



GHAPP

Gastroenterology & Hepatology
Advanced Practice Providers

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Advanced Practice Providers

Positioning Biologics in IBD

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Disclosures

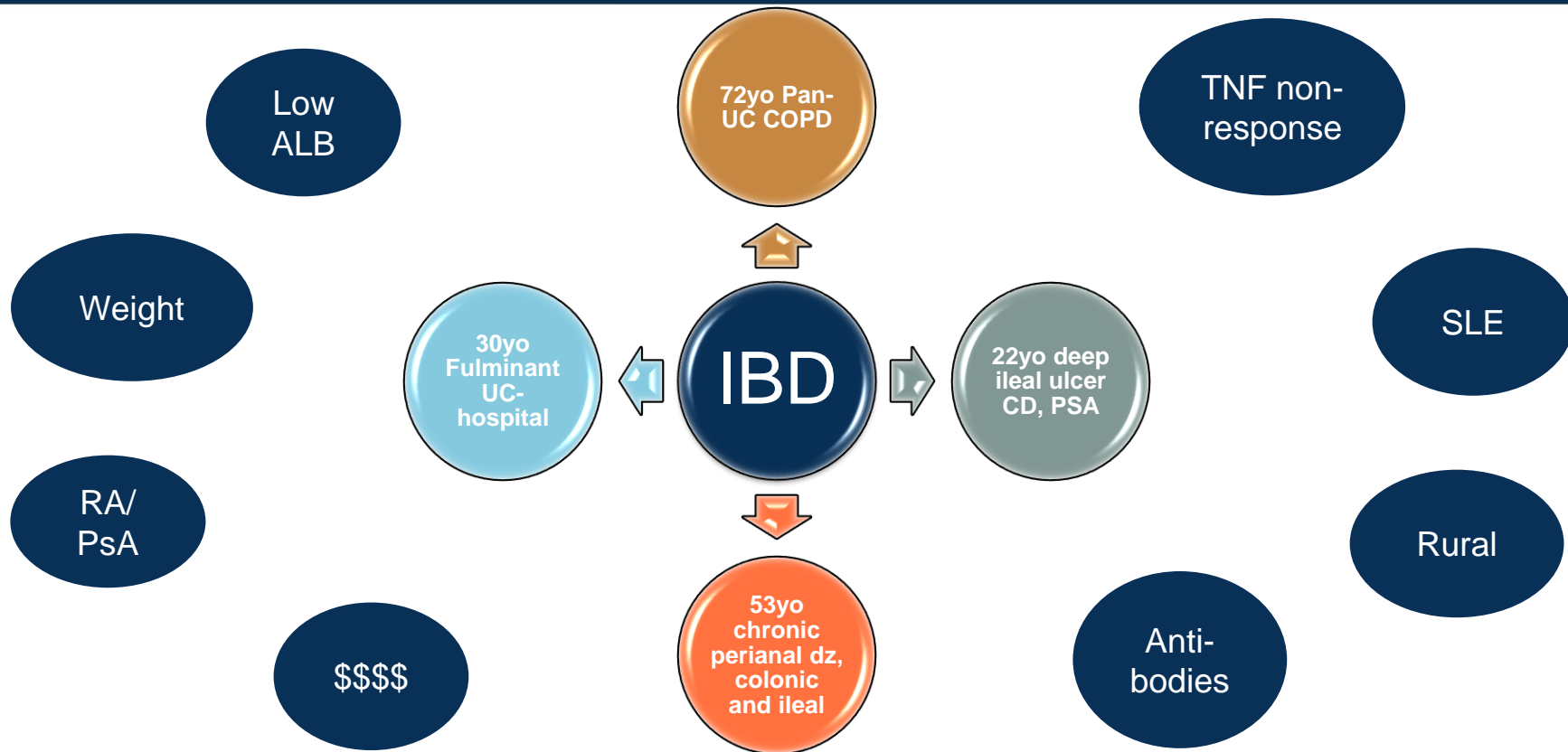
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Disclosures

Heidi Drescher, MMS, PA-C

Speakers Bureau: Abbvie, Clinical Area- Immunology/IBD

IBD Is Heterogeneous – So Are Patient Situations

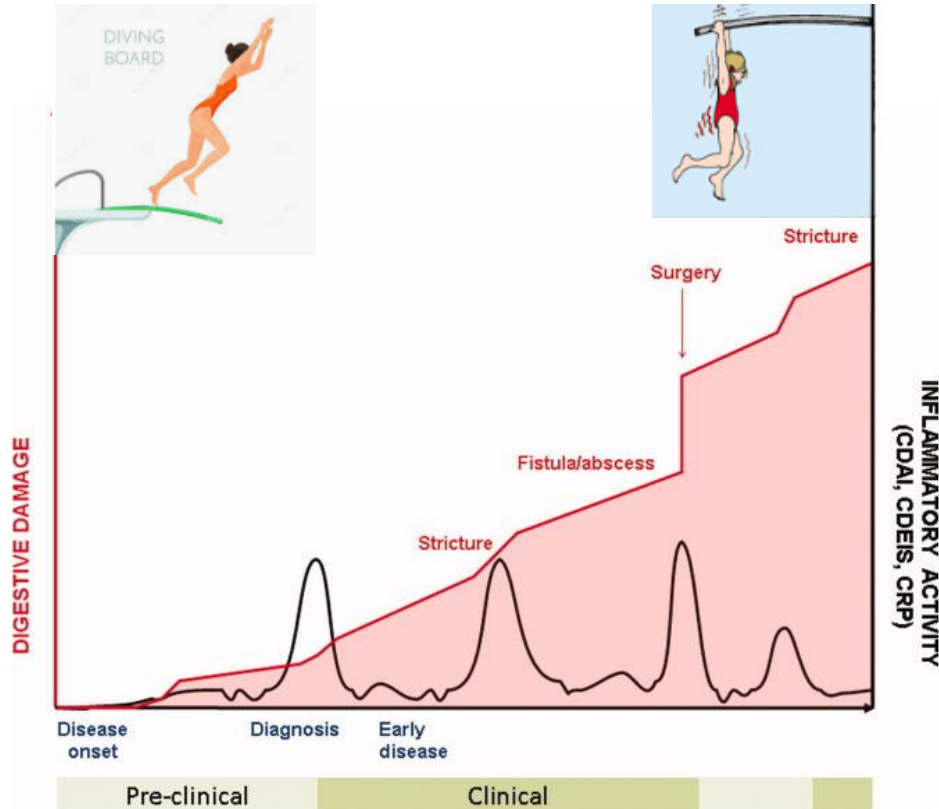


Objectives

- Discuss importance of **Prognosticating**
- Illustrate importance of **Timing** of Medication Introduction
- Review Medication **Efficacy** and **Safety** Profiles
- Examine **Comorbidities**
- Practical **Consideration\$**



