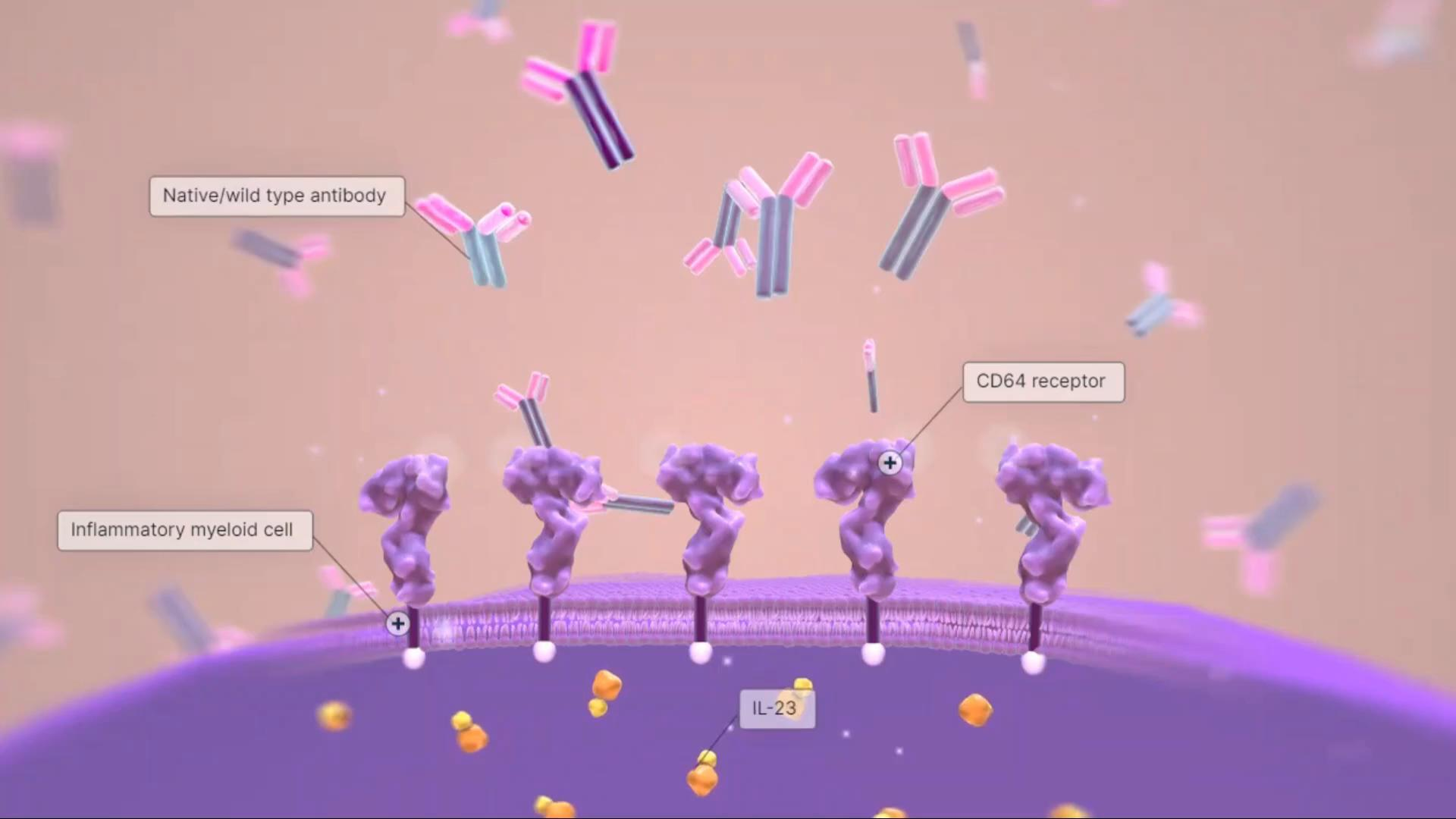
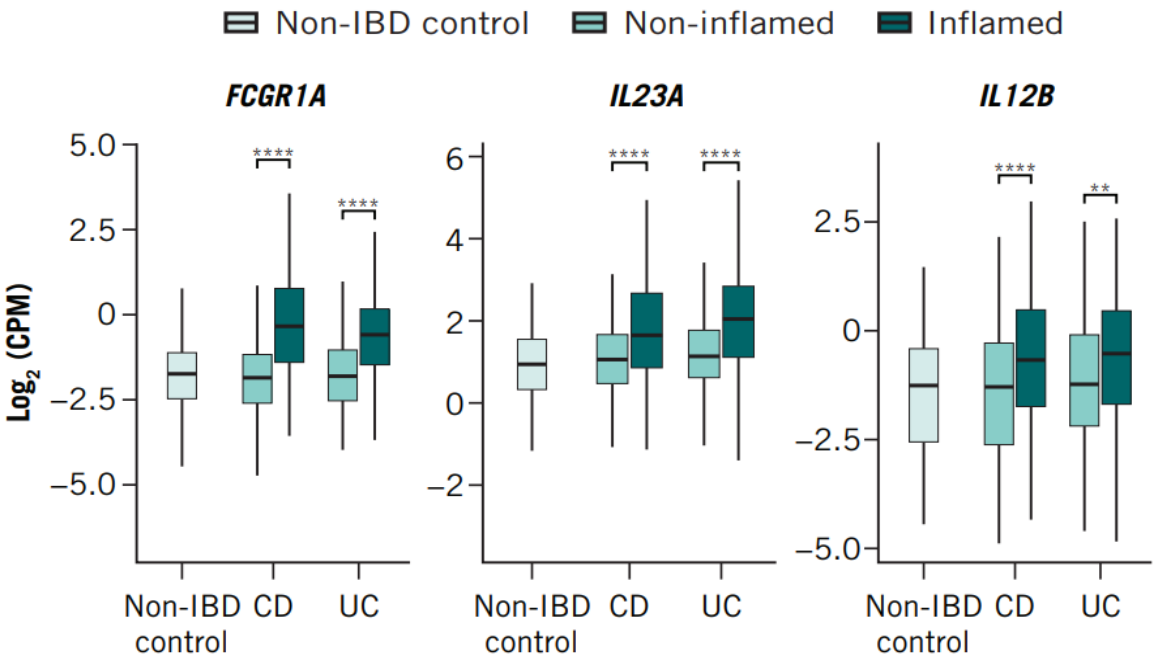

Contains mutated (LALA) Fc fragment
CD64 receptor
Inflammatory myeloid cell
IL 23


Native/wild type antibody
CD64 receptor
Inflammatory myeloid cell
IL-23

CD64 Expression in Diseased IBD Tissue



- *FCGR1A* (CD64), *IL23A* (IL-23p19), and *IL12B* (IL-23p40) expression were significantly increased in inflamed vs non-inflamed IBD gut biopsies

Atreya R, et al. *J Crohns Colitis*. 2024;18(Supplement 1):i470-i470.

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Audience Response

Which of the following is true regarding binding affinity of IL-23i's to CD64 receptors?

A. Binding of CD64 occurs with only risankizumab
B. Binding of CD64 occurs with only guselkumab
C. Binding of CD64 occurs with only mirikizumab
D. Binding of CD64 occurs with risankizumab, guselkumab, and mirikizumab
E. I don't know

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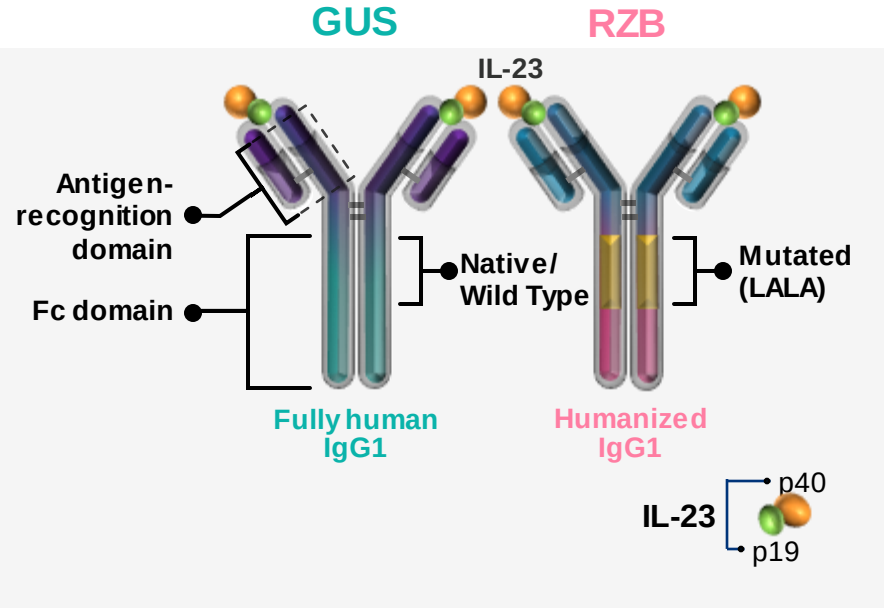
Clinically Relevant Differences Between Anti-IL-23 Therapeutic Antibodies May Be Related to Their Unique Molecular Attributes

- Guselkumab (GUS) and risankizumab (RZB) are mAbs that selectively target the p19 subunit of IL-23
- GUS and RZB have shown efficacy in the treatment of inflammatory bowel diseases*
- Potential differences in the therapeutic profiles may be related to their unique molecular attributes
- GUS and RZB have differences in the Fc region that affect binding to Fc-gamma receptors



mAb = monoclonal antibody; Fc = fragment crystallizable; LALA = leucine to alanine substitutions at positions 234 and 235; IgG = immunoglobulin G.
*GUS is approved for adult patients with moderate-to-severe plaque psoriasis and active psoriatic arthritis. RZB is approved for adult patients with moderate-to-severe plaque psoriasis, active psoriatic arthritis, and moderately to severely active Crohn's disease.

1. D'Haens G, et al. *Lancet*. 2022;399(10340):2015-2030. 2. Ferrante M, et al. *Lancet*. 2022;399(10340):2031-2046. 3. Sandborn WJ, et al. *Gastroenterology*. 2022;162(6):1650-1664. 4. Dignass A, et al. *J Crohns Colitis*. 2022;16(Supplement 1):i025-i026. 5. Louis E, et al. *Aliment Pharmacol Ther*. 2004;19(5):511-519. 6. Vos AC, et al. *Gastroenterology*. 2011;140(1):221-230. 7. Wojtal KA, et al. *PLoS One*. 2012;7(8):e43361.

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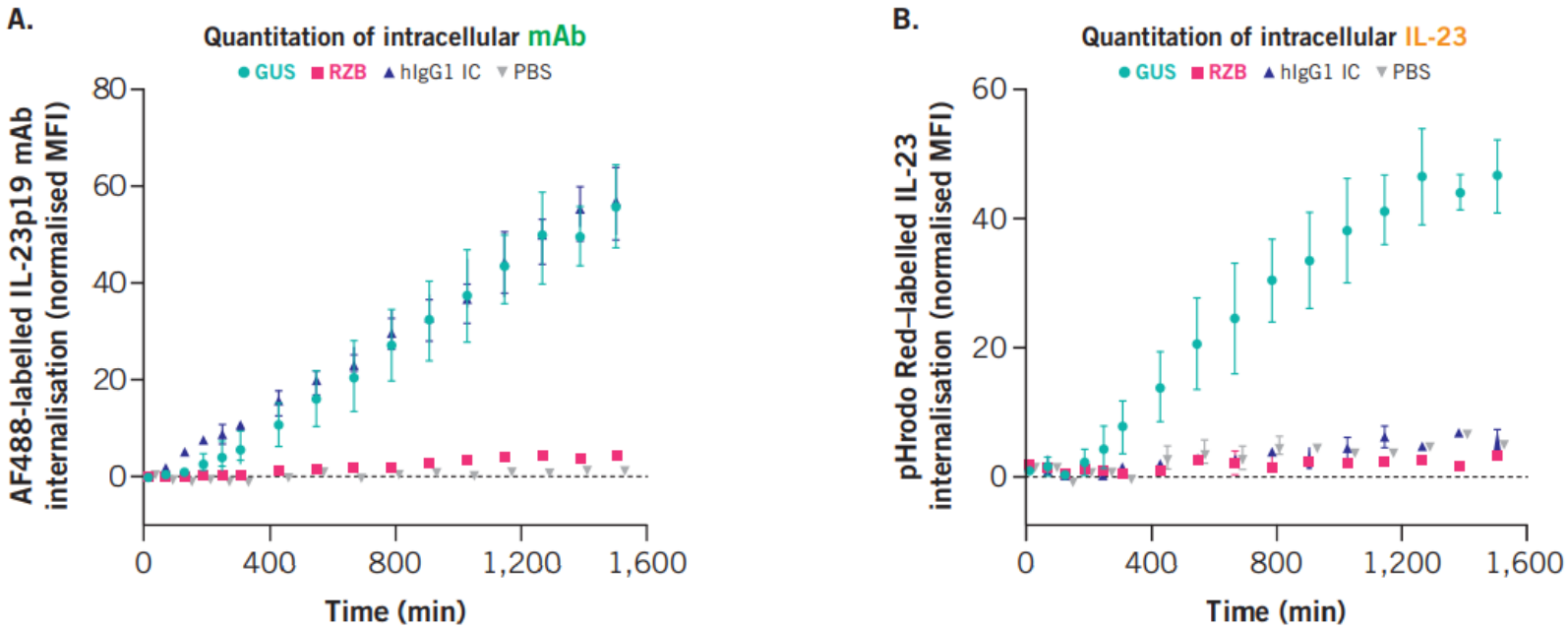
In-Vitro Evaluations of CD64 and IL-23 Binding: GUS and RZB

Quantitation of (A) mAb MFI and (B) IL-23 MFI in intracellular compartments of CD64+ inflammatory macrophages following treatment with IL-23p19 mAbs and IL-23



MFI = Mean fluorescence intensity

Atreya R, et al. *J Crohns Colitis*. 2024;18(Supplement 1):i470-i470.

