

2022 Rising Star Award

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Designing Fit-for-Purpose Clinical Trials in IBD

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UNIVERSITY OF
CALGARY



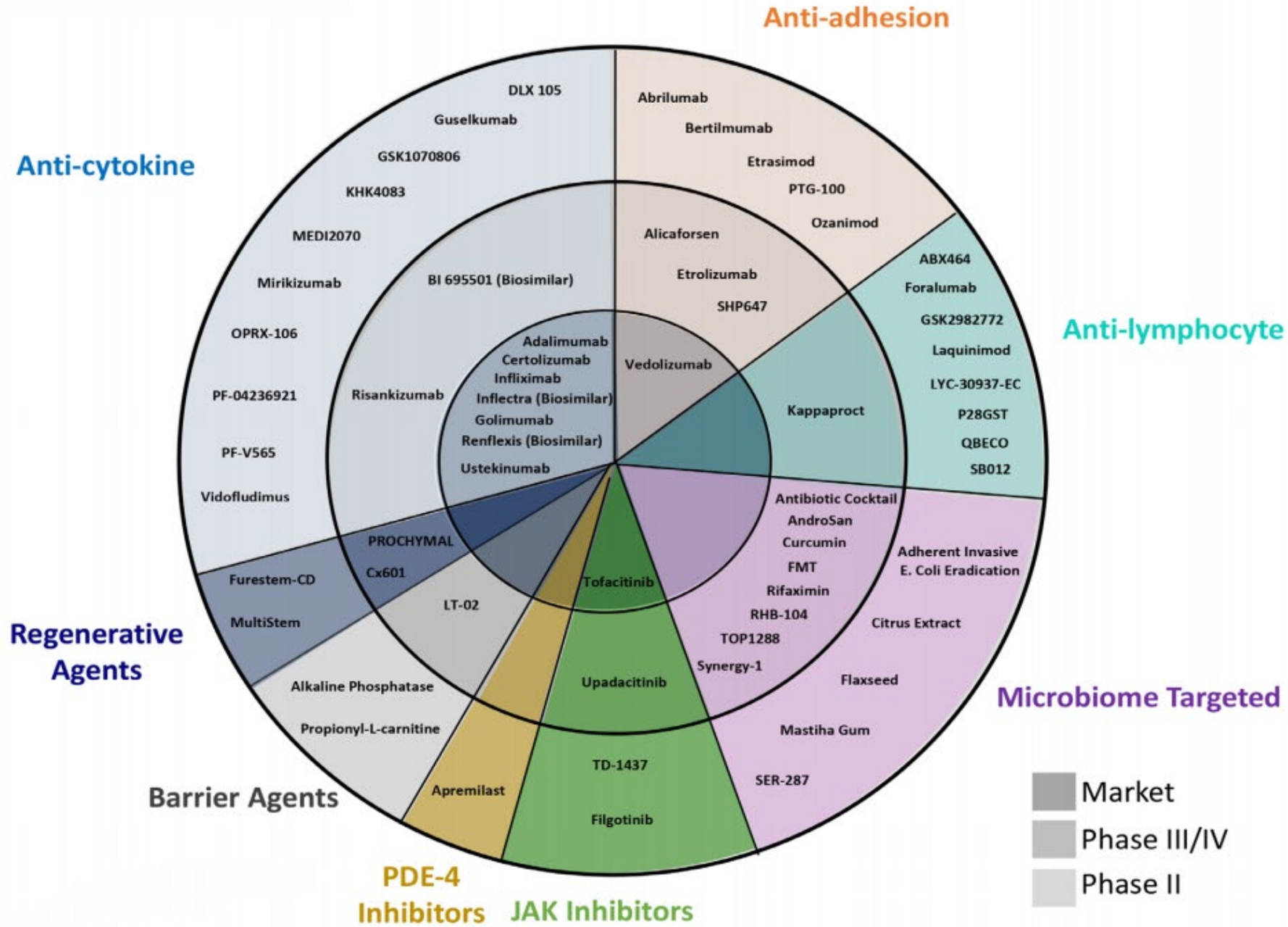
INFLAMMATORY
BOWEL DISEASE UNIT
UNIVERSITY OF CALGARY