Thoughtful Positioning Preserves Organs



Prognosticating = Severity

- CD-High Risk

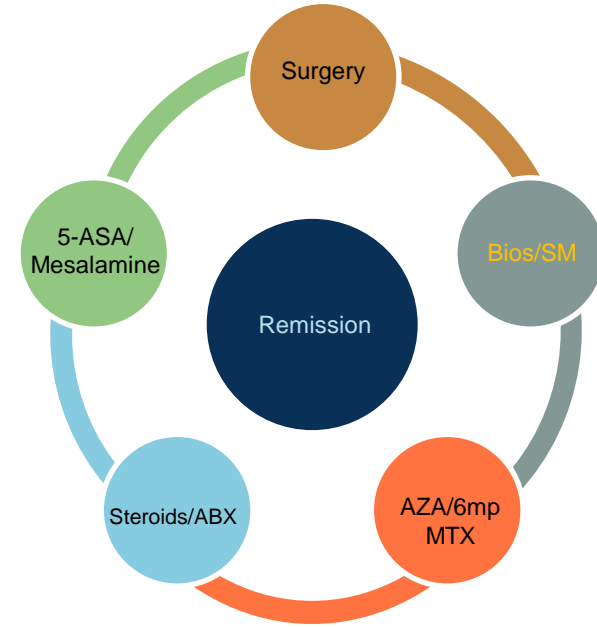
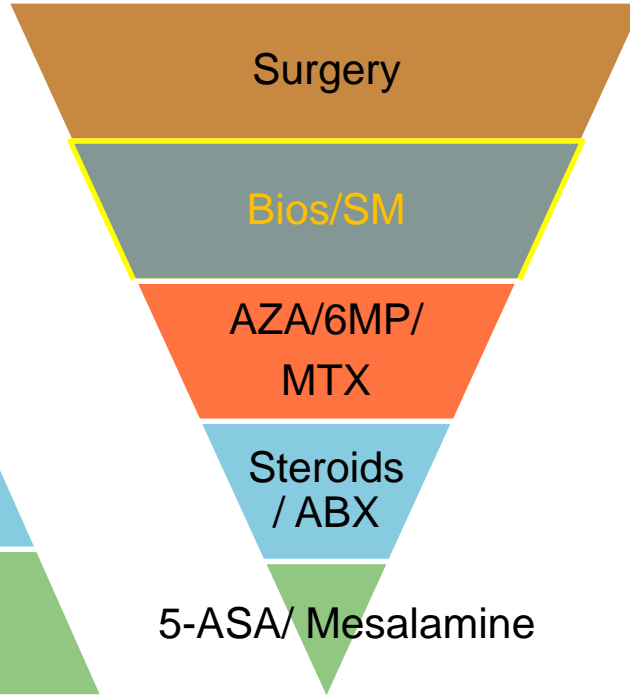
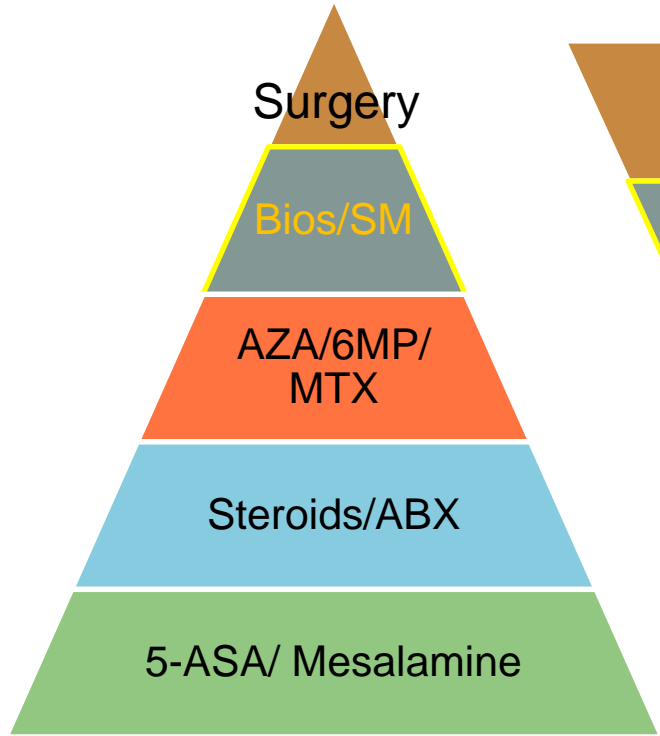
- <30yo
- Deep Ulcers
- Extensive anatomical involvement
- Perianal/severe rectal disease
- Prior Surgery
- Stricture/penetrating disease

- UC-HIGH Risk

- <40yo
- Deep ulcers
- Extensive colitis
- High CRP and ESR
- Steroids at diagnosis
- Requires hospitalization
- *C. difficile*
- CMV



Timing Therapy



IBD Scenarios – Prognosticating Severity and **ACTIVITY**

- 72yo **PanUC** COPD – (1)
- **22yo deep ileal ulcer** CD, PSA (2)
- 53yo chronic **perianal dz, colonic and ileal** (2-3)
- **30yo** Fulminant **UC** – **hospital** (2)

ESTABLISH TYPE OF THERAPY YOU WILL

STEP IN WITH

Match Intensity of Treatment with the **Inflammatory Burden**

Armamentarium for Moderate to Severe Disease

Anti-TNF	Anti-integrin	Anti-interleukins	JAK	S1P1	PDE4
Infliximab & Biosims	Vedolizumab	Ustekinumab	Tofacitinib	Ozanimod	Apremilist
Adalimumab	Natalizumab	Risankizumab	Filgotininb		
Golimumab	?Etrolizumab*	Brazikumab	Updacidinib		
Certolizumab	Ontamalimab	Mirikizumab			
	Abrilumab	Guselkumab			

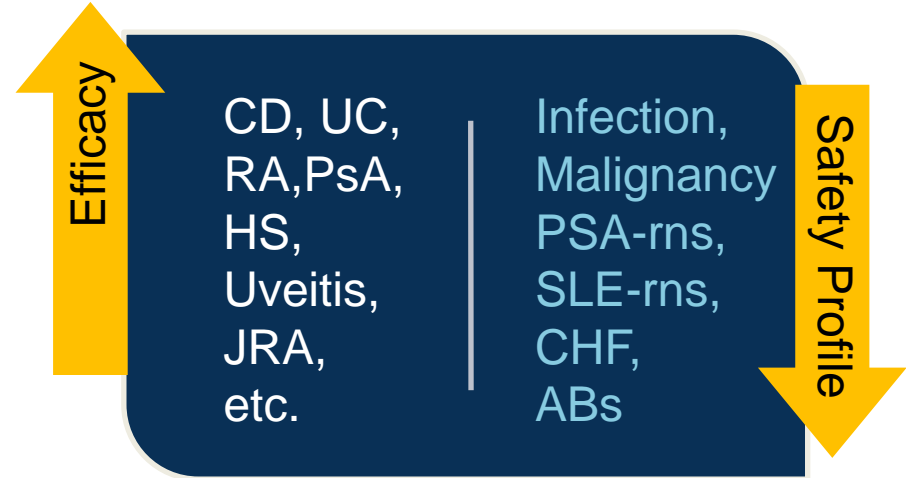
*Did not meet primary endpoint for disease Maintenance for UC in Phase 3 Trials.