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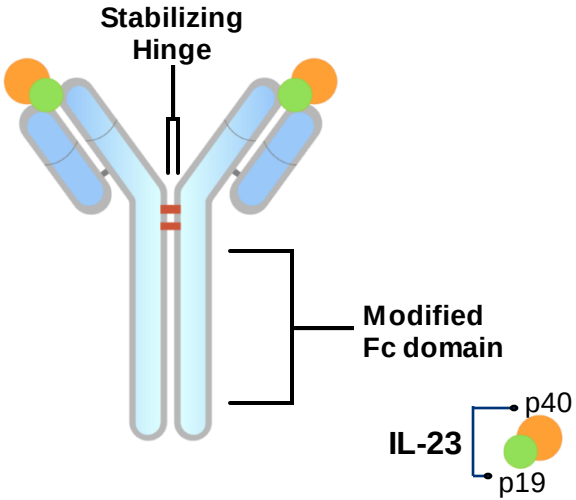
In-Vitro Evaluations of CD64 and IL-23 Binding: Mirikizumab

Mirikizumab Antibody



- Humanized IgG4 monoclonal antibody that selectively binds to the p19 subunit of human IL-23 cytokine and inhibits its interaction with the IL-23 receptor
- IgG4κ isotype containing the hinge-stabilizing S/P mutation
- Mirikizumab was additionally modified to significantly reduce FcγR binding and interaction
- Reduces the potential for unwanted interactions with the immune system and other possible toxicities

Strohl WR. *Antib Ther*. 2024;7(2):132-156.

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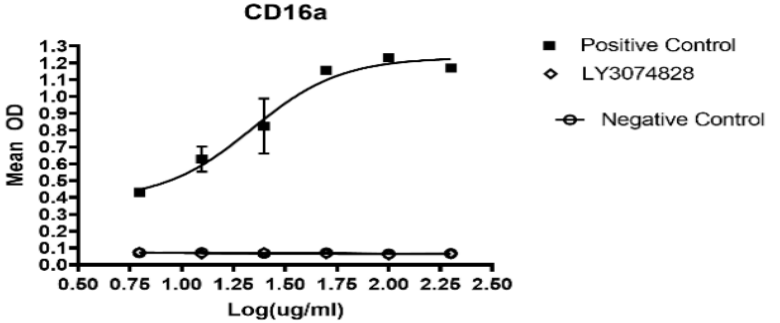
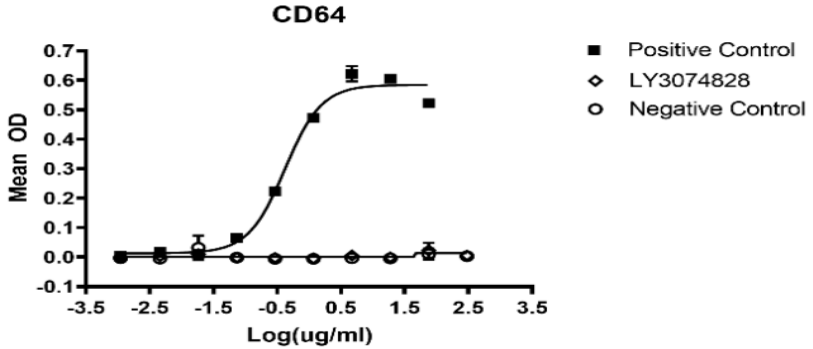
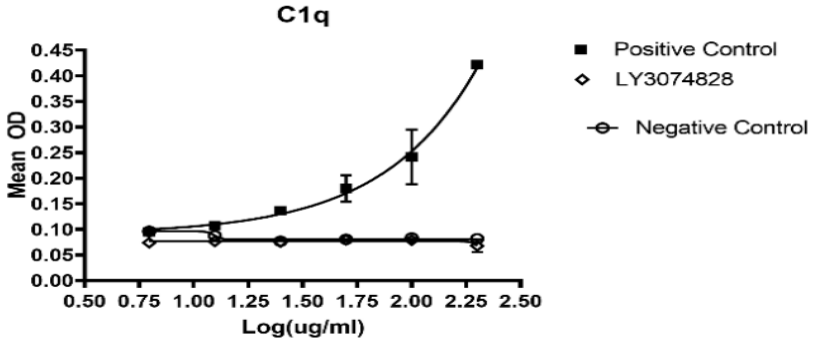
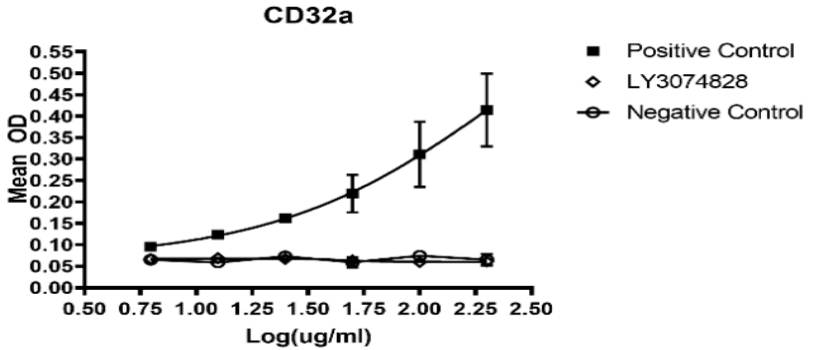
In-Vitro Evaluations of CD64 and IL-23 Binding: Mirikizumab

Assessment of Fc Receptor Activation and Complement Binding









IgG1= immunoglobulin G subclass 1; IgG4= immunoglobulin G subclass 4; SD= standard deviation; Note: Data are mean+SD of duplicate w ells

Steere B, et al. *J Pharmacol Exp Ther*. 2023;387(2):180-187.

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Audience Response

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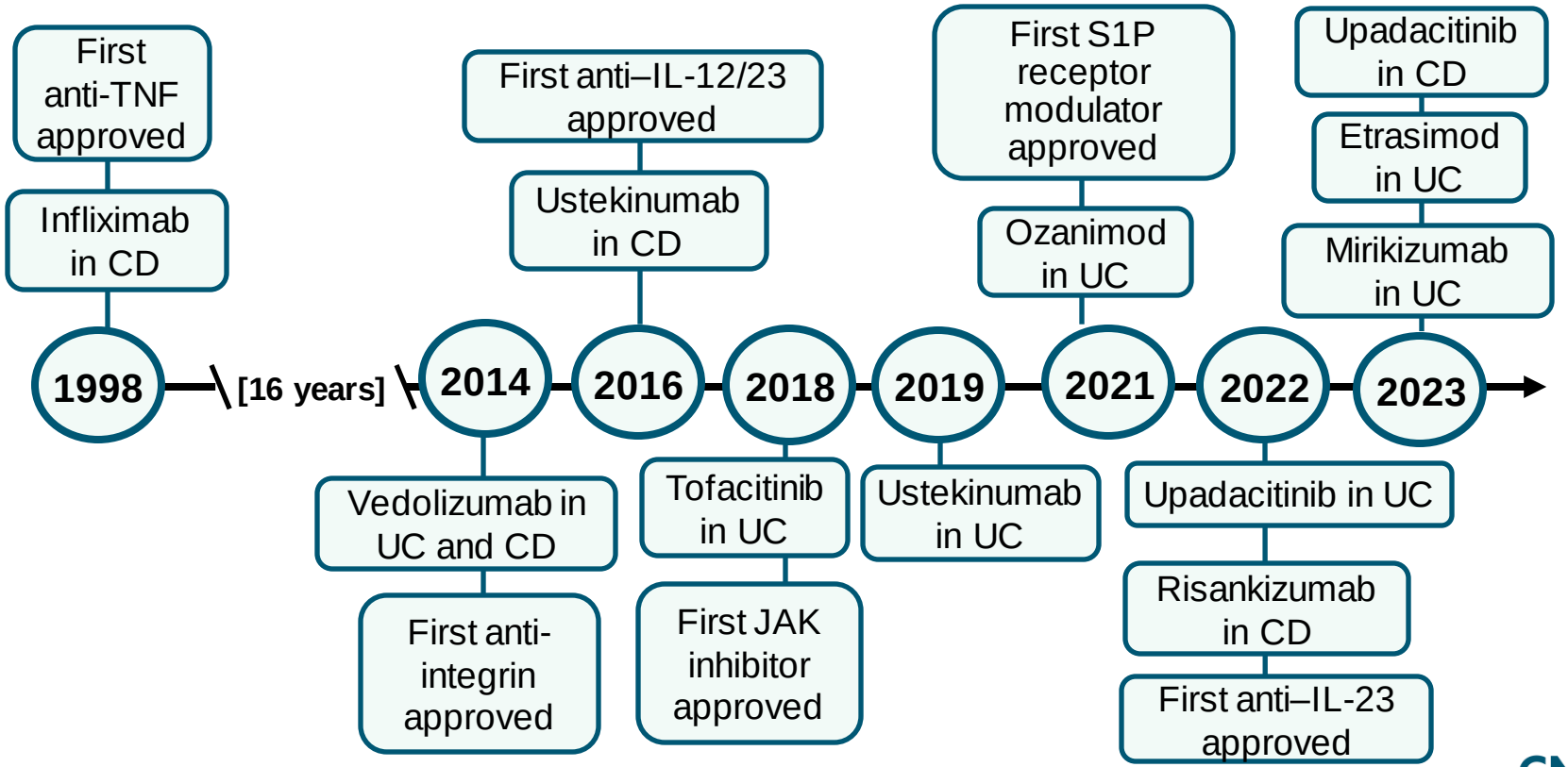
Section 3

Review of IL-23 Inhibitor Current Studies

Edward V. Loftus, Jr., MD

Evolution of IBD Treatment Landscape



CD = Crohn's disease; IBD = inflammatory bowel disease; IL = interleukin; JAK = Janus kinase; TNF = tumor necrosis factor; UC = ulcerative colitis.
Modified from Pouillon L, et al. *Nat Rev Gastroenterol Hepatol.* 2021;18(2):143. OMVOH® (mirikizumab-mrkz) [package insert]. Indianapolis, IN: Eli Lilly and Company. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761279s000lbl.pdf

