Northwestern

Medical Management of Ulcerative Colitis in Modern Era

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Disclosures

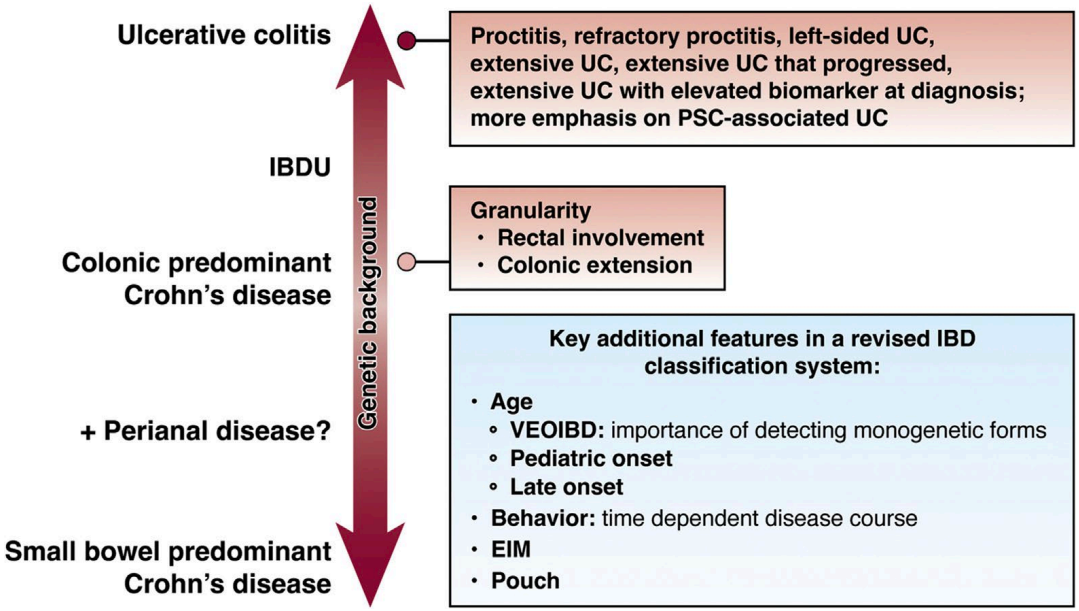
- Abbvie, Abivax, Adiso, Alimentiv, Bristol Meyer Squibb, Celltrion, Genentech, Geneoscopy, Janssen, Pfizer, Takeda

Objectives

- How do we currently ‘bucket’ UC?
- How do treatments compare across key phenotypic features or subgroups of UC?
- Can we personalize decisions using clinical phenotypes in routine practice?
- What is coming down the pipeline?

IBD Phenotypes

Set of observable characteristics of an individual resulting from the interaction of its genotype with the environment



Influenced by what we do (or don't do) during disease course

Verstockt B. et al. *Gastro* 2022

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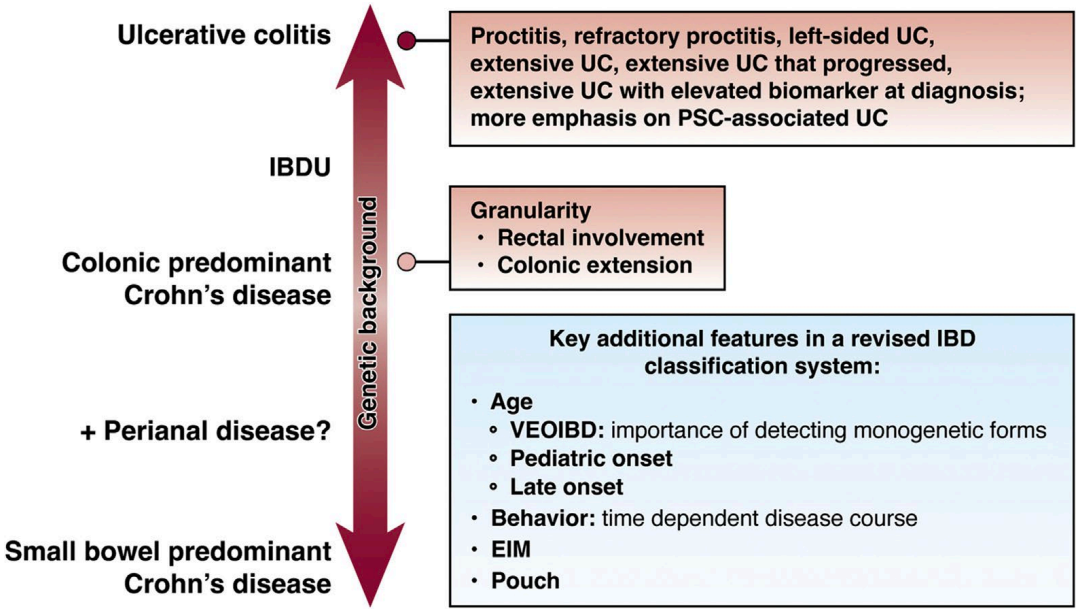