ANTI-TNFs – Versatile

Inject and Infuse options

- IFX and Biosimilars
- ADA
- CTZ
- GOL

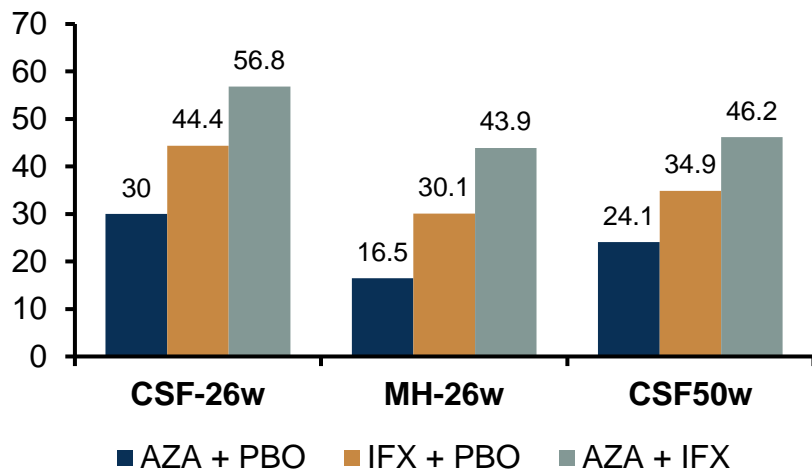
Multiple Indication



Efficacy of Infliximab

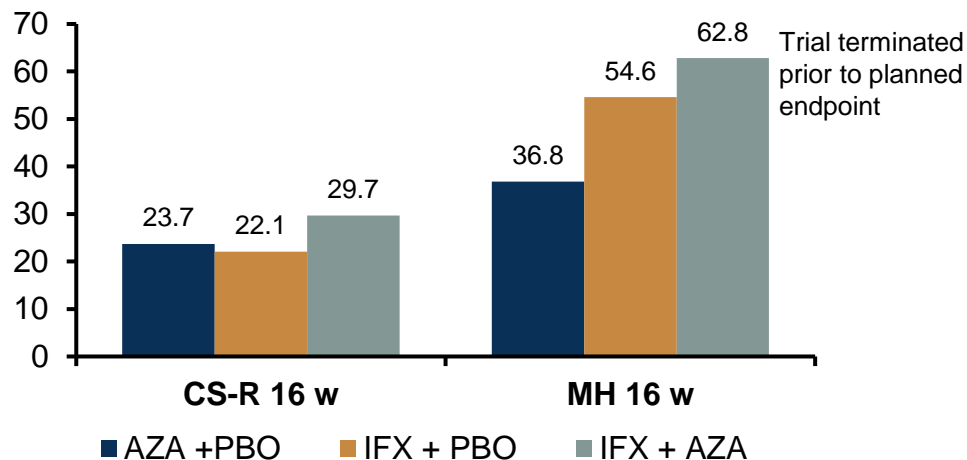
Comparative Efficacy – CD

SONIC¹



Comparative Efficacy – UC

UC SUCCESS²



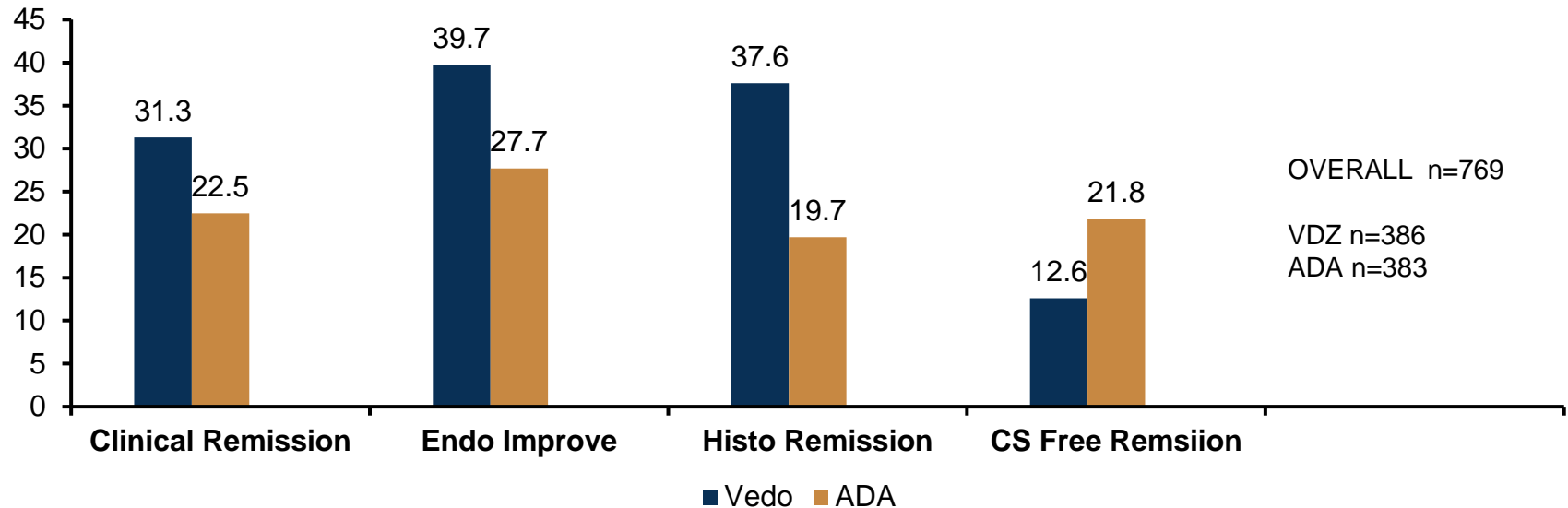
Comparative Effectiveness Between Anti-TNF

- No head-to-head trials between Anti-TNFs
- Many meta-Analyses/retrospective Studies
- Why did your Anti-TNF Fail
 - Mechanistic Failure?
 - Inadequate Drug on Board?
 - **Interval draw? Target?**
 - Develop Antibodies?
 - Adherence?
 - Infection or Inflammation?