Disclosures & Territorial Acknowledgments

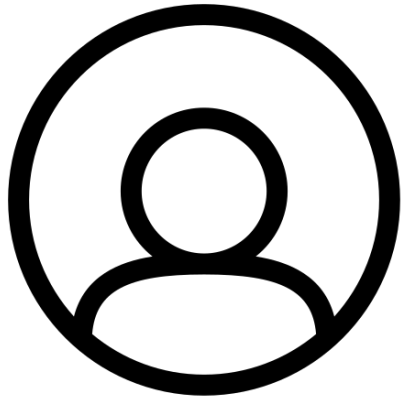
- **Consulting:** AbbVie, Alimentiv, American College of Gastroenterology, Amgen, AVIR Pharma Inc, BioJAMP, Bristol Myers Squibb, Celltrion, Ferring, Fresenius Kabi, Janssen, McKesson, Mylan, Takeda, Pendopharm, Pfizer, Roche, Sanofi
- **Speaking:** AbbVie, Amgen, AVIR Pharma Inc, Alimentiv, Bristol Myers Squibb, Ferring, Fresenius Kabi, Janssen, Takeda, Pendopharm, and Pfizer
- **Royalties:** Springer Publishing
- **Research Support:** Ferring, Pfizer

We would like to acknowledge the traditional territories of the people of the Treaty 7 region in Southern Alberta, which includes the Blackfoot Confederacy (comprising the Siksika, Piikani, and Kainai First Nations), as well as the Tsuut'ina First Nation, and the Stoney Nakoda (including the Chiniki, Bearspaw, and Wesley First Nations). The City of Calgary is also home to Métis Nation of Alberta, Region 3.

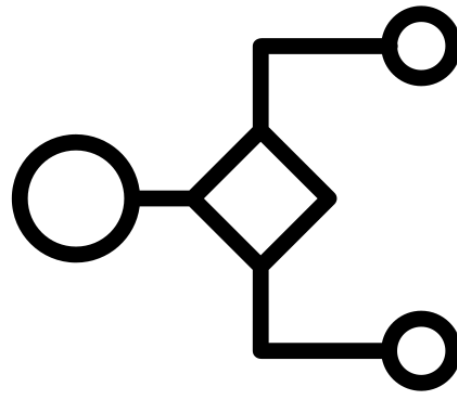




The “typical” IBD RCT



**Moderate-to-severe
adult UC or CD with
inadequate response
or intolerance to
conventional therapy**

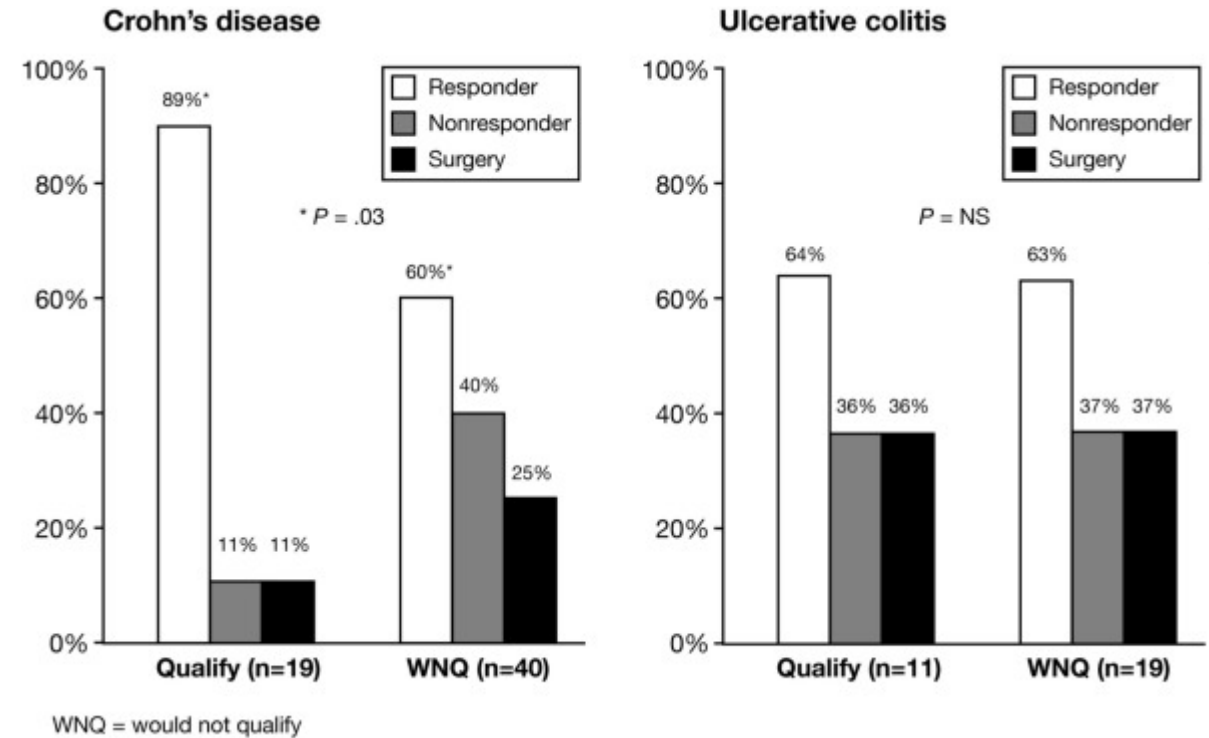
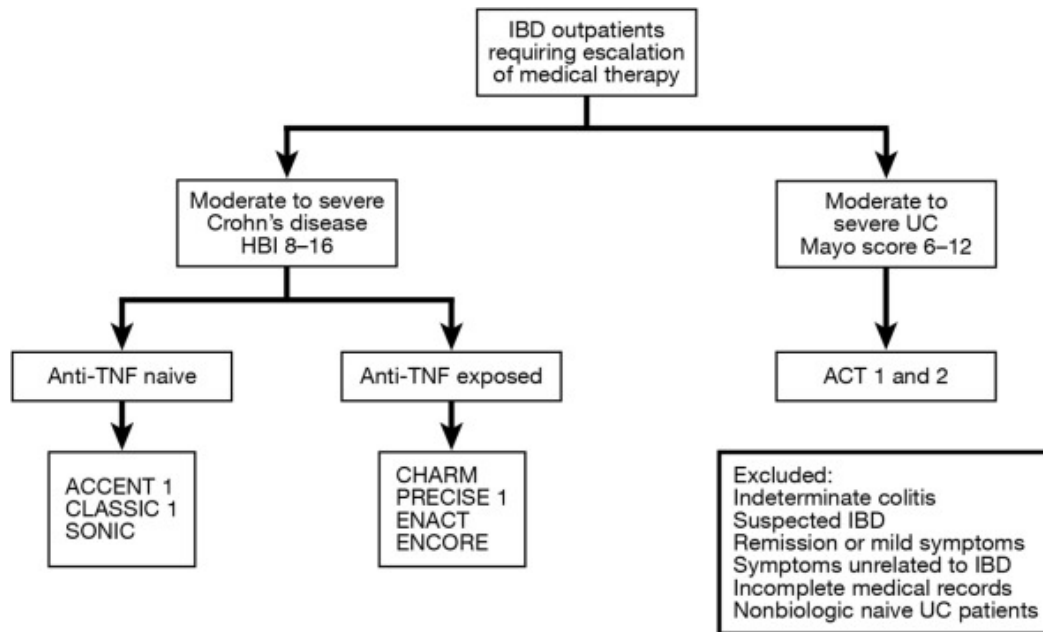