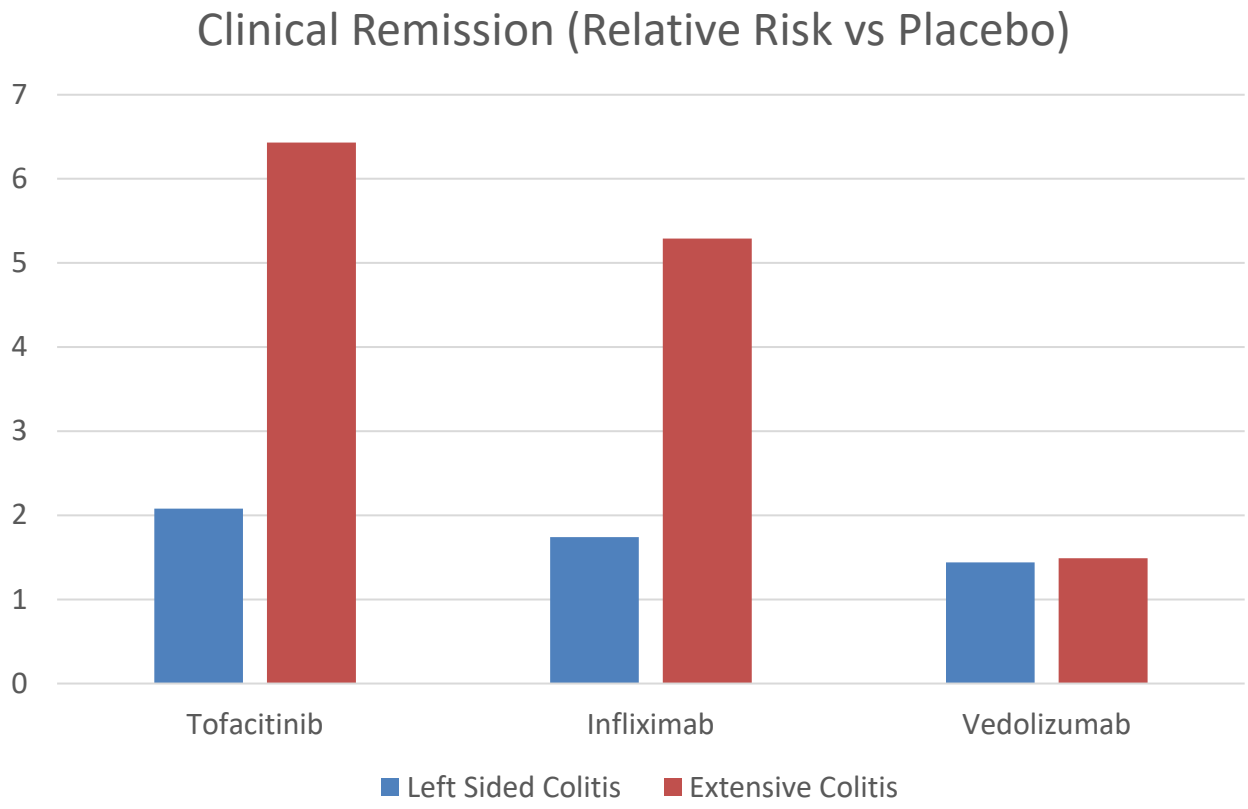
Location?

Extensive?

Influenced by what we do (or don't do) during disease course

Verstockt B. et al. *Gastro* 2022

Comparative Effectiveness of Biologics and Small Molecules based on Disease Extent in UC



Patient level meta-analysis of phase 3 trial programs – Disease extent an effect modifier of treatment response, with Infliximab and Tofacitinib being favored in extensive colitis

Vuyyuru SK et al. *EClinicalMedicine* 2024

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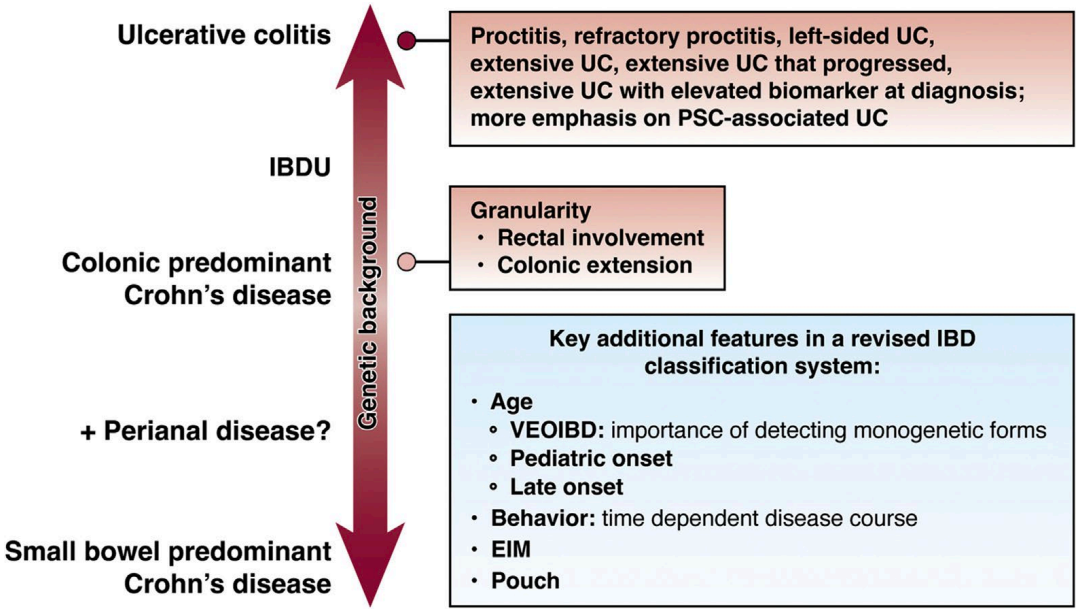


Location?