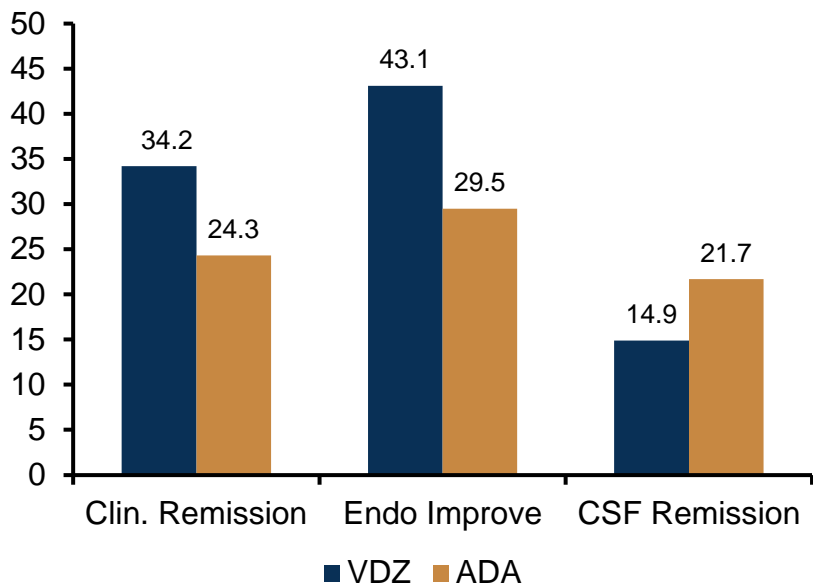
Comparative Effectiveness: VARSITY

52 Week Multi Center Study Comparing Efficacy of Vedolizumab vs. Adalimumab In **Ulcerative Colitis**

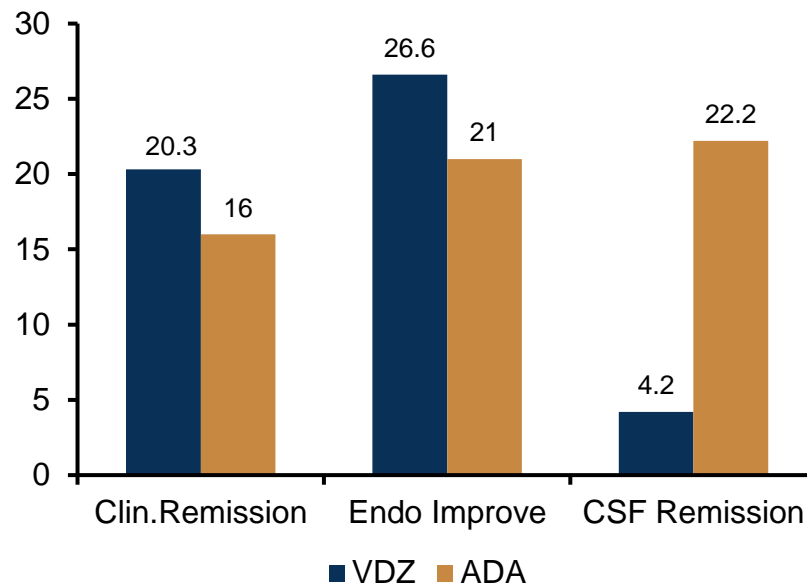


VARSIITY: UC

TNF Naïve UC



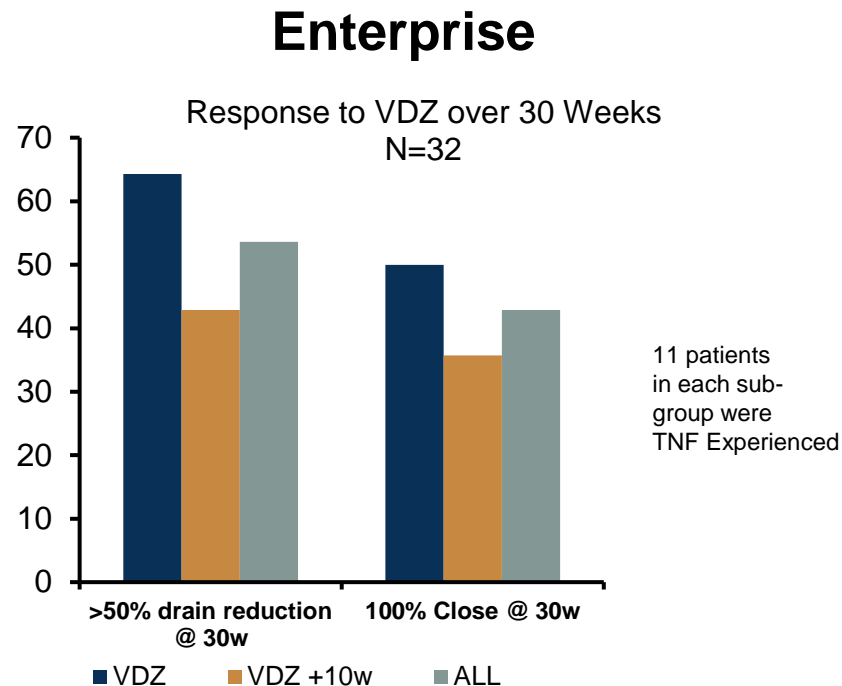
TNF Experienced UC



Perianal CD and Vedoliziumab

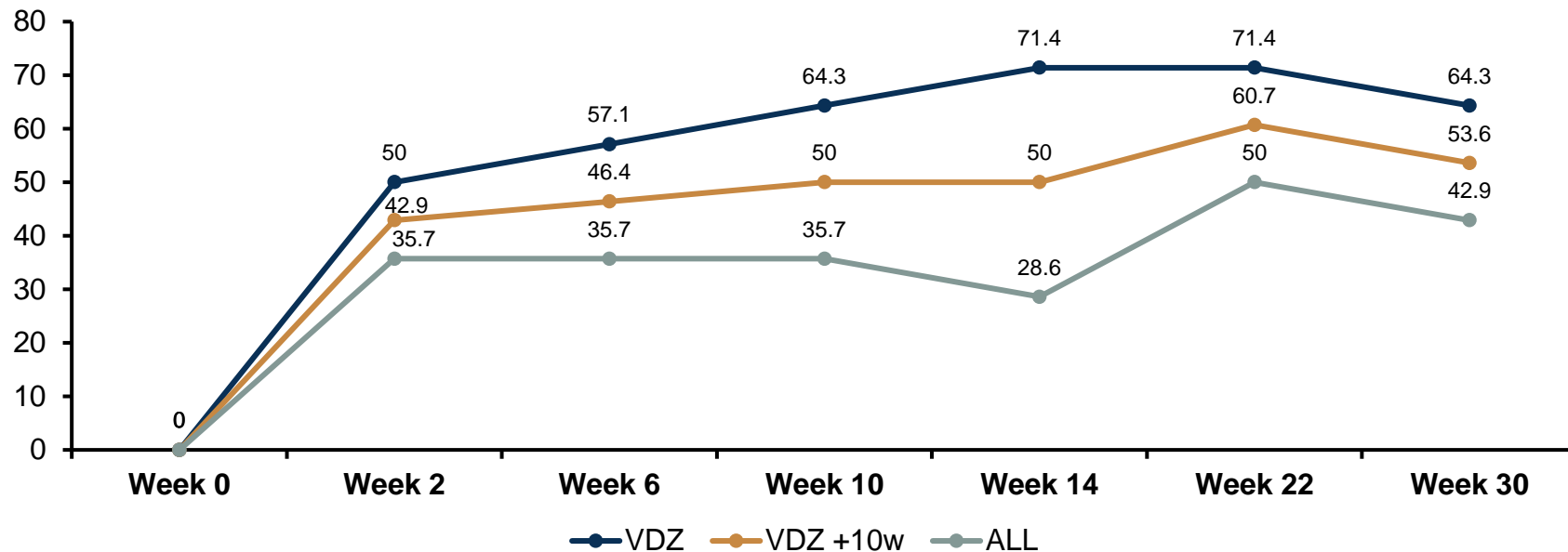
Can we add to our armamentarium?

- VDZ may be an option
- Previous & traditional options
 - ABX, AZA, tacrolimus, cyclosporine, infliximab (only case control trials)



Enterprise

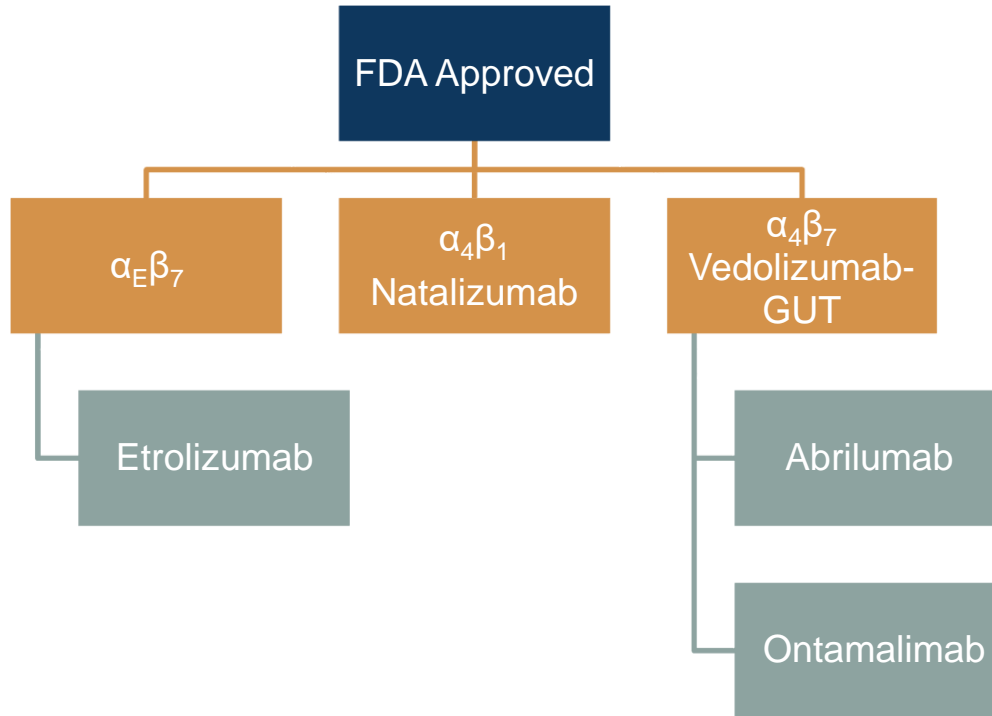
Fistula Response (<50 Drainage from Baseline) at week 30