**Parallel group,
induction
responders then re-
randomized into
maintenance**



**Strict inclusion and
exclusion criteria:
pregnancy,
comorbidities,
phenotype, etc.**

Historically, RCTs have not represented patients we see in clinic

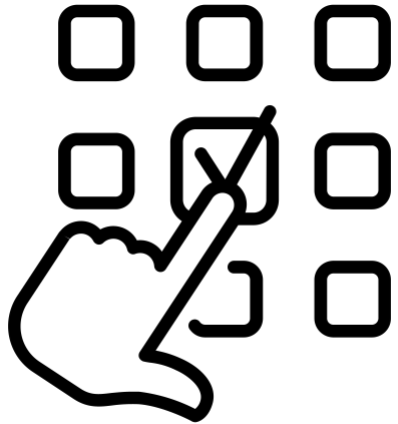




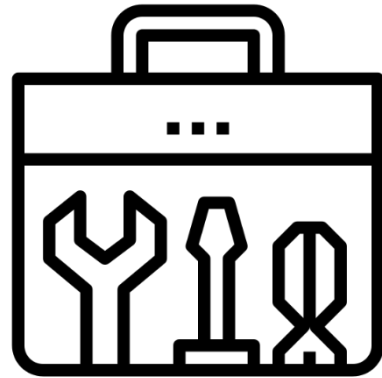
The “typical” IBD RCT vs. the “typical” IBD patient



What are the considerations for being more inclusive?



What are the appropriate eligibility criteria?



What is the appropriate trial design? Do we have the right tools?



What are the logistical implications of the trial design?



What are the patient and treatment characteristics that are appropriate?