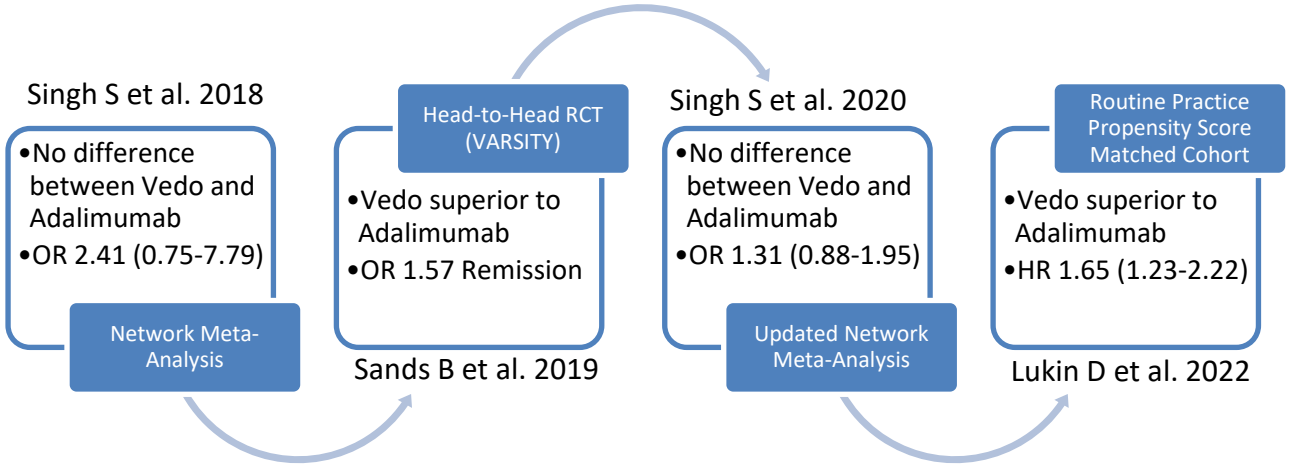
Extensive?

Exposure (Refractory)?

Influenced by what we do (or don't do) during disease course

Verstockt B. et al. *Gastro* 2022

UC Vedo vs. anti-TNF



- Network meta-analysis failed to identify a significant difference (when one exists)
- Network meta-analysis remained non-significant after including head-to-head trial
- Patient level data with propensity score matching (VICTORY) provided comparable estimates to the prospective head-to-head trial (VARSITY)
  - Sub-group of greatest benefits – moderate activity, anti-TNF naive

Biologics and Small Molecules UC

- VARSITY Trial: Vedolizumab superior to Adalimumab
  - Anti-TNF/biologic naïve, moderate severity
- Propensity matched: Infliximab superior to Vedolizumab
  - Infliximab higher rates of 1-year remission
  - Limited to anti-TNF/biologic naïve
  - Infliximab evidence for prevention of colectomy/hospitalization
- NMA: Infliximab ranked highest efficacy first line therapy, and Upadacitinib highest second line
- NMA: Vedolizumab ranked highest safety

Dulai PS et al. *Gastroenterology* 2024

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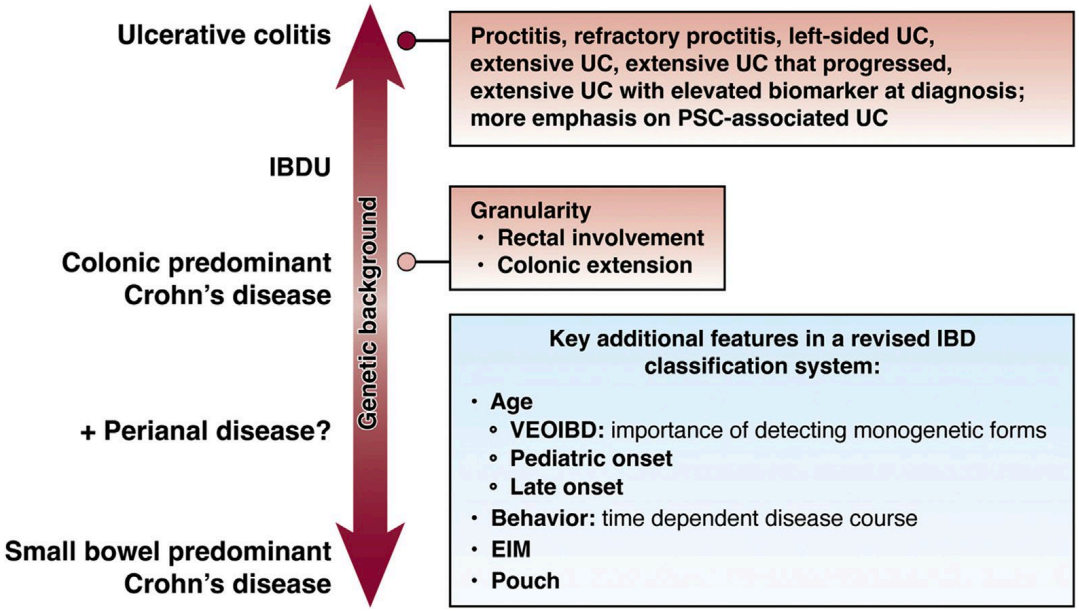

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Concomitant Ds/EIMs?