Anti-Integrins – Vedolizumab a4B7

- Organ Specific Therapy
- Low Immunogenicity
- Safety Signals are Low
- Demonstrates Superiority in UC vs ADA in RCT
 - **NAIVE**
- ? Fistulas
- UC and CD

Anti-Intergrins

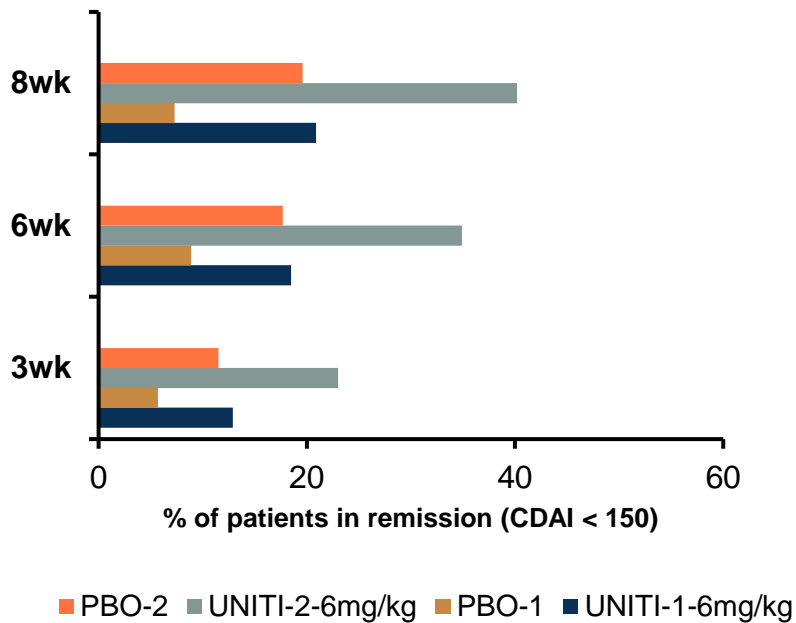


Ustekinumab-IL 12/23 Thru p40

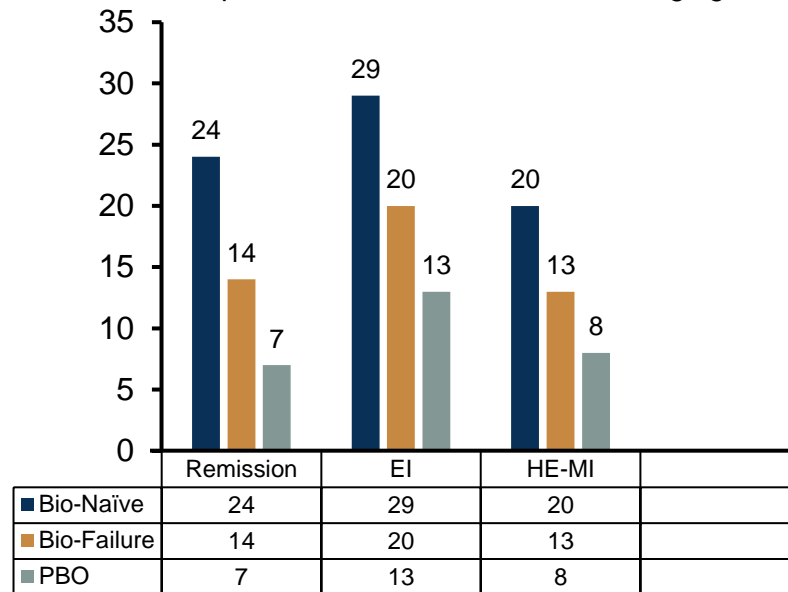
- Indicated for both CD and UC
- Indicated in PsA and Plaque Psoriasis
- Low Immunogenicity
- Injection after loading infusion
- Favorable Safety Profile
- Durable

Ustekinumab Induction in CD and UC

Induction of Clinical Remission in CD



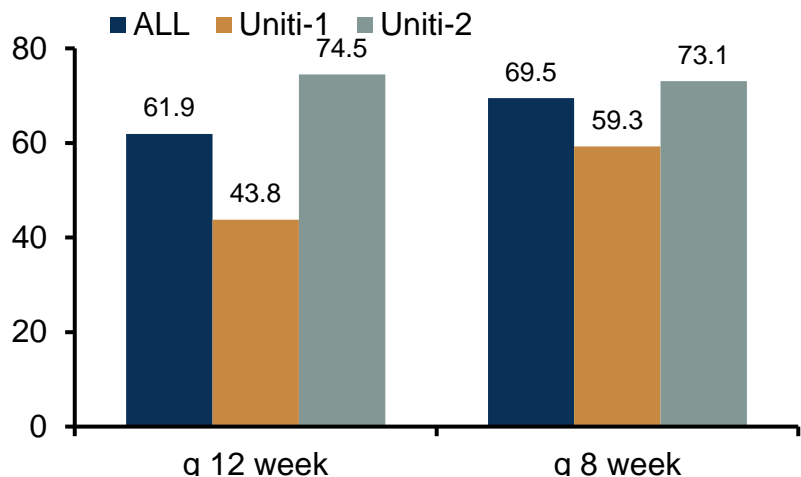
% of UC patient meeting Endpoints after UST IV Induction – 6mg/kg



Ustekinumab Maintenance in CD and UC

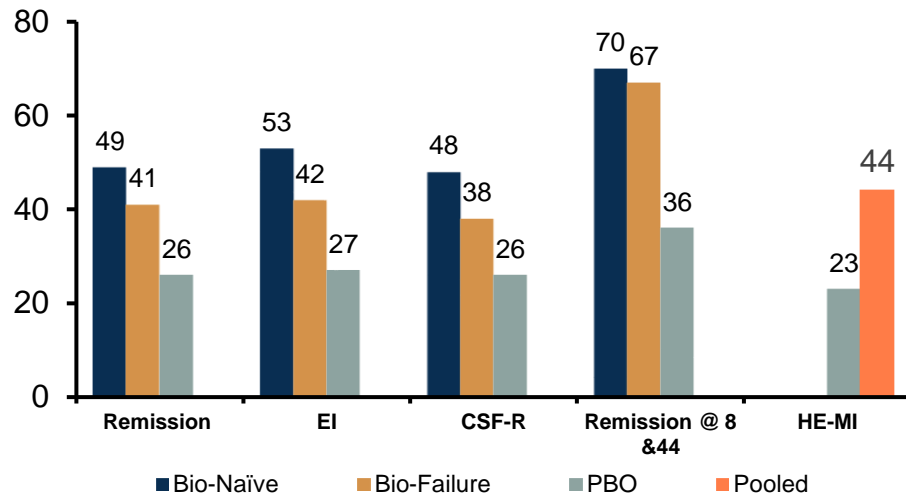
Ustekinumab 152 week remission (CDAI ≤ 150) in CD