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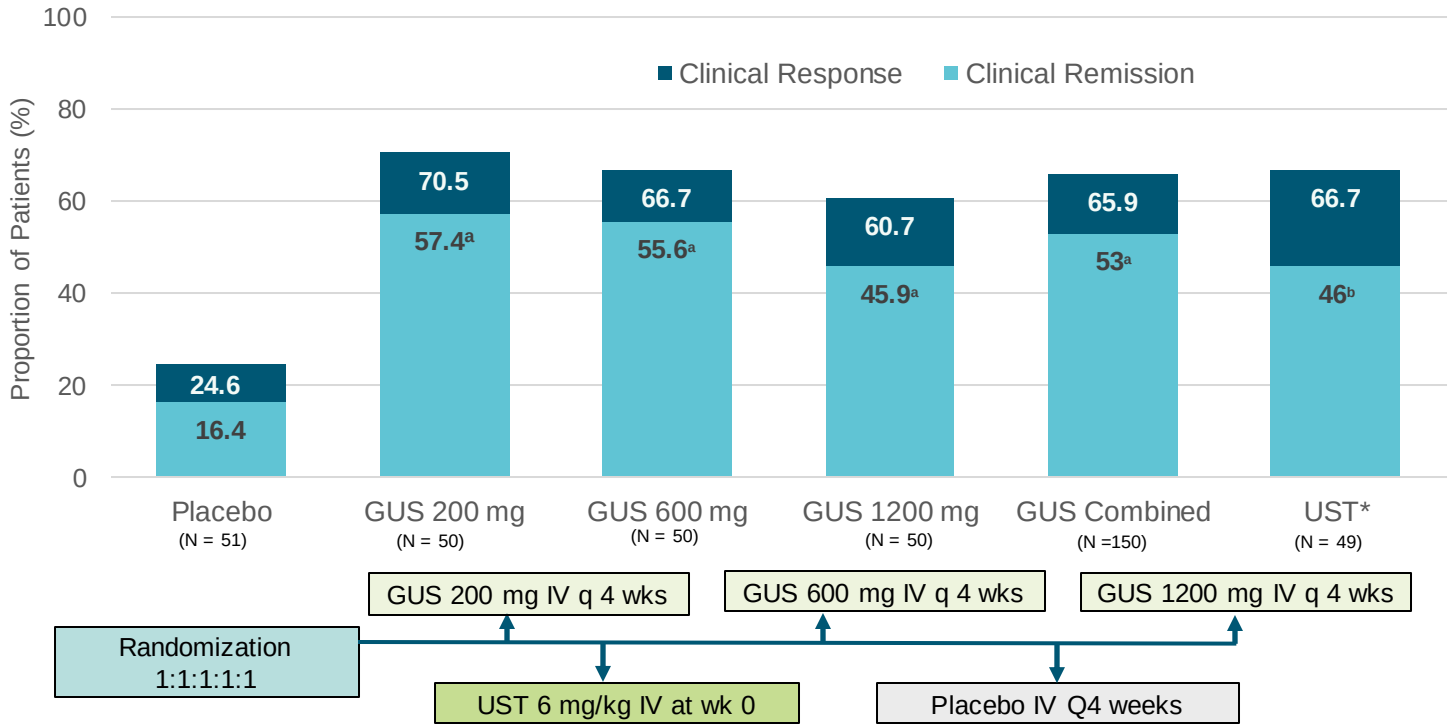
GALAXI-1: Guselkumab Induction in CD**



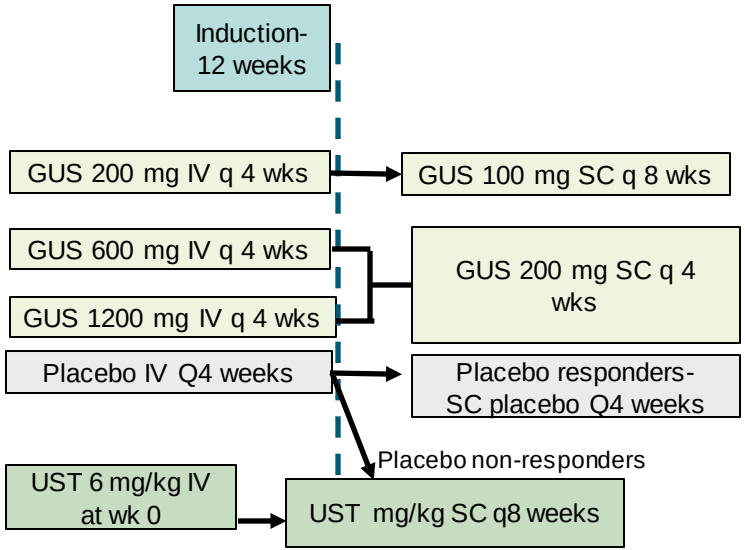
[A]p = <0.001 b p = 0.001; *UST approx. 6 mg/kg IV ⟹ 90 mg SC. Clinical Response = 100-point reduction from baseline CDAI score or CDAI < 150; Clinical Remission = CDAI < 150

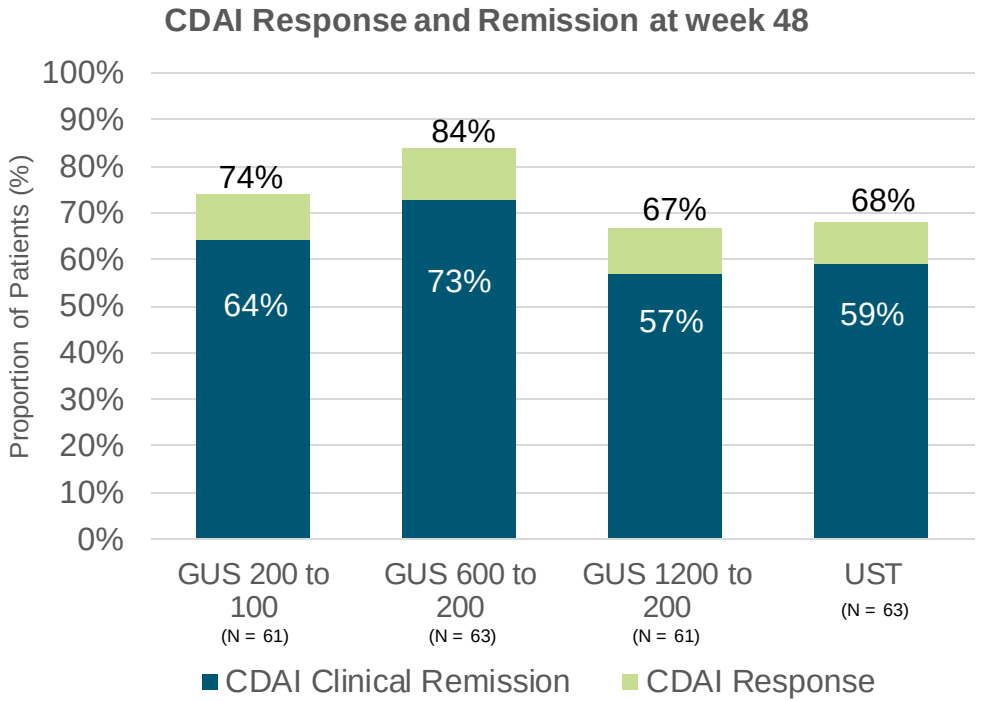
**guselkumab is not FDA-approved for the treatment of CD.

Sandborn W, et al. *Gastroenterology*. 2022;162(6):1650-1664.e8.

CME OUTFITTERS

GALAXI-1: Guselkumab Maintenance in CD*

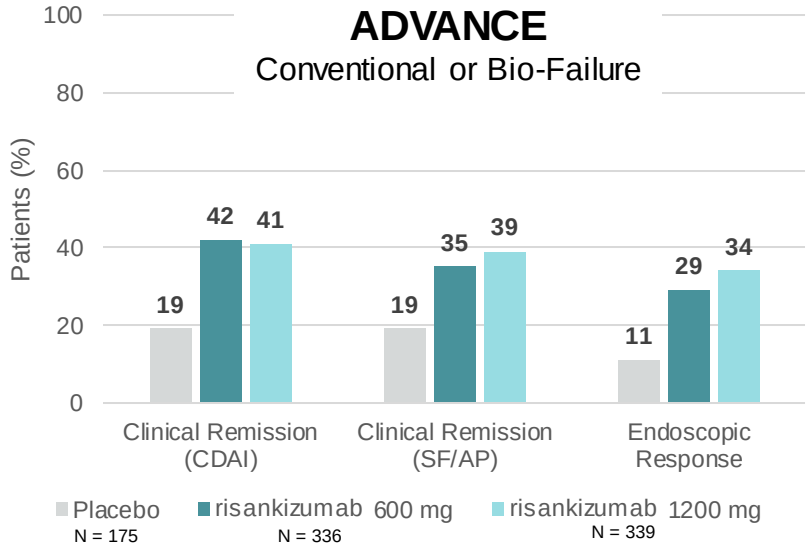


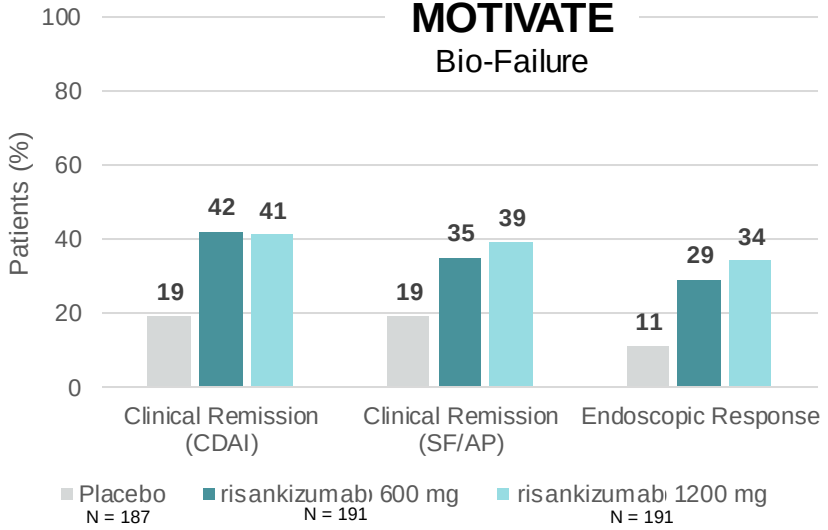


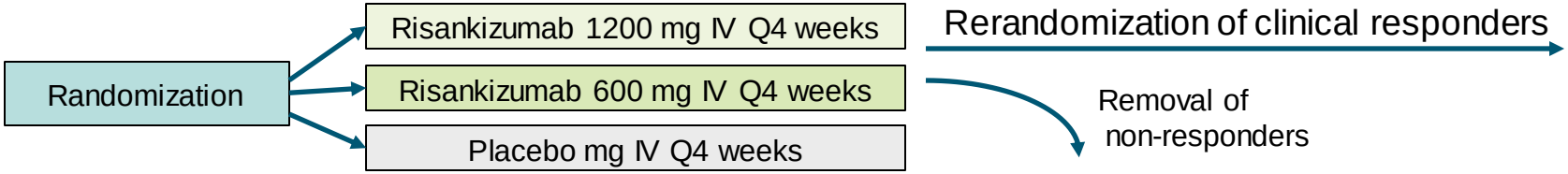
*guselkumab is not FDA-approved for the treatment of CD.
Clinical Response = 100-point reduction from baseline CDAI score or CDAI < 150; Clinical Remission = CDAI < 150
Danese S, et al. *Lancet Gastroenterol Hepatol.* 2024;9(2):133-146.