Influenced by what we do (or don't do) during disease course

Verstockt B. et al. *Gastro* 2022

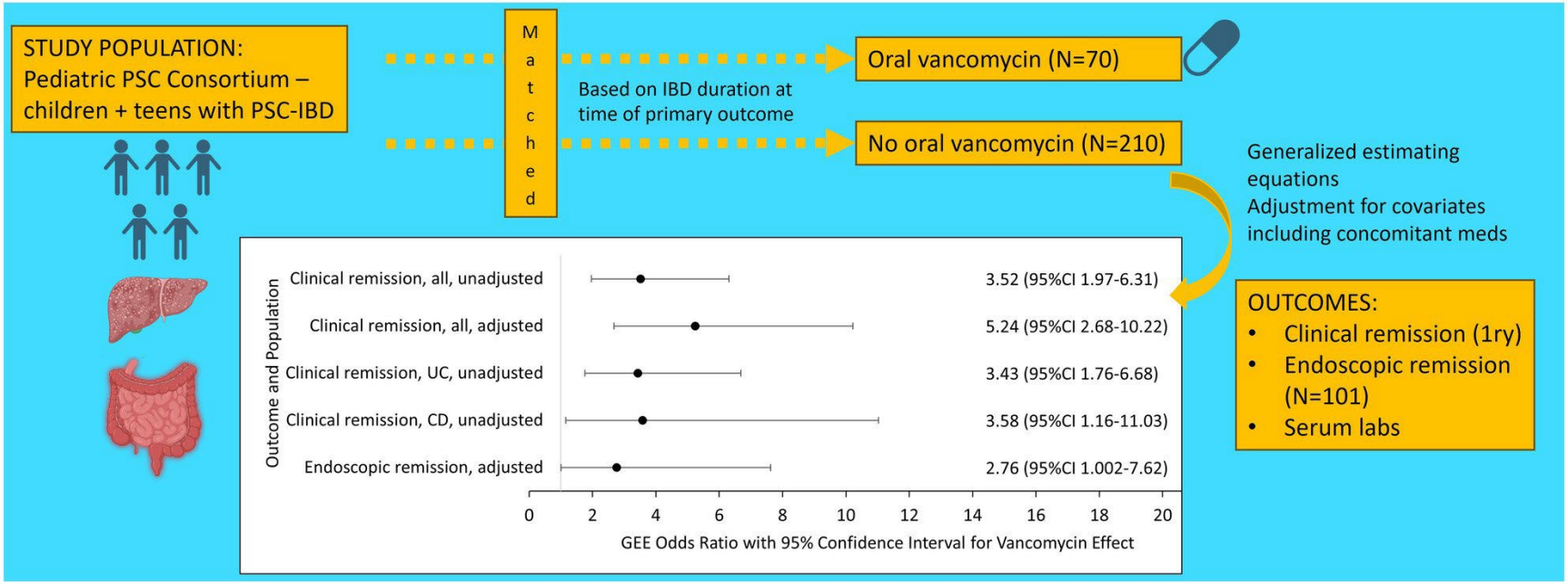
Biologics and Small Molecules for Treatment of EIMs

	Anti-TNF				Anti-Integrin	IL12/23	JAK
	IFX	ADA	CZP	GOL	VDZ	UST	TOF/UPA
Arthritis							
SpA							
PG							
Uveitis							
EN							

Greuter T et al. Gut 2022

PSC-IBD

Oral vancomycin is associated with improved inflammatory bowel disease clinical outcomes in primary sclerosing cholangitis-associated inflammatory bowel disease (PSC-IBD): A matched analysis from the Paediatric PSC Consortium