UNITI-IM Long-term extension

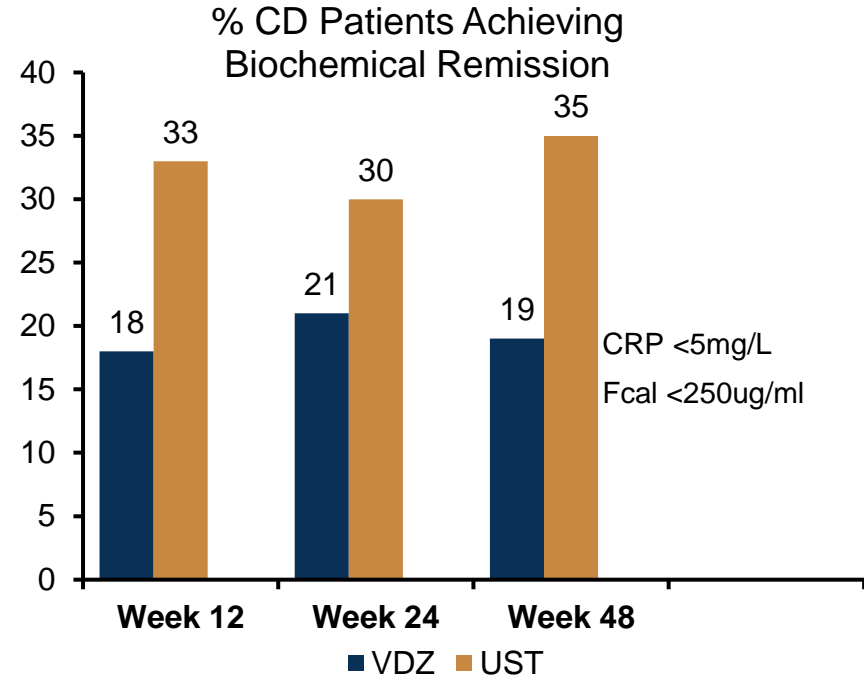
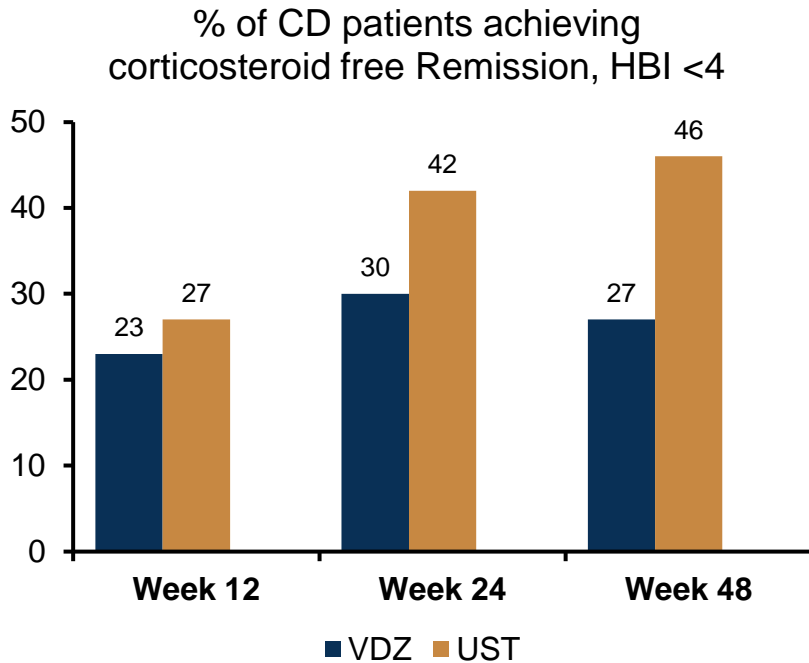


Remission defined as CDAI ≤ 150

44 week SC maintenance after Induction- including Histologic-Endoscopic Mucosal Improvement



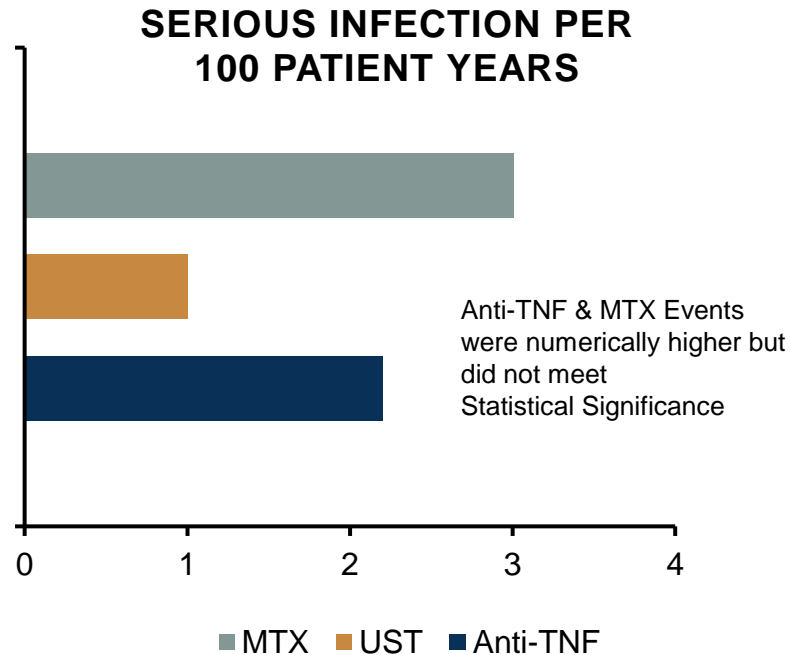
Positioning Ustekinumab in CD Patients With Anti-TNF Failure



PSOLAR – Malignancy Risk Profile

Odds ratio (95% CI)	UST	Anti-TNF	MTX
Overall Malignancy	0.98 (0.63-1.53)	<u>1.54</u> (1.10-2.15)	0.98 (0.63-1.53)
w/ Monotherapy Malignancy	0.76 (0.42-1.37)	<u>1.29</u> (0.84-1.98)	0.95 (0.3-3.02)