CME OUTFITTERS

ADVANCE and MOTIVATE: Risankizumab Induction in CD





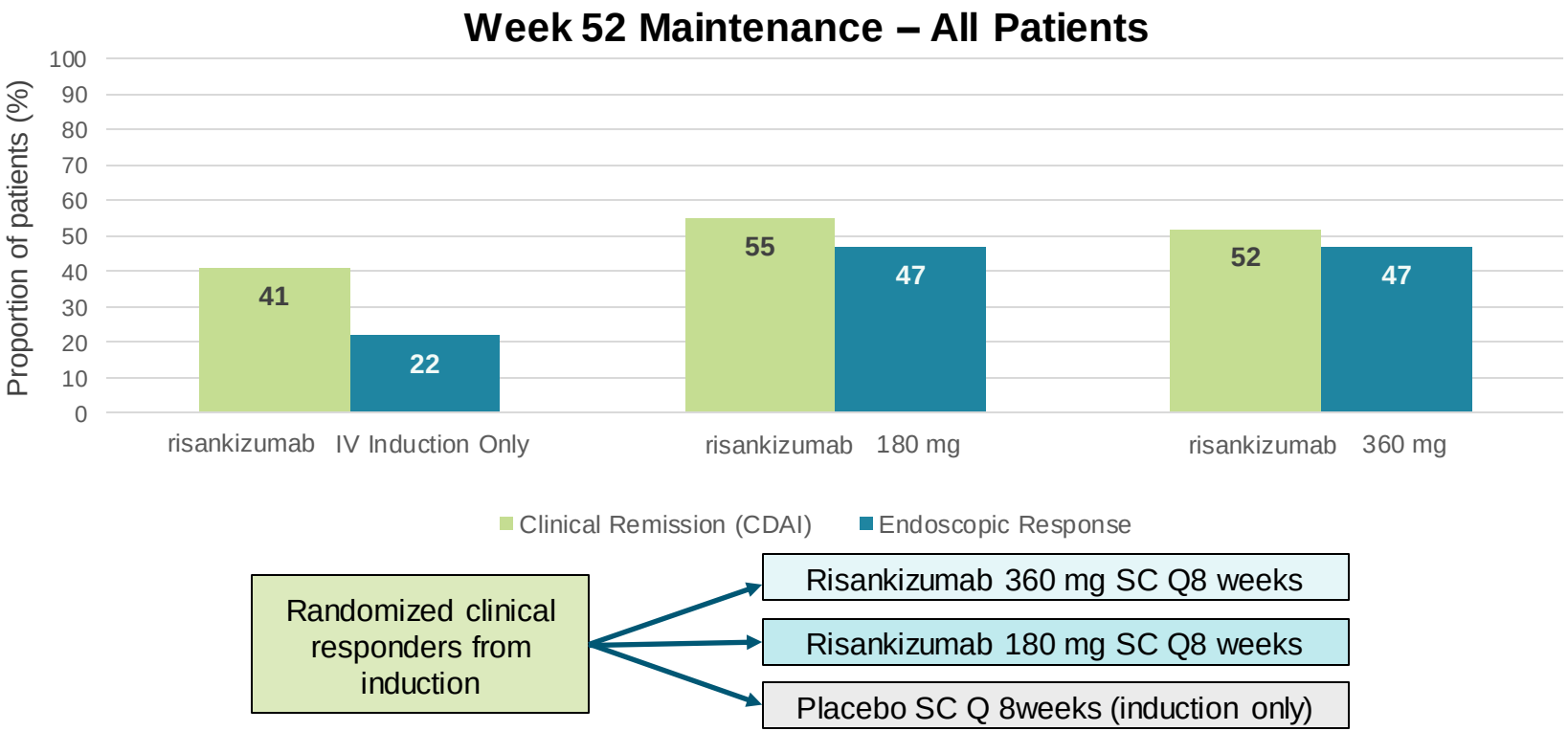


CDAI =Crohn's disease activity index; SF/AP = stool frequency/abdominal pain.; *Clinical responders defined as ≥30% decrease in average daily stool frequency or APS and not worse than baseline; *Endoscopic response defined as >50% decline in SES-CD vs BL by central reviewer (or in pts with SES-CD of 4 at BL, ≥2-point decrease vs BL); CDAI clinical remission a CDAI < 150.

D'Haens G, et al. *Lancet*. 2022;399(10340):2015-2030. Ferrante M, et al. *Lancet*. 2022;399(10340):2031-2046.

CME OUTFITTERS

FORTIFY: Risankizumab Maintenance in CD



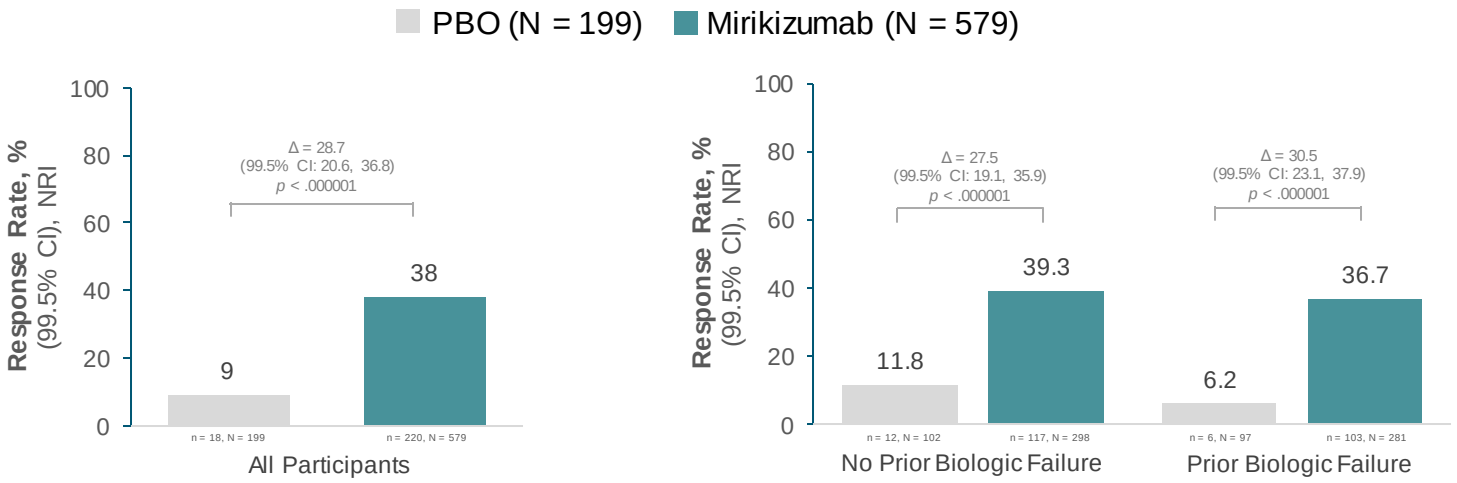
Endoscopic response defined as >50% decline in SES-CD vs BL by central reviewer (or in pts with SES-CD of 4 at BL, ≥2-point decrease vs BL); CDAI clinical remission a CDAI < 150.

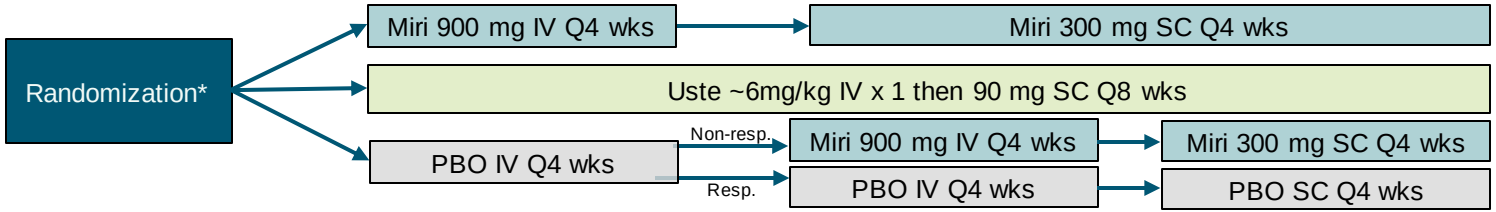
Ferrante M, et al. *Lancet*. 2022;399(10340):2031-2046.

CME OUTFITTERS

VIVID-1: Mirikizumab Comparison in Moderate-to-Severe CD

Clinical Response by PRO at Week 12 and Endoscopic Response by SES-CD at Week 52



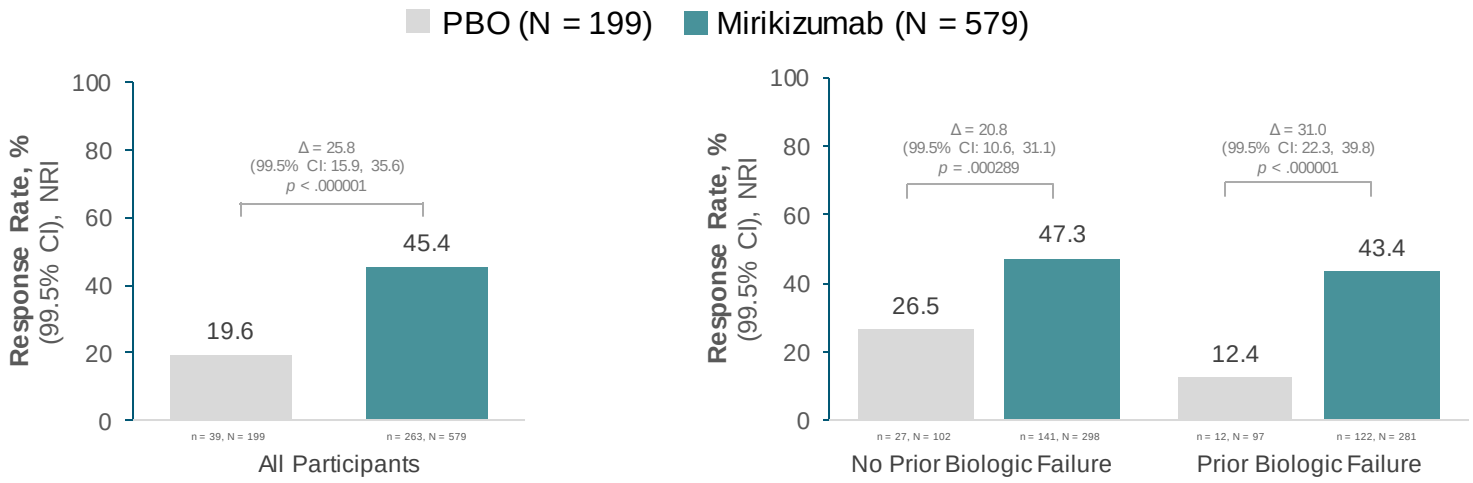


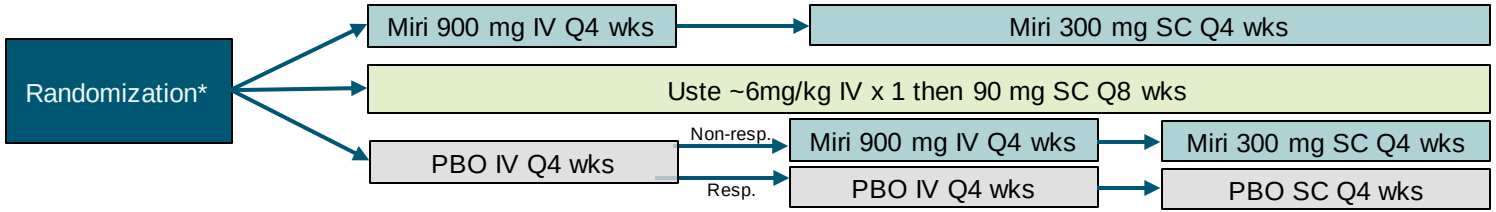
*Randomized 6:3:2 to mirikizumab, ustekinumab, and placebo. Ferrante M, et al. *J Crohns Colitis*. 2024;18(Supplement 1):i7-i9.

CME OUTFITTERS

VIVID-1: Mirikizumab Comparison in Moderate-to-Severe CD

Clinical Response by PRO at Week 12 and Clinical Remission by CDAI at Week 52

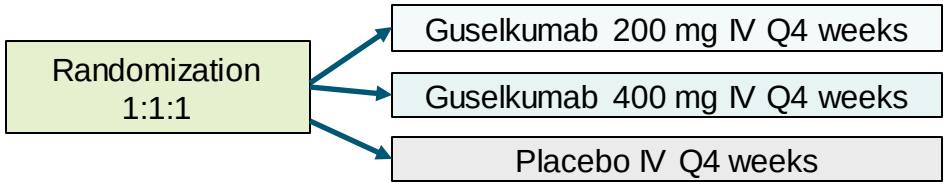


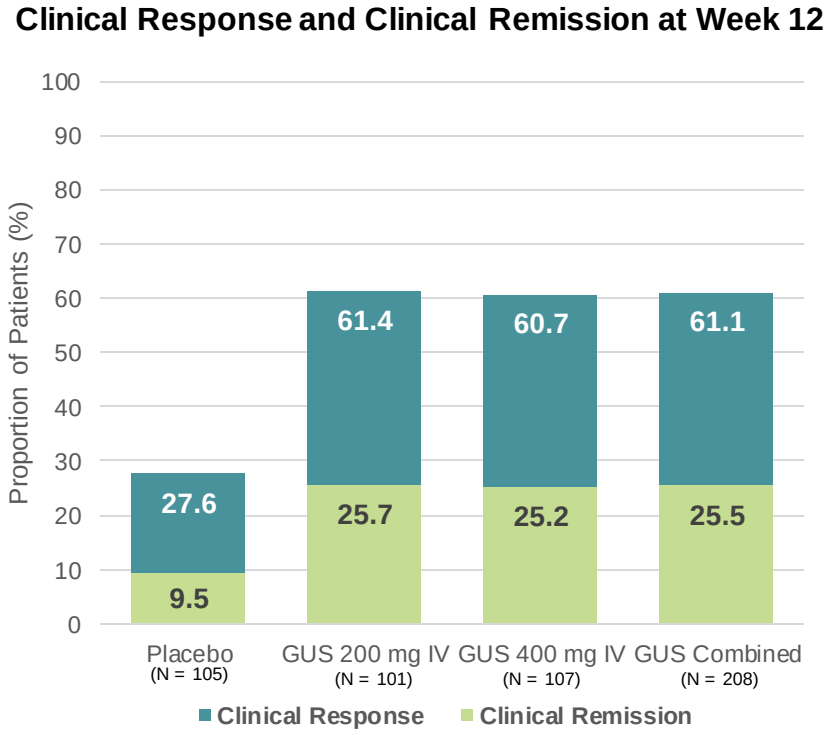


*Randomized 6:3:2 to mirikizumab, ustekinumab, and placebo. Ferrante M, et al. *J Crohns Colitis*. 2024;18(Supplement 1):i7-i9.