Unmet Needs: Mild to Moderate Disease

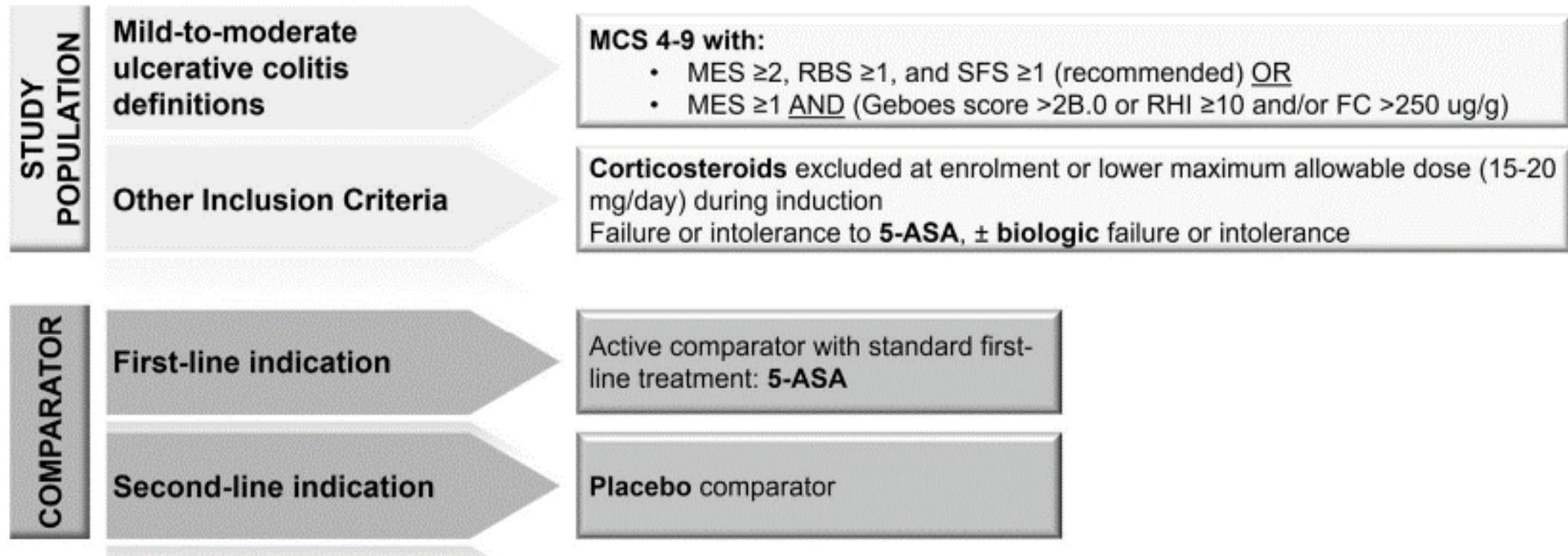
Considerations	Pros	Cons
Drug and patient factors	May be more suitable for some mechanisms of action	Uncertain natural history of milder disease phenotypes
Enroll patients on the basis of endoscopically active disease	Reduce placebo rate Increase trial efficiency	Burdensome for patients Defining “mild-to-moderate” IBD endoscopically
Allowance and handling of corticosteroids	Avoids masking relatively milder symptoms	Enrolment logistics and barriers
Using a placebo comparator	Improves assay sensitivity	Appropriateness of placebo vs. active vs. historical comparator
Defining remission and response using existing instruments	Consistency in outcome definitions	Unknown operating properties of our existing tools for mild-to-moderate disease

Sedano R *et al.* Gastroenterology. 2022;162(4)

Hanzel J *et al.* Gastroenterology. 2021;162(7)



Unmet Needs: Mild to Moderate Disease

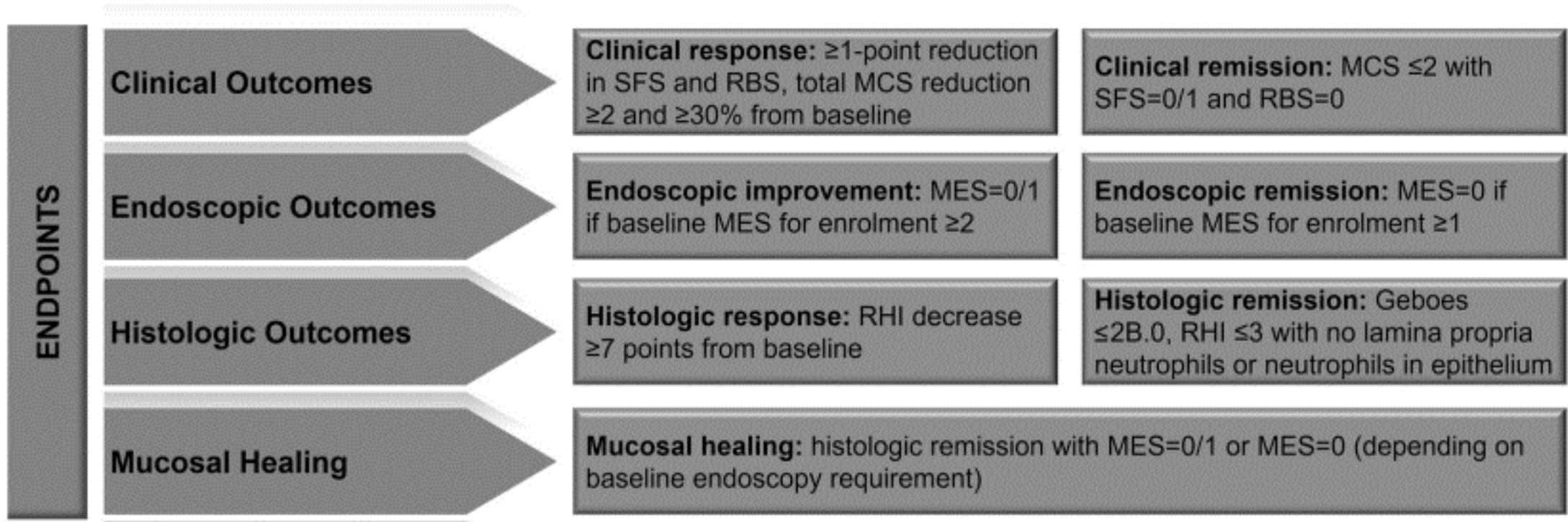


Sedano R *et al.* Gastroenterology. 2022;162(4)