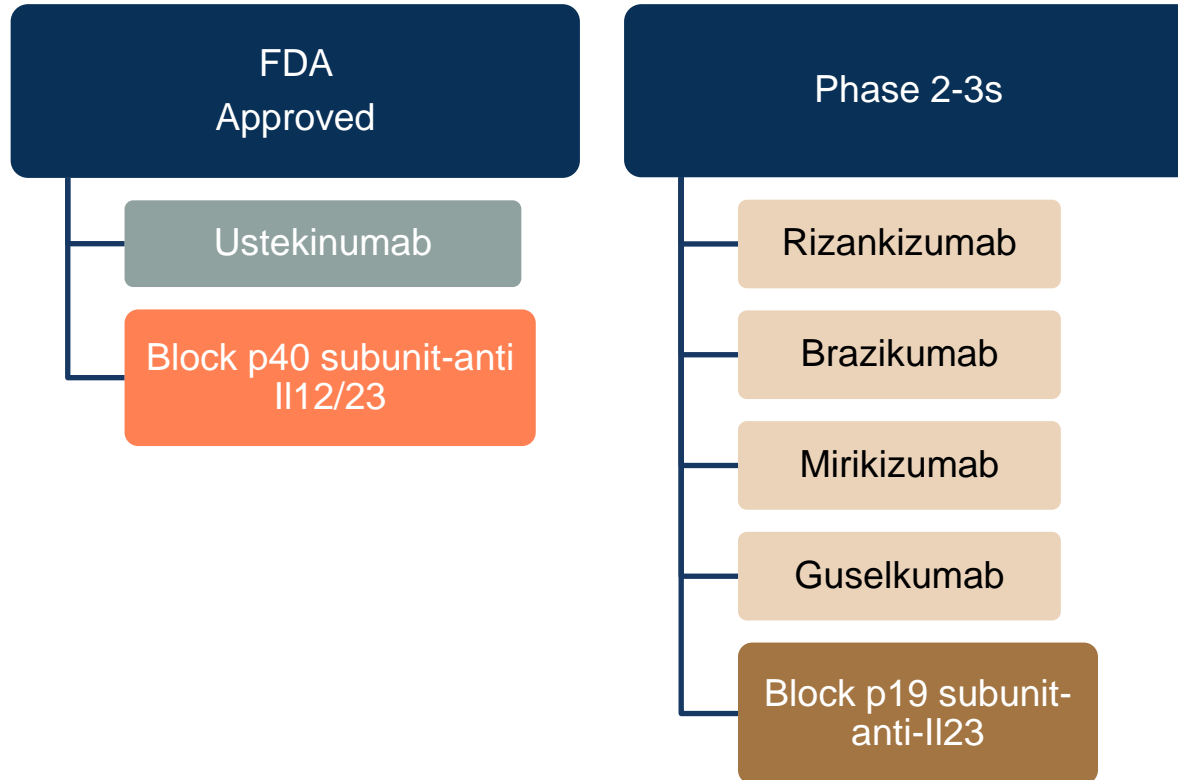
2019 PSOLAR Serious Infection Data



- Dynamic 8-year study
- Most common infections of this cohort
 - Pneumonia
 - Cellulitis



Anti-Interleukins

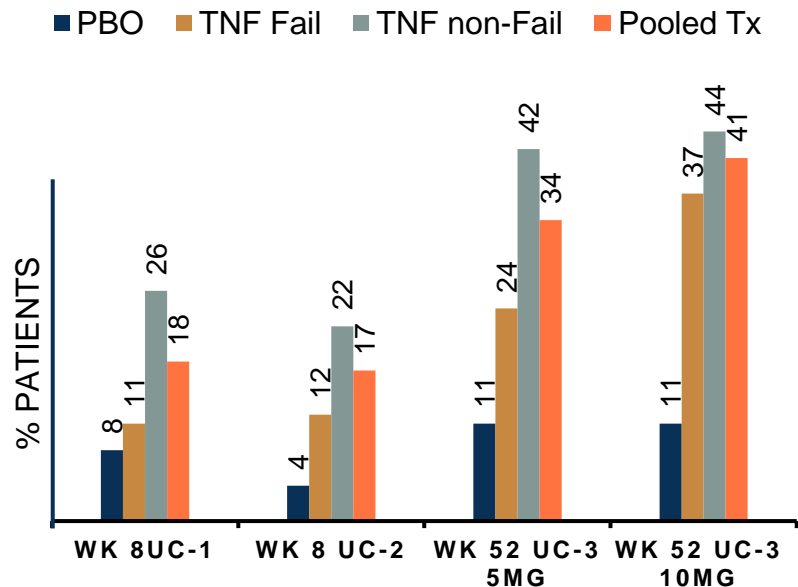


Tofacitinib – JAK/STAT

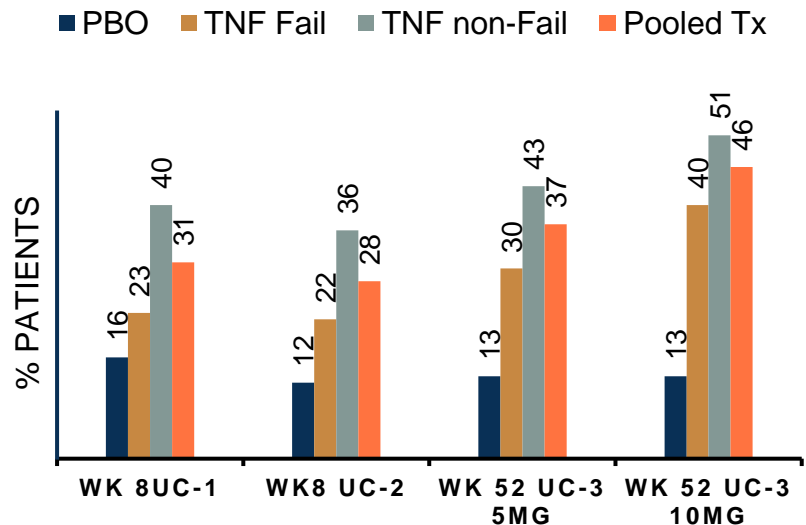
- UC
- Small Molecule – no Immunogenicity
- Not bound to Albumin
- Oral
- Approved for RA, PsA
- **Multi-inhibition of Pre-inflammatory signaling**

Tofacitinib Efficacy – Octave 1, 2, 3

Remission UC

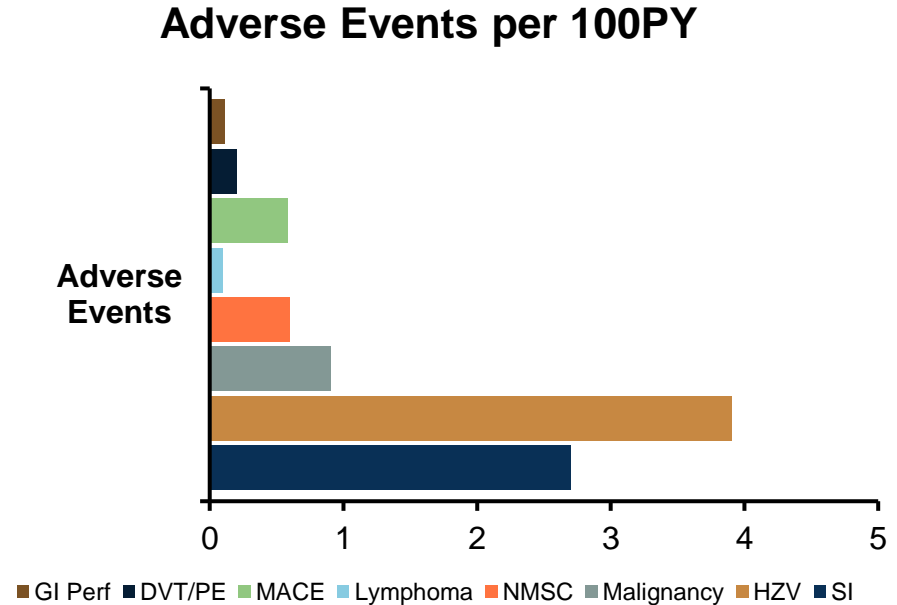


UC Endoscopic Improvement



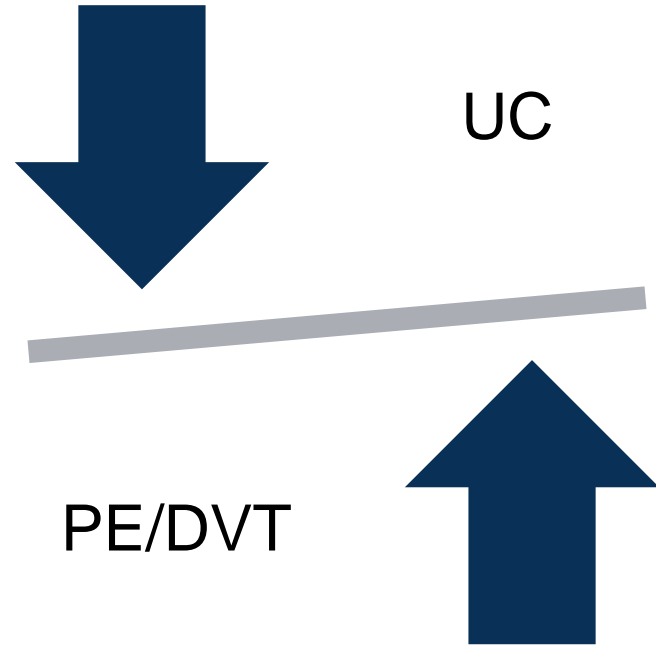
Tofacitinib Safety

- Serious Infections
- HZV
- Malignancy
- NMSC
- Major Cardiac Event
- DVT/PE
- GI Perforation



Tofacitinib

- In the RA population on 10mg BID
 - Thrombosis
 - DVT/PE
 - Cardiac Mortality
 - >50yo
 - 1 or >cardiac risk factor



More Small Molecules to Come...