CME OUTFITTERS

QUASAR: Guselkumab Induction in UC*





*guselkumab is not FDA-approved for the treatment of UC. GUS = guselkumab.

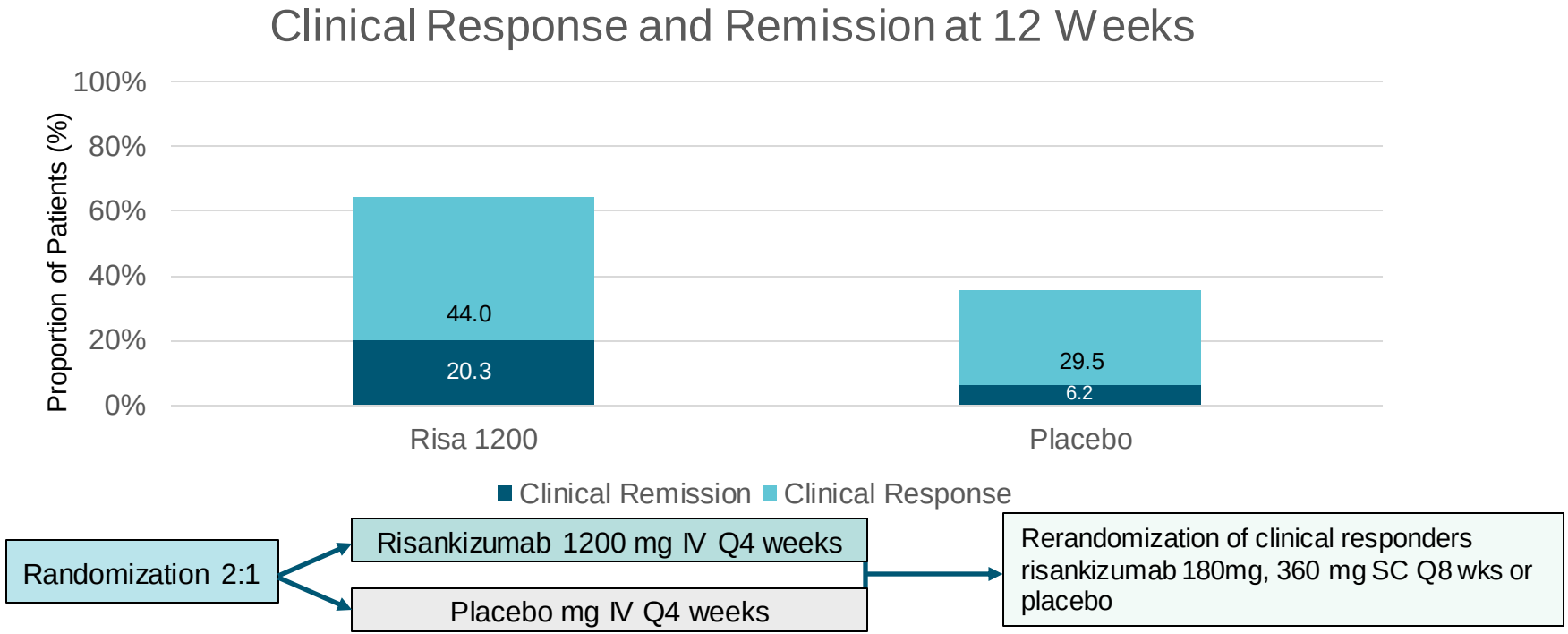
Clinical response = modified Mayo score decrease ≥30% and ≥2 points, rectal bleeding subscore ≥1-point decrease or subscore of 0/1;

Clinical remission = Mayo stool frequency subscore of 0 or 1 and not increased from induction baseline, a Mayo rectal bleeding subscore of 0, and a Mayo endoscopy subscore of 0 or 1 with no friability present on the endoscopy

Peyrin-Biroulet L, et al. *Gastroenterology* 2023;165(6):1443-1457.

CME OUTFITTERS

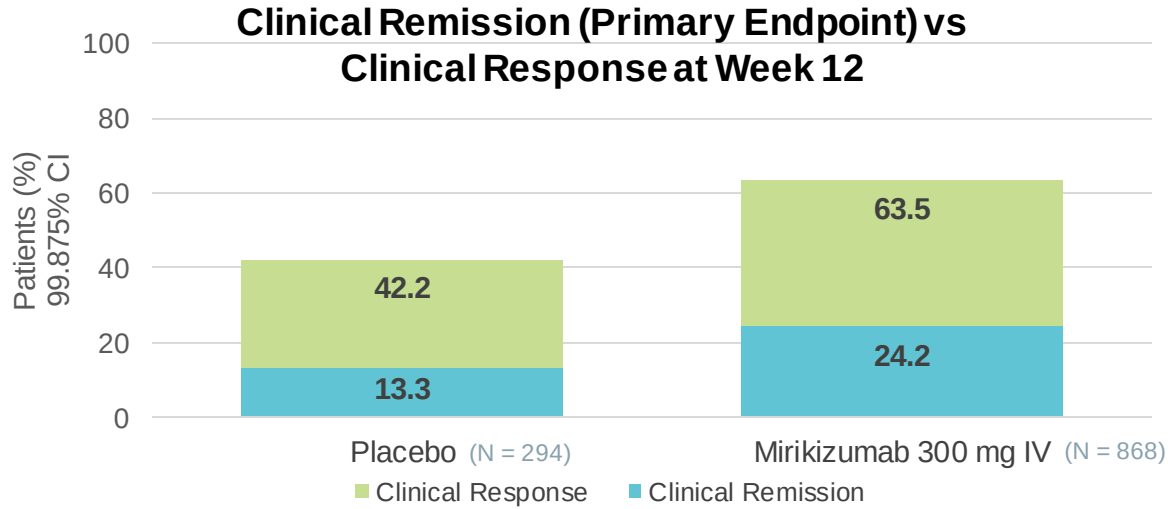
INSPIRE: Risankizumab Induction in UC*

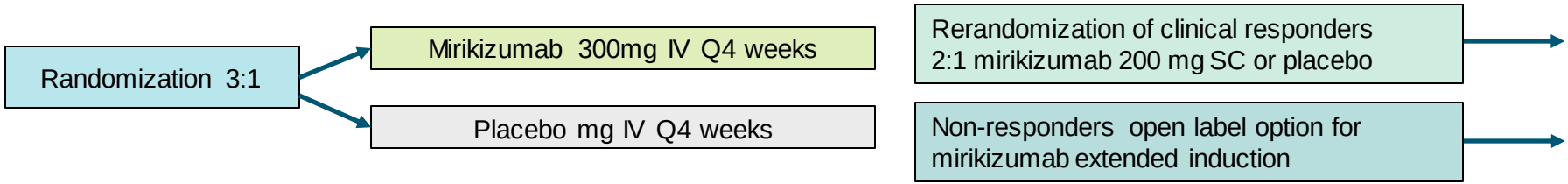


*risankizumab is not FDA-approved for the treatment of UC.
*Clinical responders defined as ≥30% decrease in average daily stool frequency or APS and not worse than baseline; *Endoscopic response defined as >50% decline in SES-CD vs BL by central reviewer (or in pts with SES-CD of 4 at BL, ≥2-point decrease vs BL); CDAI clinical remission a CDAI < 150.
Louis E, et al. *Am J Gastroenterol*. 2023;118(10S):S624-S625.

CME OUTFITTERS

LUCENT-1: Mirikizumab Induction in UC



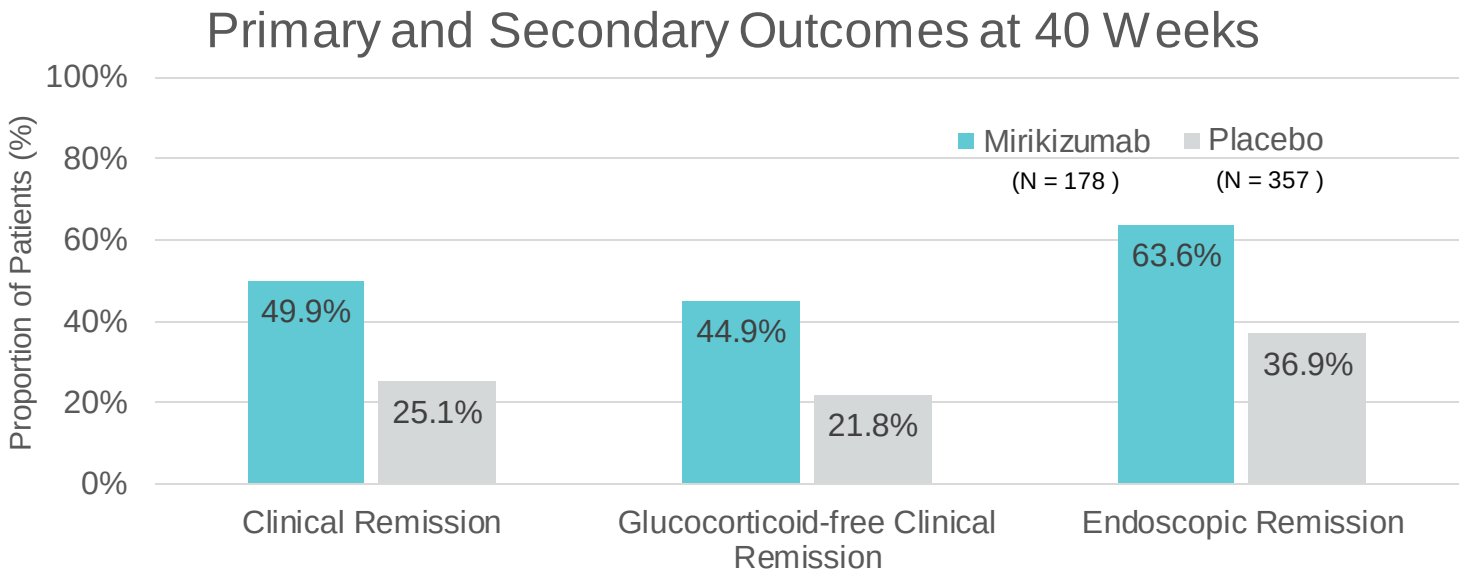


Clinical Remission: Stool frequency (SF) = 0, or SF = 1 with a ≥1-point decrease from baseline; rectal bleeding (RB) = 0; endoscopic subscore (ES) = 0 or 1 (excluding friability); clinical response: MMS of ≥2 points and ≥30% decrease from baseline, and a decrease of ≥1 point in the RB subscore from baseline or a RB score of 0 or 1

D'Haens G, et al. *N Engl J Med*. 2023;388(26):2444-2455

CME OUTFITTERS

LUCENT-2: Mirikizumab Maintenance in UC



Clinical Remission: Stool frequency (SF) = 0, or SF = 1 with a ≥1-point decrease from baseline; rectal bleeding (RB) = 0; endoscopic subscore (ES) = 0 or 1 (excluding friability), Endoscopic Remission: ES = 0 or 1 (excluding friability), clinical remission at week 40, remission of symptoms at week 28, and no glucocorticoid use for ≥12 weeks before week 40

D'Haens G, et al. *N Engl J Med*. 2023;388:2444-2455.