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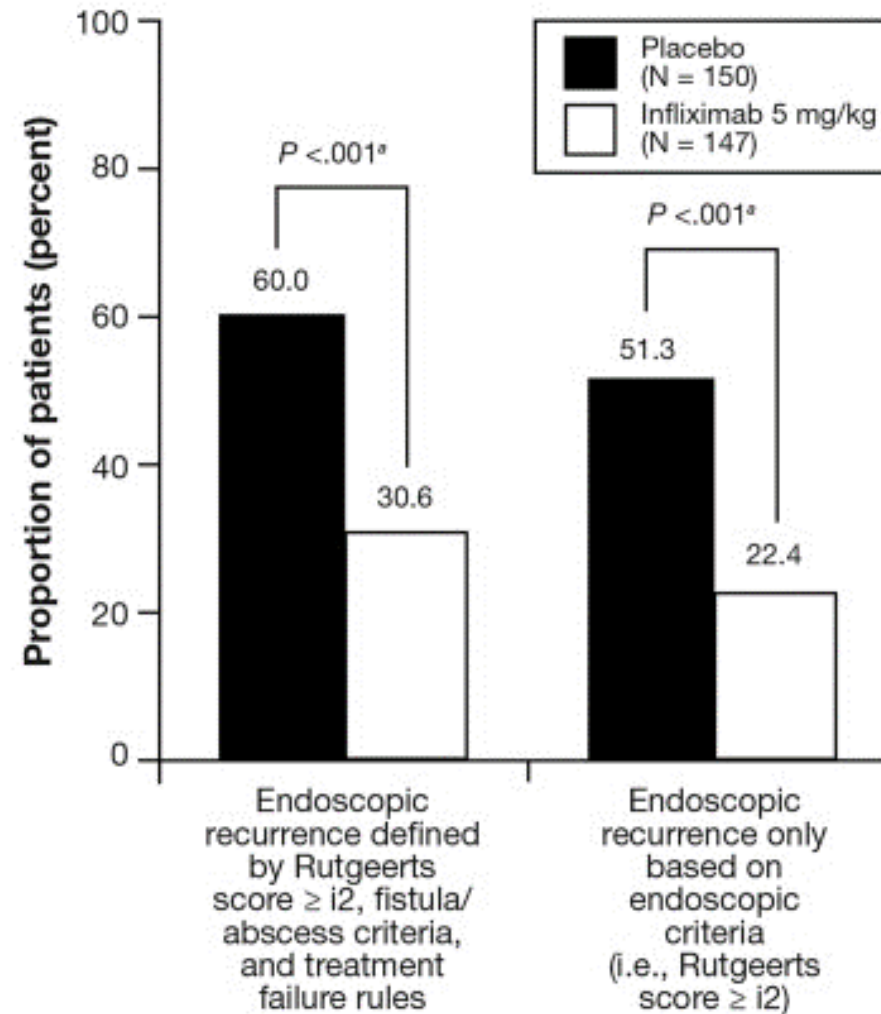
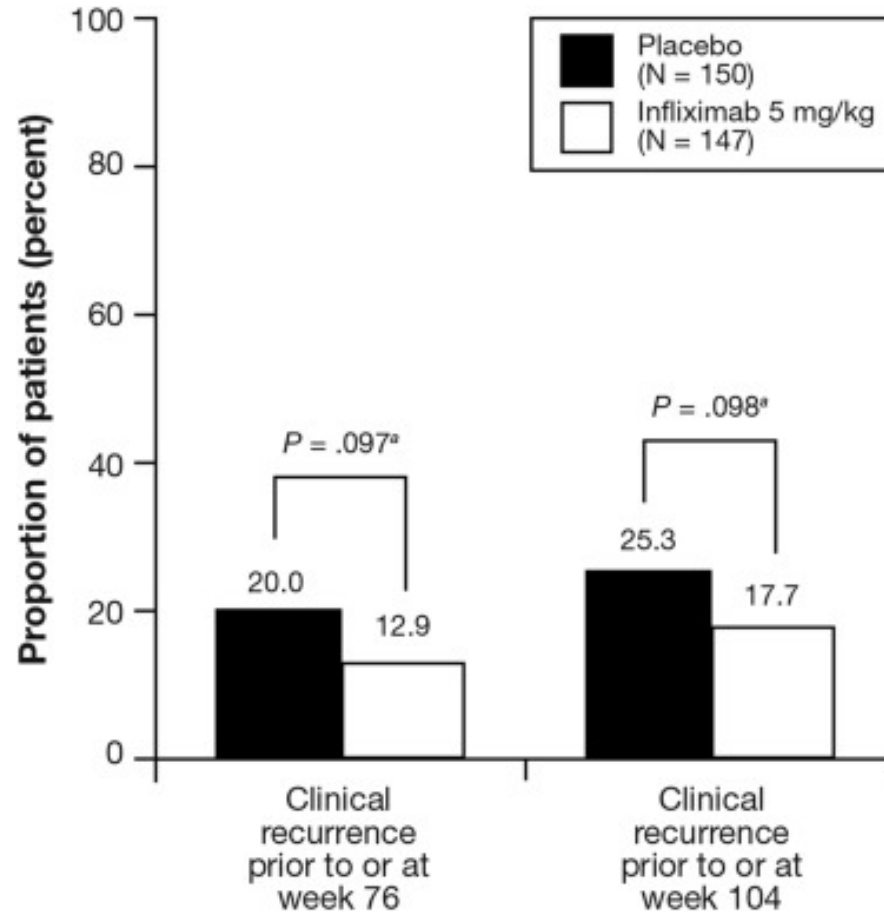
Unmet Needs: Mild to Moderate Disease