JAK-Inhibitors

Tofacitinib

Filgotinib

Upadacitinib

S1P1 Receptor Blocker

Ozanimod

PDE4 Inhibitors

Apremalist

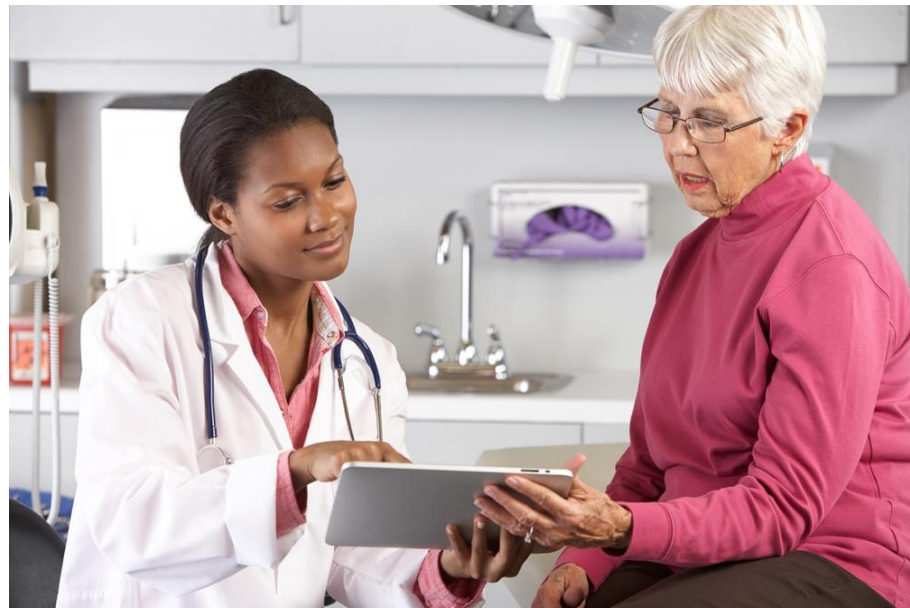
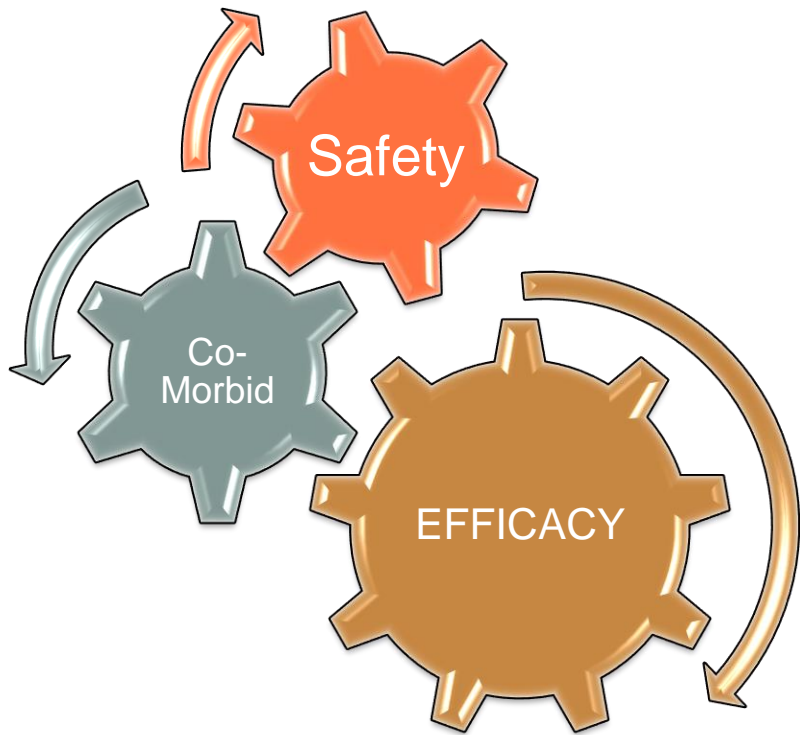
AGA Technical Review on the Management of UC

TNF NAÏVE	Quality of Evidence	TNF EXPERIENCED	Quality of Evidence
IFX >ADA	Moderate	UST, TOF >ADA VDZ	Low
VDZ >ADA	Moderate	VDZ >ADA	Low
IFX & VDZ >other Bios	Very Low	UST >/<TOF (uncertain)	Very Low
TOF vs other?	Uncertain		

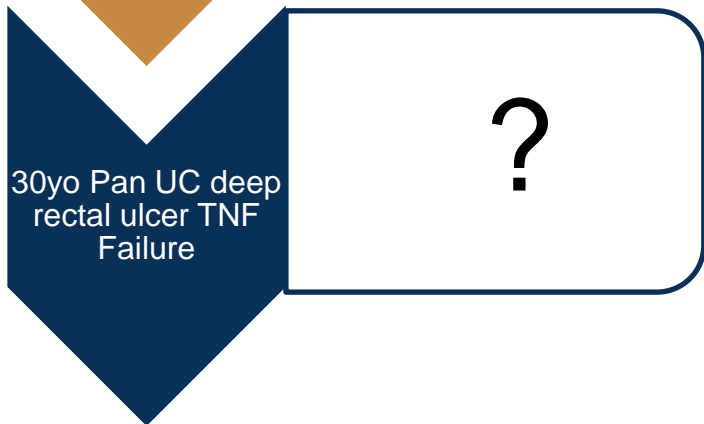
2018 Meta-Analysis of Biologics in Luminal CD

TNF NAÏVE	Quality of Evidence	TNF EXPERIENCED	Quality of Evidence
IFX, ADA Ranked #1	Moderate	UST	Moderate
UST par with VDZ	Low	ADA >VDZ, UST Unless 1* NR	Low
All superior to PBO	Moderate	VDZ	Low

Putting It All Together



Positioning Safety and Efficacy



Anti-TNF-Naïve	Quality of evidence	Anti-TNF-experienced	Quality of evidence
IFX > ADA	Moderate	UST, TOF >ADA VDZ	Low
VDZ >ADA	Moderate	VDZ > ADA	Low
IFX & VDZ >other Bios	Very Low	UST >/< TOF (uncertain)	Very Low
TOF vs other?	Uncertain		

Positioning Safety, Efficacy and Comorbidities

22yo deep ileal ulcers, CD, PSA

?

53yo CD, Perianal DZ, enterocolitis

?

Anti-TNF-Naïve	Quality of evidence	Anti-TNF-Experienced	Quality of evidence
IFX, ADA Ranked #1	Moderate	UST	Moderate
UST par with VDZ	Low	ADA >VDZ, UST Unless 1* NR	Low
All superior to PBO	Moderate	VDZ	Low

Example of Treatment Decision Process Using FDA Approved Agents

	SI	CA	CHF	PML	RPLS	AB	Hem	SLE AI Rns	HSV	MI Risk	Pt X \$	Non Alb bnd	GI
Anti TNFs	+++	++	++			++	++	+					
VDZ	+	+				+							+
NATA	+	+		+		+							
UST	+	+			+	+							
TOF	++	+					+		+++	++		+	

Thank You!!!