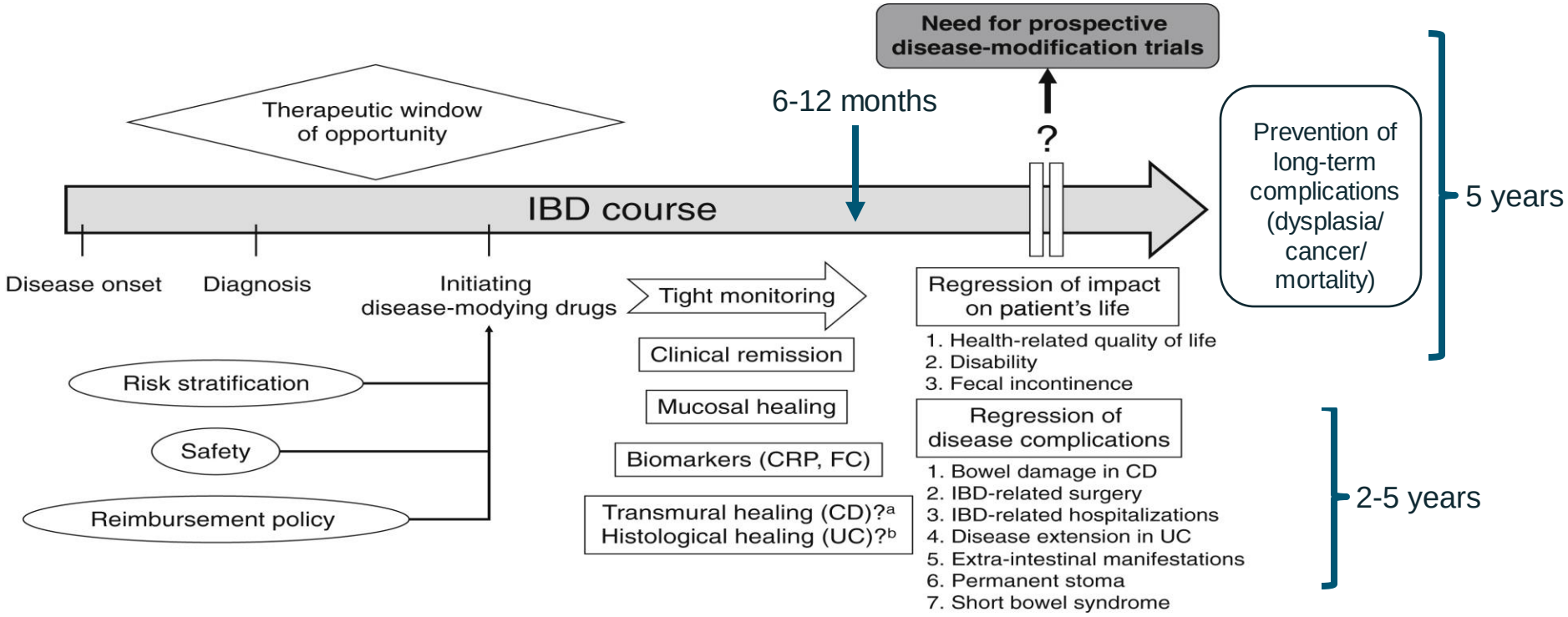
CME OUTFITTERS

Section 4

Clinical Implications to Practice

Angelina E. Collins, MSN, ANP-BC

Defining Goals for Treatment



FC = fecal calprotectin

[a]Transmural healing maybe the ultimate therapeutic goal in CD; [b]Histologic healing maybe the ultimate therapeutic goal in UC

Le Berre C, et al. *Gastroenterology*. 2022;162(5):1424-1438.

CME OUTFITTERS

Dosing of IL-23is

Drug	Dose	Induction Schedule	Indication	Trial
Guselkumab*	200-400mg IV	Q4W X 3	UC	QUASAR
Risankizumab*	1200mg IV	Q4W X 3	UC	INSPIRE
Mirikizumab	300mg IV	Q4W X 3	UC	LUCENT-1
Guselkumab*	200-1200mg IV	Q4W X 3	CD	GALAXI-1
Risankizumab	600-1200mg IV	Q4W X 3	CD	ADVANCE, MOTIVATE
Mirikizumab*	200-1000mg IV	Q4W X 3	CD	SERENITY

*Not FDA-approved for treatment

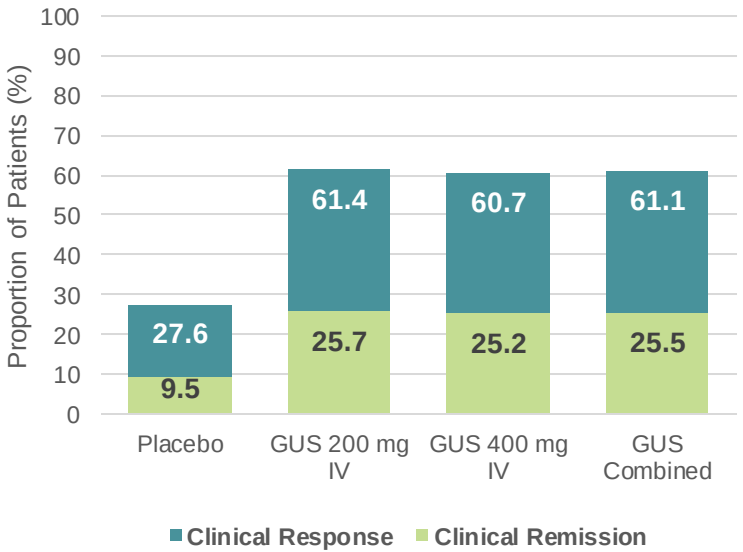
McDonald BD, et al. *J Crohn's Colitis*. 2022;16(Supplement 2):ii42-ii53.

CME OUTFITTERS

IL-23is in Treatment-Naïve and Treatment-Experienced Patients

QUASAR: Guselkumab in Ulcerative Colitis, 2b

Clinical Response and Clinical Remission at Week 12



History of inadequate response or intolerance to 1 or more advanced therapies in 47% of patients

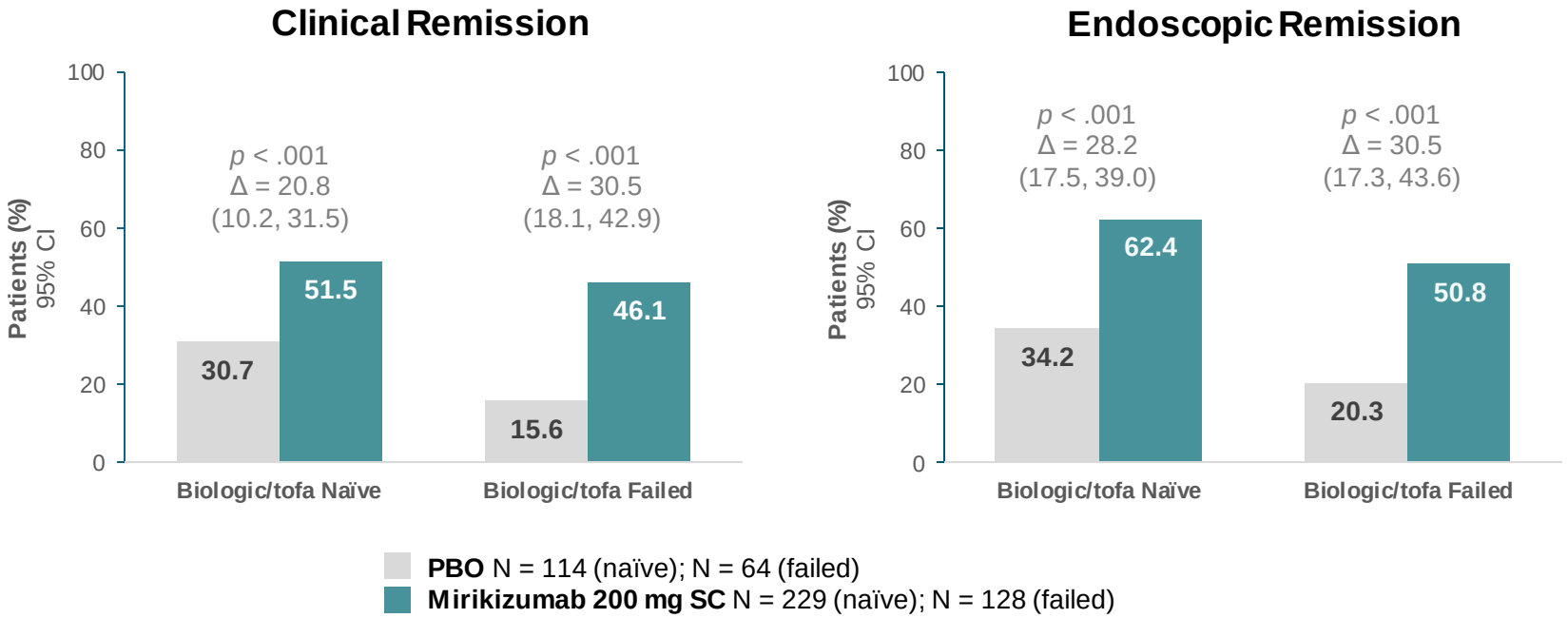
		Guselkumab		
	Placebo (N = 105)	200 mg IV (N = 101)	400 mg IV (N = 107)	Total (N = 313)
History of inadequate response/intolerance to ≥1 UC advanced therapy,[c] n (%)	51 (48.6)	46 (45.5)	51 (47.7)	148 (47.3)
≥1 TNF-α antagonist, n/n (%)	46/51 (90.2)	41/46 (89.1)	46/51 (90.2)	133/148 (89.9)
Vedolizumab, n/n (%)	29/51 (56.9)	22/46 (47.8)	27/51 (52.9)	78/148 (52.7)
Tofacitinib, n/n (%)	15/51 (29.4)	10/46 (21.7)	6/51 (11.8)	31/148 (20.9)
1 advanced therapy class, n/n (%)	23/51 (45.1)	27/46 (58.7)	25/51 (49.0)	75/148 (50.7)
≥2 advanced therapy classes, n/n (%)	28/51 (54.9)	19/46 (41.3)	26/51 (51.0)	73/148 (49.3)

Peyrin-Biroulet L, et al. *Gastroenterology* 2023;165(6):1443-1457.

CME OUTFITTERS

IL-23is in Treatment-Naïve and Treatment-Experienced Patients

LUCENT-2: Mirikizumab Endpoints by Biologic/tofacitinib Failure Status – Ulcerative Colitis



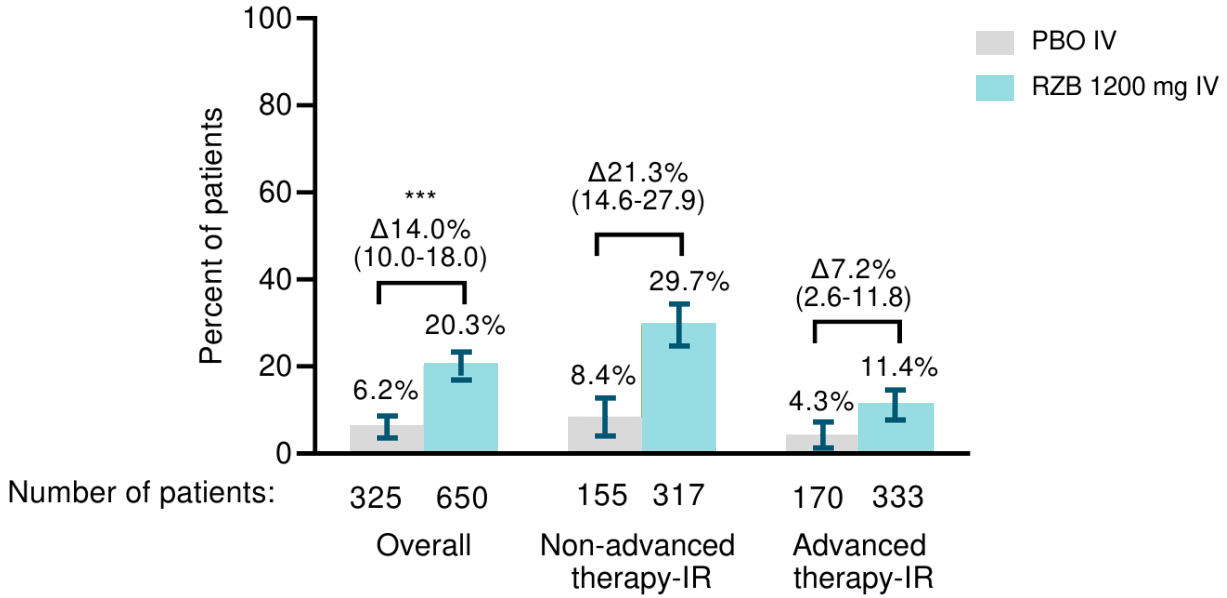
D'Haens G, et al. *N Engl J Med.* 2023;388:2444-2455.