Sedano R *et al.* Gastroenterology. 2022;162(4)

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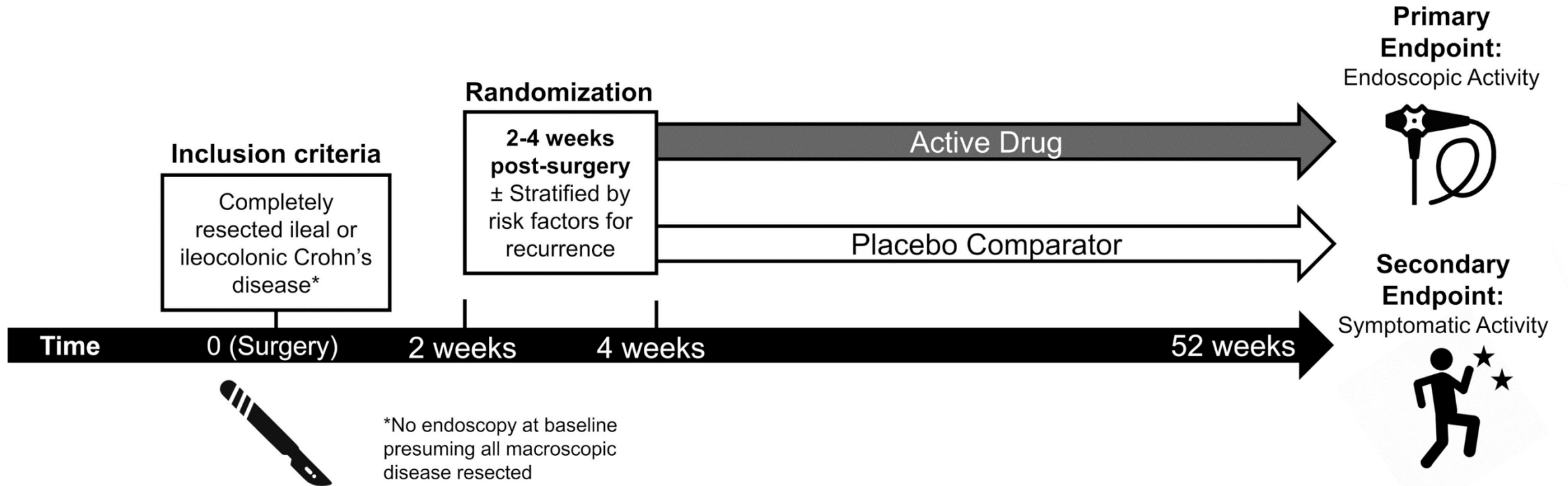
Unmet Needs: Postoperative Crohn's Disease



Regueiro M *et al.* Gastroenterology. 2016;150(7)
 Ma C *et al.* Clin Gastroenterol Hepatol. 2020;18(9)
 Hanzel J *et al.* Inflamm Bowel Dis. 2021;28(9)