Ricciuto, et al. *Aliment. Pharmacol. Ther.*

AP&T

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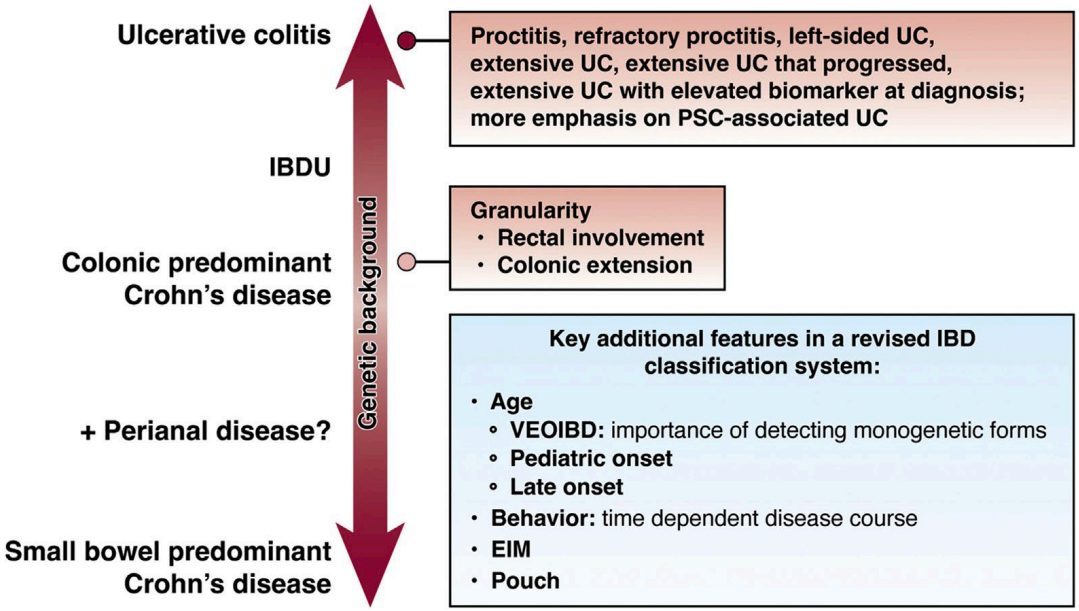

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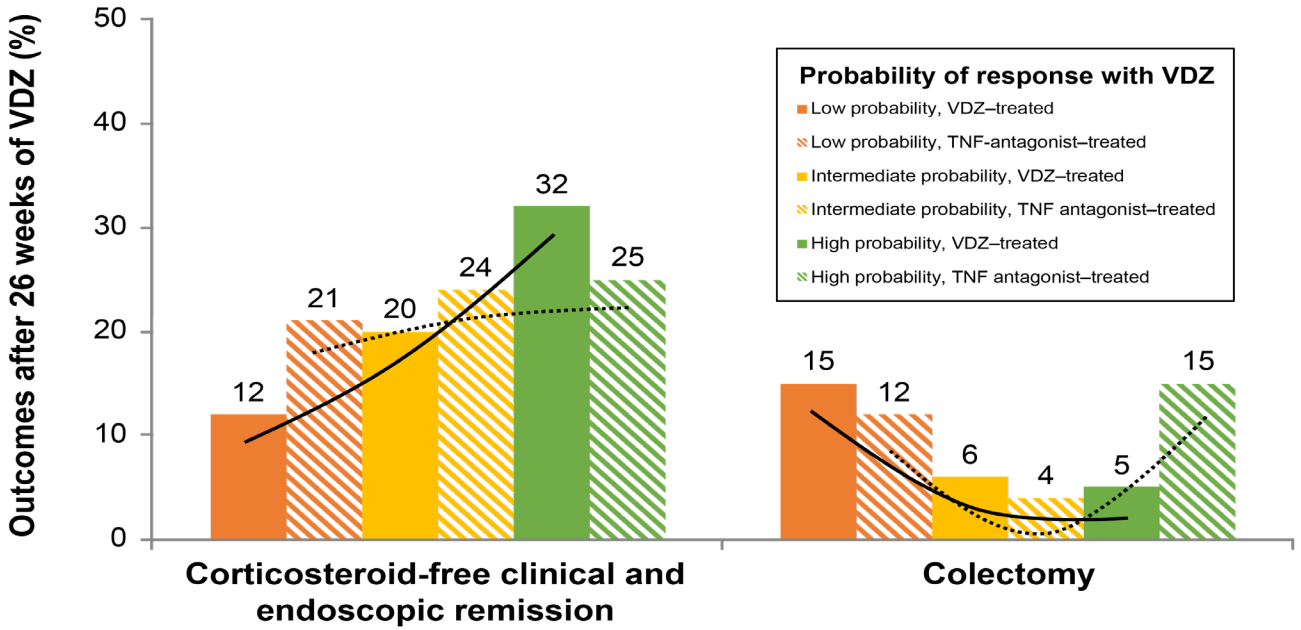
Clinical Decision Support Tools?