CME OUTFITTERS

IL-23is in Treatment-Naïve and Treatment-Experienced Patients

INSPIRE: Risankizumab Endpoints by non-Advanced and Advanced Therapy-IR – Ulcerative Colitis

Primary Endpoint: Clinical Remission at Week 12

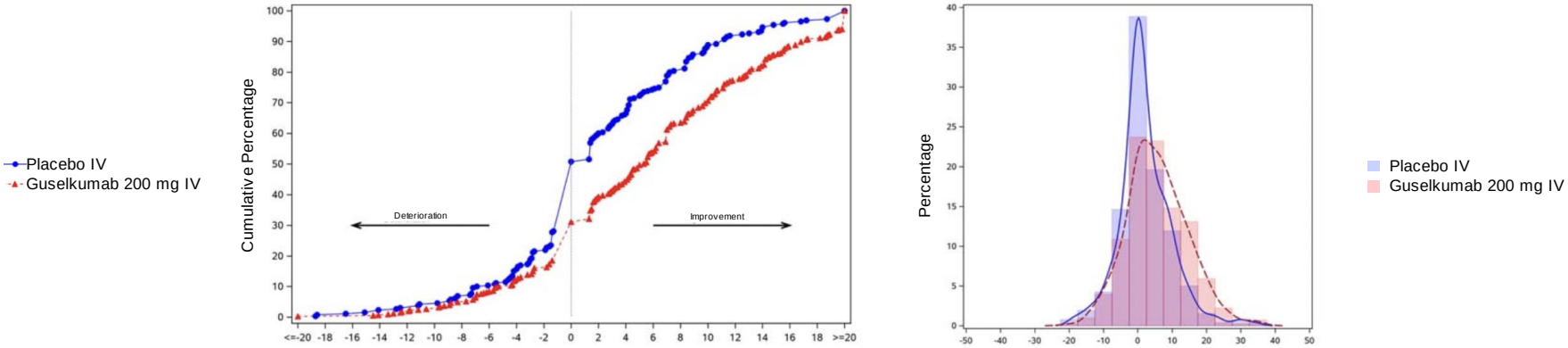


Louis E, et al. *Am J Gastroenterol*. 2023;118(Supplement 12):S2-S2.

CME OUTFITTERS

IL-23is and Fatigue in Patients with Moderate-to-Severe UC – QUASAR Trial (GUS)

Improvement from Baseline in PROMIS-Fatigue Short Form 7a T-score at Week 12



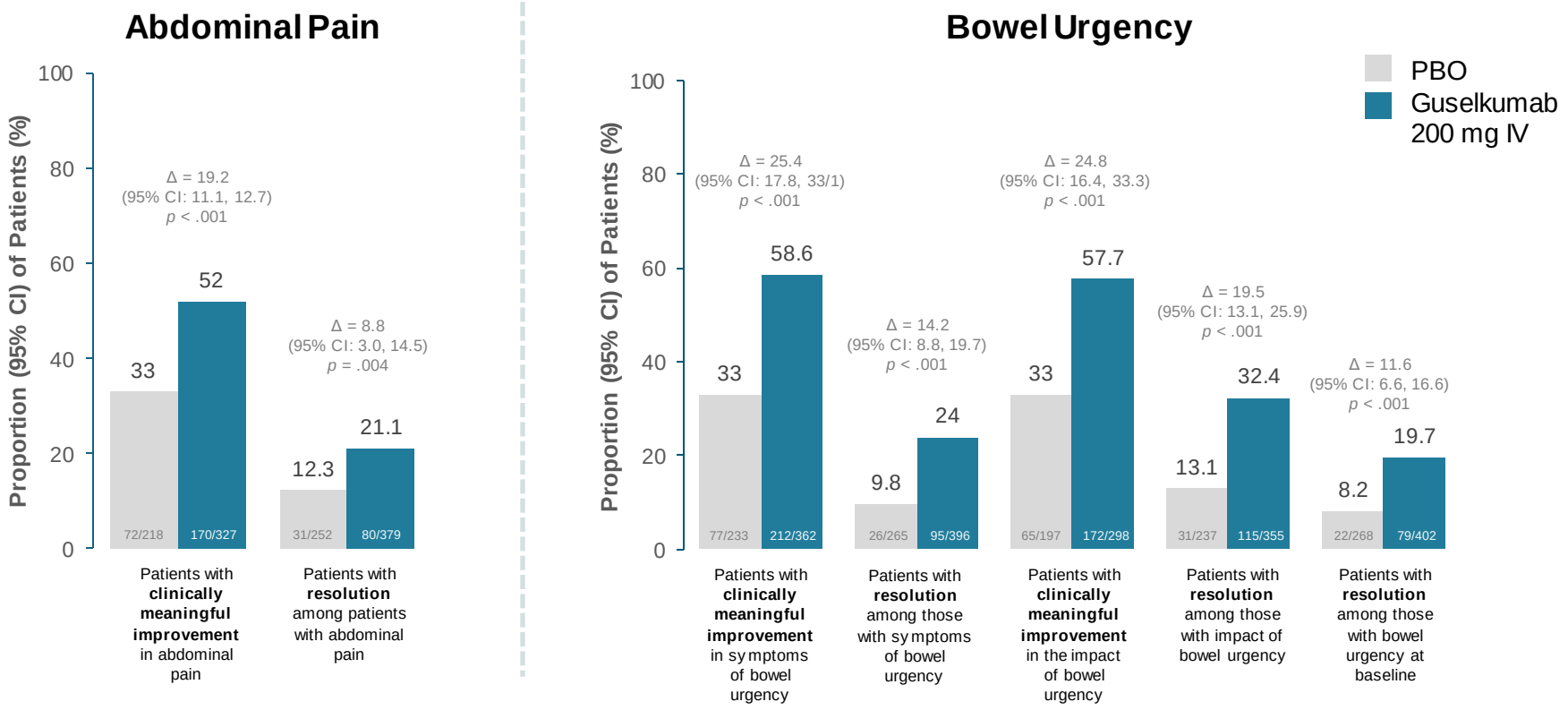
Fatigue response at Week 12: Overall and by history of inadequate response/intolerance to advanced therapy (ADT-IR)						
	Overall		Non-ADT-IR		ADT-IR	
	Placebo IV	GUS 200 mg IV	Placebo IV	GUS 200 mg IV	Placebo IV	GUS 200 mg IV
Primary analysis population, N	280	421	144	213	136	208
Fatigue response at Week 12, N (%)	60 (21.4%)	173 (41.1%)	42 (29.2%)	93 (43.7%)	18 (13.2%)	80 (38.5%)
Adjusted treatment difference, (95% CI)		19.8 (13.1%, 26.4%)**		14.5% (4.5%, 24.5%)*	25.2% (16.6%, 33.9%)**	

*Nominal p-value < 0.01; **Nominal p-value < 0.001

Dignass A, et al. *J Crohns Colitis*. 2024;18(Supplement 1):i166-i167.

CME OUTFITTERS

IL-23is and Abdominal Pain and Urgency in Patients with Moderate-to-Severe UC - QUASAR Trial (GUS)



Rubin D, et al. *J Crohns Colitis*. 2024;18(Supplement1):i1825-i1826.

CME OUTFITTERS

IL-23is and Symptom Resolution in Moderate-to-Severe UC – INSPIRE and COMMAND Trials (RZB)

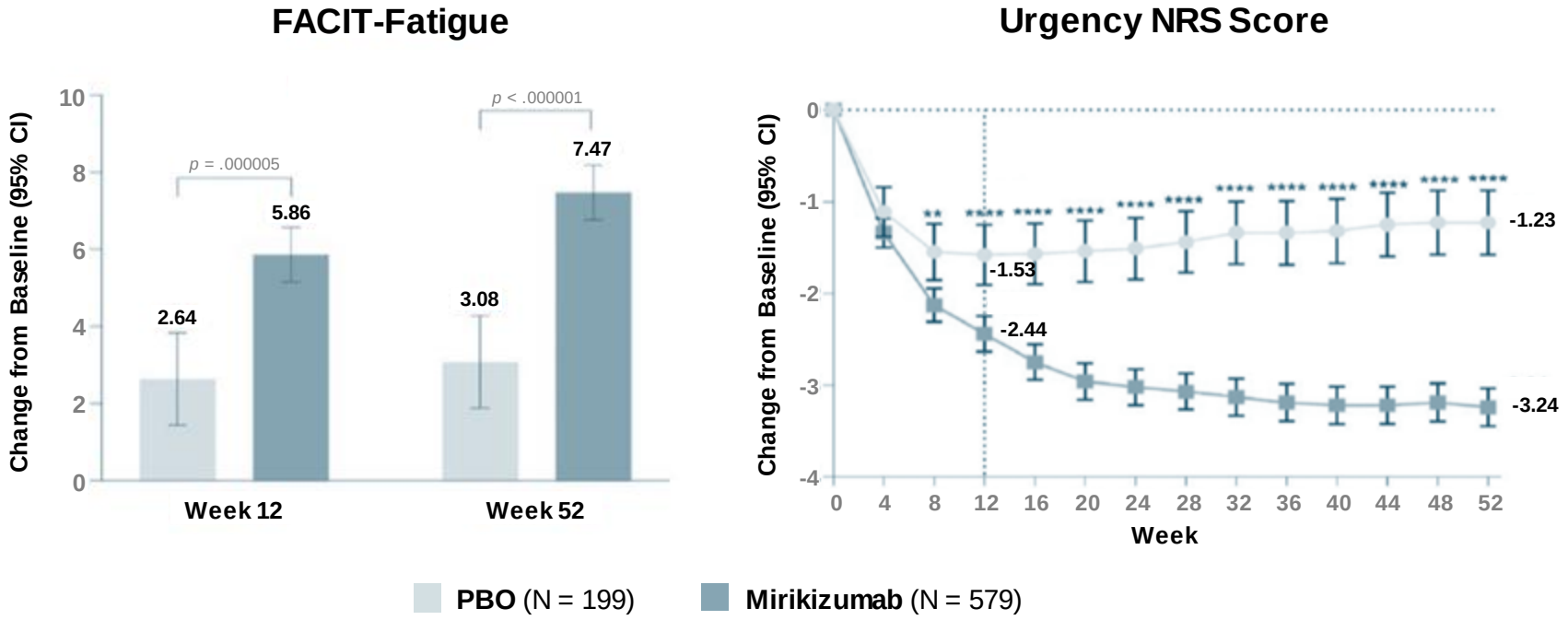
Endpoints at weeks 12 and 52 point estimate [95% CI]	Induction (week 12)		Between group diff. (RZB 1200 mg vs PBO)	Maintenance (week 52)			Between group diff. (RZB 180 mg vs PBO)	Between group diff. (RZB 360 mg vs PBO)
	PBO IV	RZB 1200 mg IV		PBO (withdrawal) SC	RZB 180 mg SC	RZB 360 mg SC		
No abdominal pain	26.5 [21.7, 31.3]	35.8 [32.1, 39.4]	9.3** [3.4, 15.3]	29.5 [22.9, 36.1]	46.9 [39.6, 54.2]	37.8 [30.8, 44.8]	17.0*** [7.4, 26.7]	8.2 [-1.3, 17.7]
No bowel urgency	27.7 [22.8, 32.6]	44.1 [40.3, 47.9]	16.3*** [10.3, 22.4]	31.1 [24.4, 37.9]	53.6 [46.3, 60.9]	49.4 [42.2, 56.6]	22.6*** [13.1, 32.2]	18.4*** [8.8, 28.0]
No tenesmus	30.2 [25.2, 35.1]	48.7 [44.9, 52.6]	18.6*** [12.4, 24.8]	23.5 [17.4, 29.6]	36.9 [29.8, 43.9]	36.8 [29.8, 43.8]	13.1** [4.6, 21.7]	14.4** [5.7, 23.0]
No fecal incontinence	58.2 [52.8, 63.5]	70.5 [67.0, 74.1]	12.5*** [6.2, 18.8]	30.6 [23.9, 37.3]	41.3 [34.1, 48.6]	39.6 [32.5, 46.6]	10.4* [1.8, 19.0]	9.8* [1.2, 18.5]
No nocturnal bowel movement	43.1 [37.7, 48.5]	67.3 [63.7, 70.9]	24.2*** [17.9, 30.5]	30.1 [23.4, 36.7]	41.9 [34.7, 49.1]	43.5 [36.3, 50.6]	12.0** [3.3, 20.6]	14.8*** [6.1, 23.5]
No sleep interruption	40.3 [35.0, 45.6]	62.3 [58.6, 66.0]	22.0*** [15.6, 28.4]	30.1 [23.4, 36.7]	39.7 [32.5, 46.8]	44.0 [36.9, 51.2]	9.5* [0.9, 18.1]	15.3*** [6.6, 24.0]
Comprehensive symptom resolution	9.5 [6.3, 12.7]	21.8 [18.7, 25.0]	12.2*** 7.8, 16.7	14.2 [9.1, 19.3]	23.5 [17.3, 29.7]	19.4 [13.7, 25.1]	8.9* [1.5, 16.3]	5.7 [-1.8, 13.1]

*$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$

Tinoco da Silva Torres J, et al. *J Crohns Colitis*. 2024;18(Supplement 1):i214-i215.