Unmet Needs: Postoperative Crohn's Disease





Unmet Needs: Postoperative Crohn's Disease

Item	Reliability (ICC with 95% CI)	
	Inter-rater	Intra-rater
Anastomotic lesions		
Aphthous ulcer(s) <5mm	0.12 [0.02, 0.21]	0.48 [0.30, 0.62]
Large ulcer(s) ≥5mm	0.37 [0.24, 0.49]	0.60 [0.52, 0.69]
Neoterminal ileum lesions		
Aphthous ulcer(s) <5mm	0.17 [0.04, 0.27]	0.48 [0.25, 0.64]
Large ulcer(s) ≥5mm	0.40 [0.24, 0.55]	0.60 [0.48, 0.71]
CI confidence interval, ICC intraclass correlation coefficient		

**Primary
Endpoint:**

Endoscopic Activity

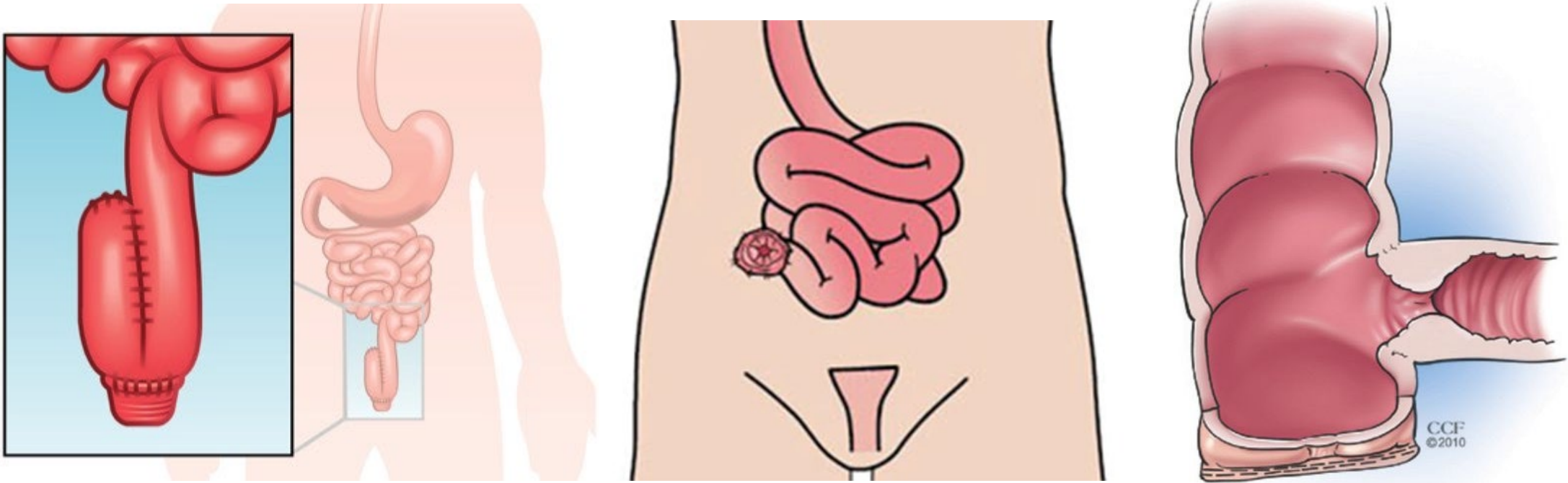


**Secondary
Endpoint:**

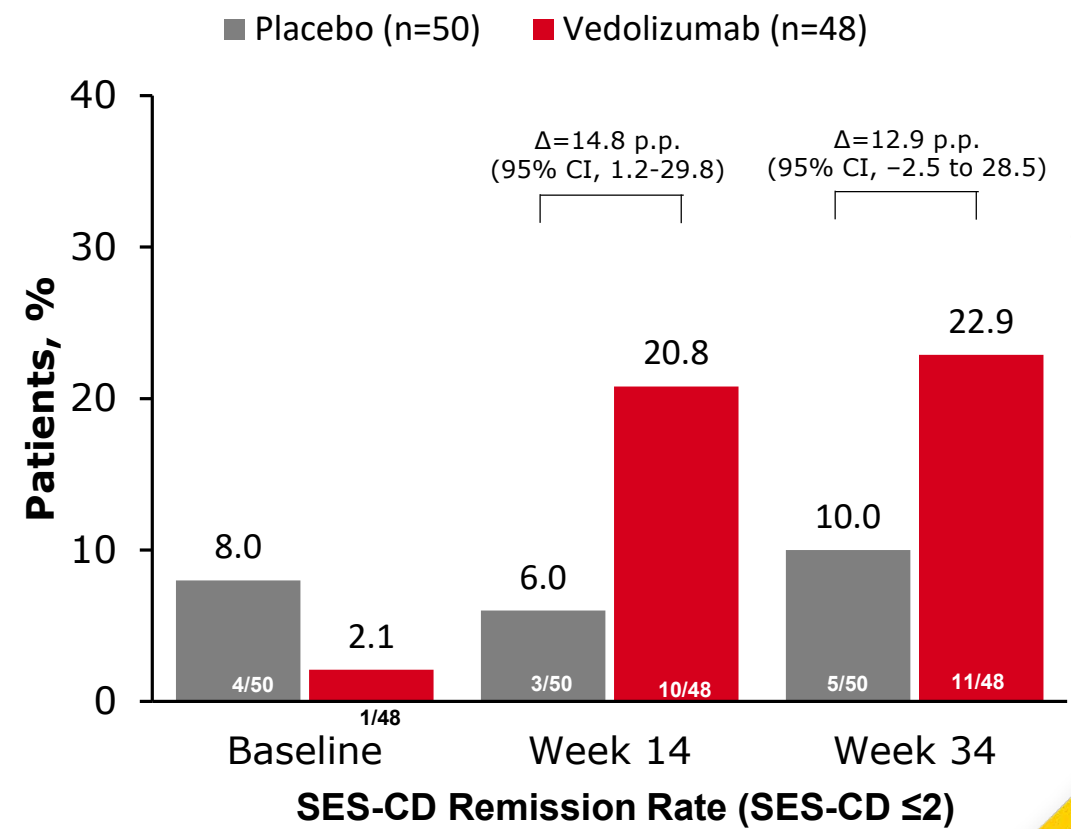
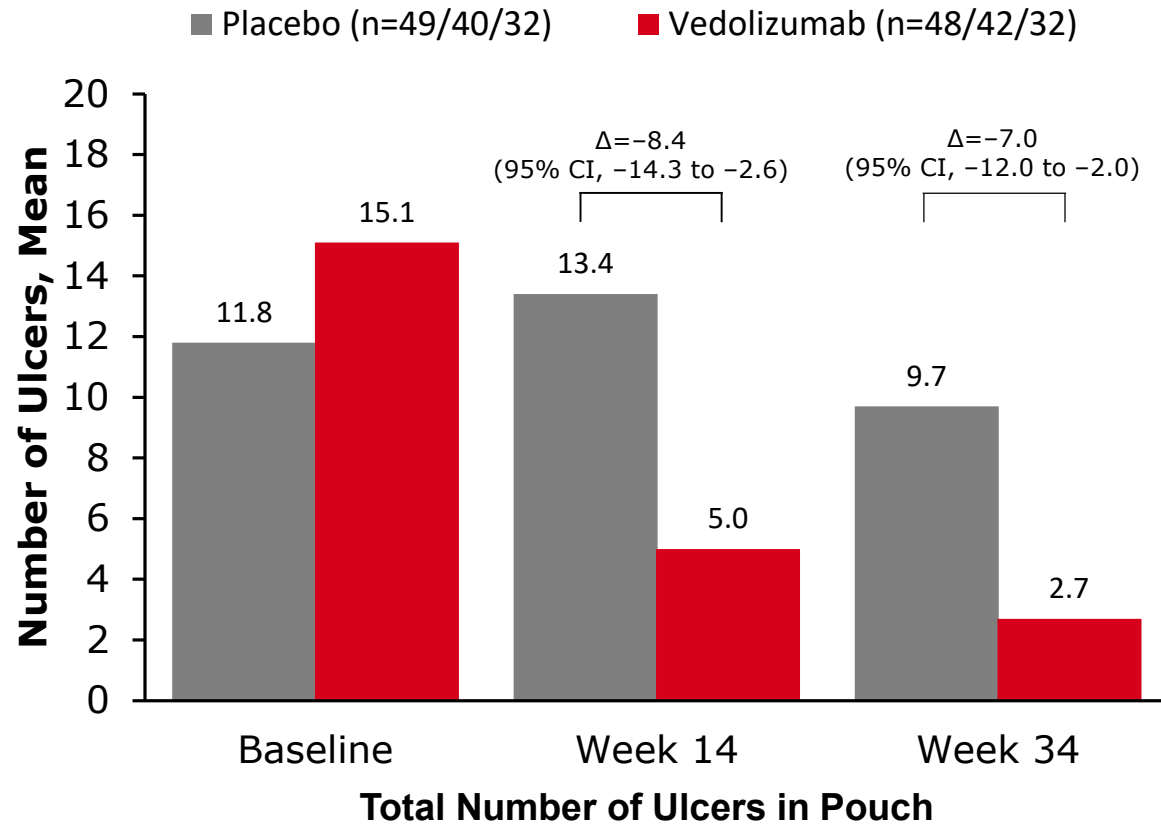
Symptomatic Activity



Unmet Needs: Different Anatomy, Different Phenotypes



Sedano R *et al.* Aliment Pharmacol Ther. 2021;53(10)
Goodsall T *et al.* J Crohns Colitis. 2020;15(1)
Rieder F *et al.* Aliment Pharmacol Ther. 2018;48(3)





Conclusions