Influenced by what we do (or don't do) during disease course

Verstockt B. et al. *Gastro* 2022

VICTORY cohort treatment outcomes stratified by UC CDST

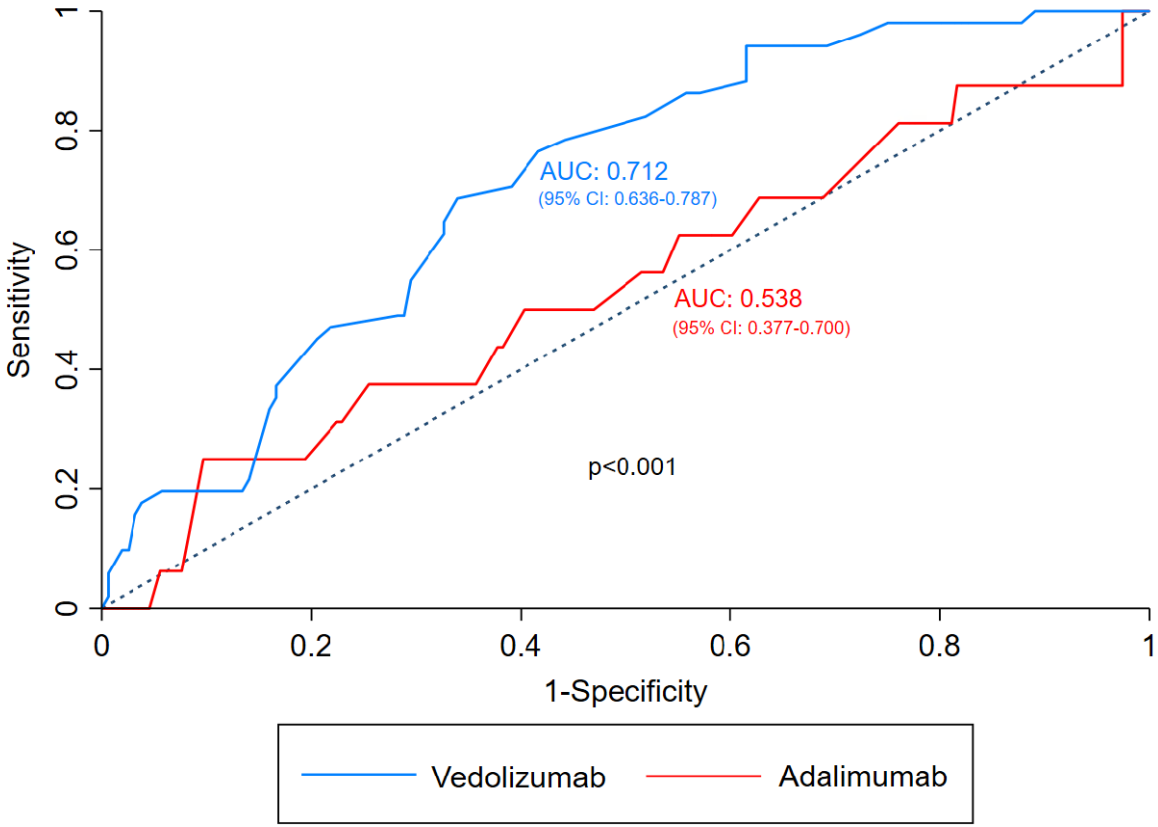
Disease duration ≥2 years	No prior TNF antagonist	Baseline endoscopy moderate activity	Baseline albumin concentration
+3 points	+3 points	+2 points	+0.65 points per unit (g/L)



CDST: clinical decision support tool; TNF: tumor necrosis factor; VDZ: vedolizumab.
Dulai PS, et al. *Clin Gastroenterol Hepatol.* 2020;18:2952–961.

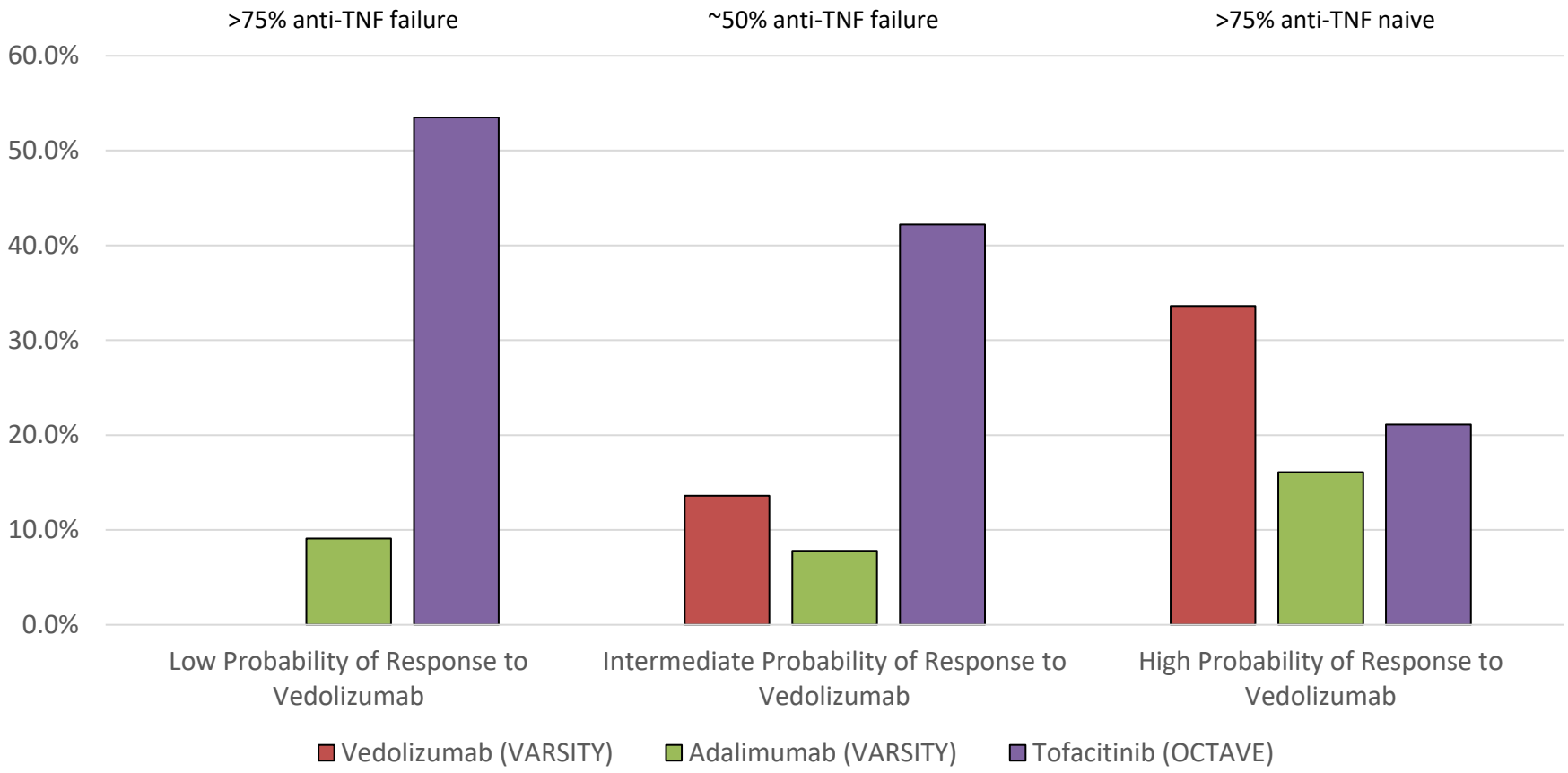
VARSITY (head-to-head RCT) validation of vedolizumab UC CDST