CME OUTFITTERS

IL-23is and Fatigue and Bowel Urgency in Moderate-to-Severe CD – VIVID-1 Trial (MIRI)



**$p < 0.01$, ****$p < 0.0001$

FACIT-Fatigue = functional assessment of chronic illness therapy– fatigue; NRS = numeric rating scale.

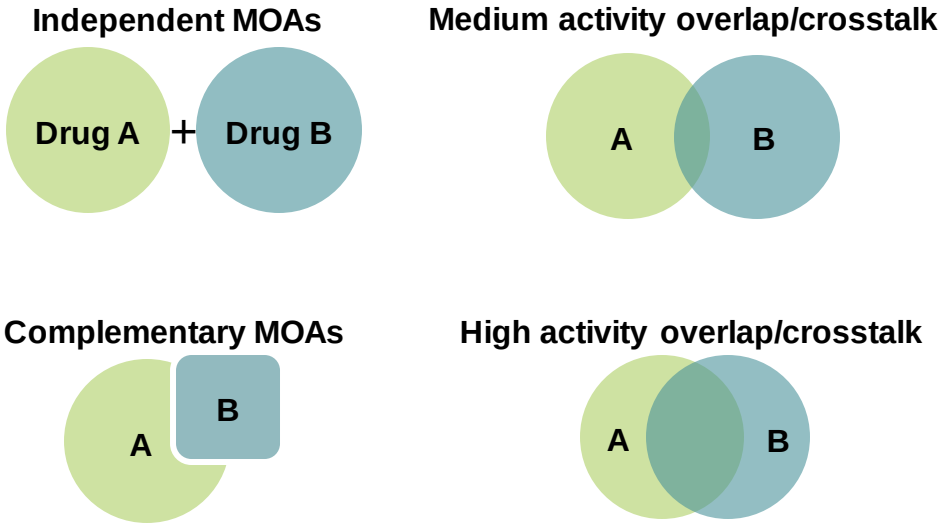
Travis S, et al. *J Crohns Colitis*. 2024;18(Supplement 1):i21-i23.

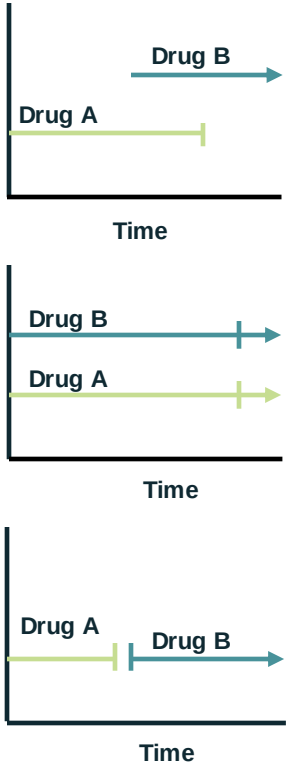
CME OUTFITTERS

How do we position IL-23 therapies in practice?

Faculty Discussion

Considerations for Combination Therapy





MOA = mechanism of action.
Adapted from Stalgis C, et al. *Gastroenterology*. 2021;161(2):394-399.

CME OUTFITTERS

Advanced Combination Therapy

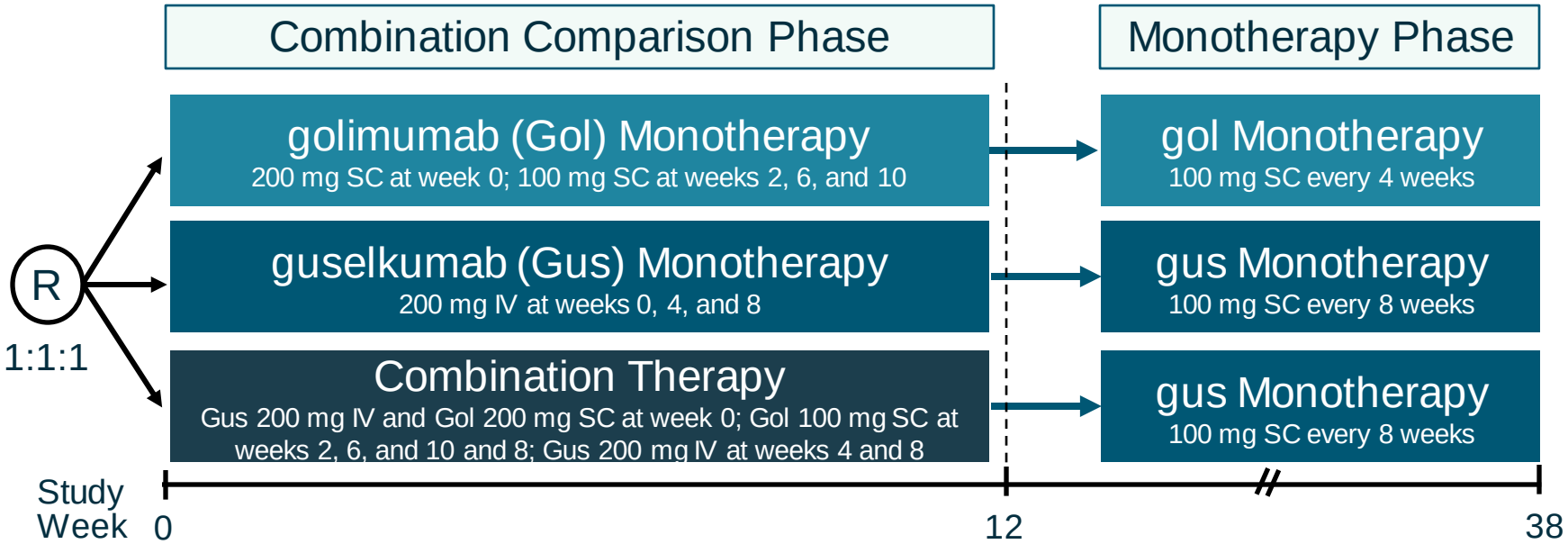
- Anti-IL-23 + anti-TNF
  - VEGA
  - DUET-CD
  - DUET-UC
- Anti-integrin + anti-TNF + methotrexate
  - EXPLORER

Solitano V, et al. *Gastroenterol Hepatol (NY).* 2023;19(5): 251-263. Noor NM. *Nat Rev Gastroenterol Hepatol.* 2023;20(12):761.

CME OUTFITTERS

VEGA: Golimumab, Guselkumab*, or Combination Therapy in UC

- Included TNF-naïve patients refractory to conventional therapy (e.g., immunomodulators, corticosteroids)

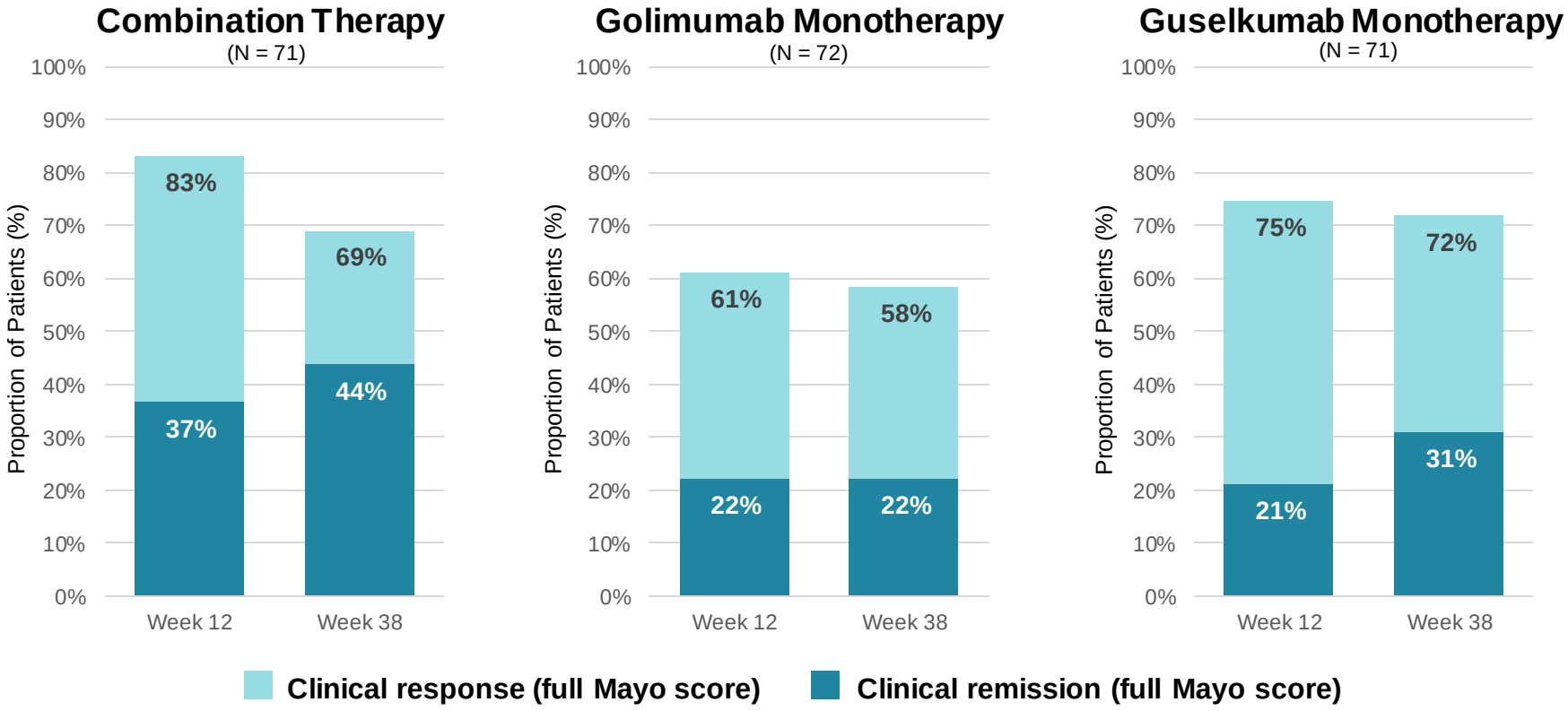


*Guselkumab is not FDA-approved for the treatment of UC.

Feagan BG, et al. *Lancet Gastroenterol Hepatol.* 2023;8(4):307-320.

CME OUTFITTERS

VEGA: Golimumab, Guselkumab*, or Combination Therapy in UC



*Guselkumab is not FDA-approved for the treatment of UC.

Feagan BG, et al. *Lancet Gastroenterol Hepatol*. 2023;8(4):307-320.

CME OUTFITTERS

How do we translate this data into clinical practice?

Faculty Discussion

How do we optimize an interdisciplinary team approach to care?

In large centers?

In community settings?

Faculty Discussion

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Consider the underlying mechanisms behind the inflammatory pathways implicated in IBD, such as those impacting IL-23 and Th17 pathways, when considering treatment options
- Differentiate between IL-23-targeted therapies and their unique characteristics to individualize and optimize patient treatment
- Increase utilization of clinical data from treatments targeting IL-23 when developing treatment plans for patients with IBD

CME OUTFITTERS


QUESTIONS
&
ANSWERS
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