Comparative accuracy of the vedolizumab CDST for histoendoscopic mucosal improvement with vedolizumab vs adalimumab in ulcerative colitis



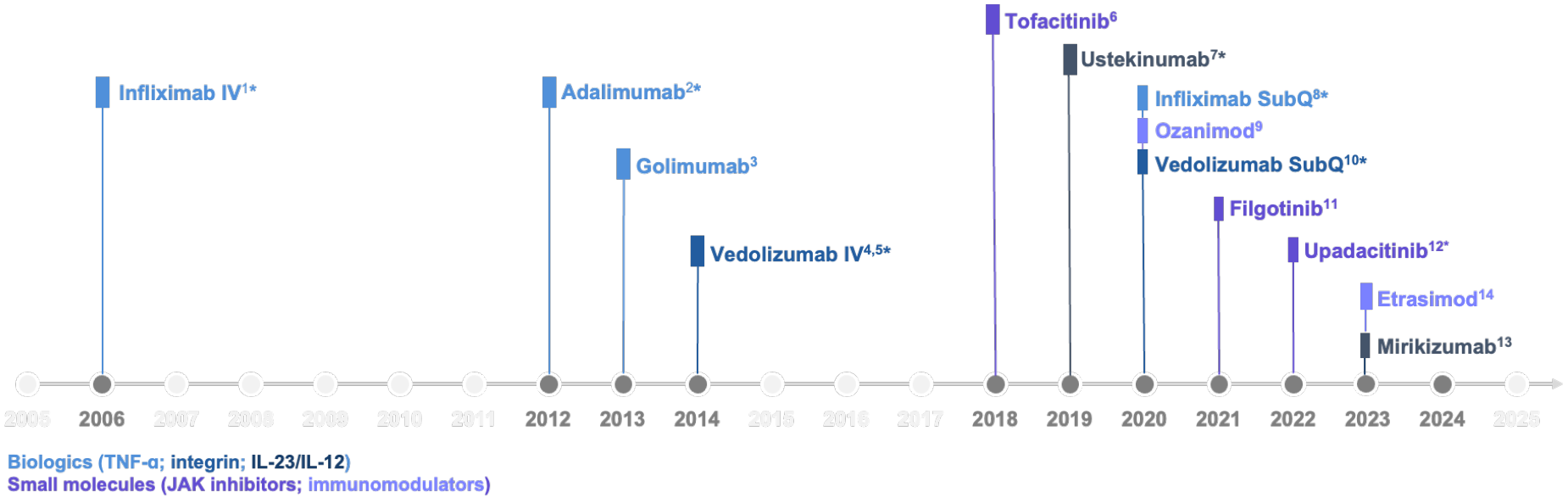
Dulai PS, et al. *Inflamm Bowel Dis.* 2021

Vedo-UC CDST Individualized Choice of Therapy



Dulai PS, et al. *Inflamm Bowel Dis.* 2021

Number of Advanced Therapies in UC is growing considerably

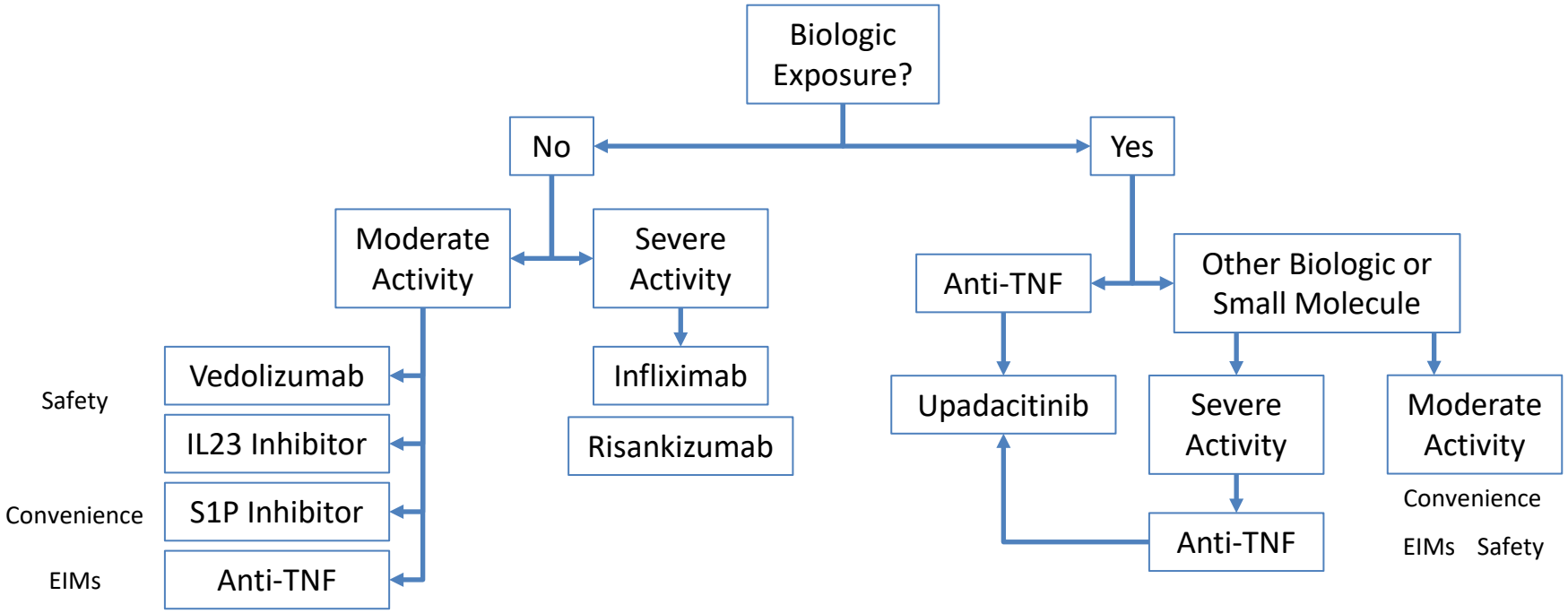


Overall landscape is changing

	S1PR Modulator		JAK1 Inhibitors		Anti-α4β7	Anti-TNFα		Anti-IL12/23	Anti-IL23
Molecule Manufacturer US Launch Year	**Zeposia® BMS 2021**	**Velsipity® Pfizer 2023**	**Xeljanz® Pfizer 2019**	**Rinvoq® AbbVie 2022**	**Entyvio® Takeda 2014**	**Remicade® Janssen 2005**	**Humira® AbbVie 2012**	**Stelara® Janssen 2019**	**Omvoh® Eli Lilly 2023**
Molecule	ozanimod	etrasimod	tofacitinib	upadacitinib	vedolizumab	infliximab	adalimumab	ustekinumab	mirikizumab
ROA	Oral	Oral	Oral	Oral	IV	IV	SC	IV/SC	IV/SC
Pre-Initiation Requirements	ECG, Ocular, LFTs, CBC, VZV Abs	ECG, Ocular, Skin,LFTs, CBC, VZV Abs	CBC, LFT, TB	CBC, LFT, TB	None	TB	CBC, LFT, TB	TB	TB, LFT
Safety	Mild to Moderate AE	Mild to Moderate AE	Black Box Warnings	Black Box Warnings	Warning: Allergic reactions and infections	Black Box Warnings	Black Box Warnings	Warning: Allergic reactions and infections	Warning: Allergic reactions and infections
Clinical Remission Rate (Induction)	**10 weeks** 18% 6%	**12 weeks** 27% 7%	**8 weeks** 17% 4%	**8 weeks** 33% 4%	**6 weeks** 17% 5%	**8 weeks** 38% 15%	**8 weeks** 17% 9%	**8 weeks** 19% 7%	**12 weeks** 24% 15%
Clinical Remission Rate among Induction Responders (Maintenance)	**52 weeks** 37% 19%	**52 weeks** 49% 17%	**52 weeks** 34% 11%	**52 weeks** 42% 12%	**52 weeks** 42% 16%	**54 weeks*** 35% 17%	**52 weeks*** 17% 9%	**52 weeks** 45% 26%	**52 weeks** 51% 27%

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across trials.

What's my Algorithm?



- Oral Vancomycin for PSC-UC patients (250-500mg BID)
- Concomitant IMM for anti-TNF (particularly in severe UC or those with EIMs)
- Consider utility of dose optimization attempts versus switch to alternative therapy (small molecules)
- Don't reduce JAK inhibitor dose until they are in remission

Conclusion

- Clinical phenotypes can help guide decisions on treatment selection and personalization
- Need to intervene at appropriate window
- ‘Matrix’ of phenotypic features can be addressed with evolving decision support tools for advanced therapies
- Substantial growth in the space for UC