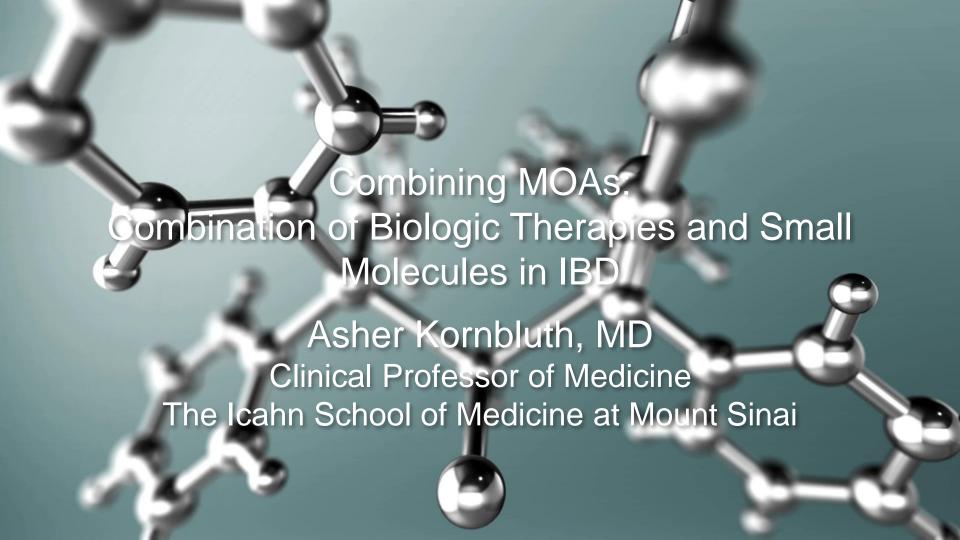
GI ReConnect

June 17-19, 2021 Napa Valley, California





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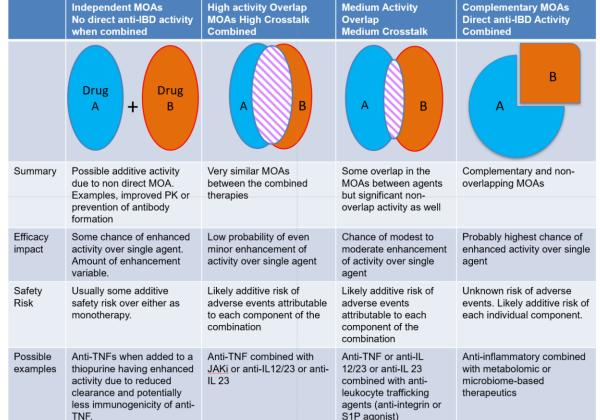
All additional planning committee members, the University of Cincinnati staff and the Gi Health Foundation staff have no relationships to disclose.

Faculty Disclosures

Asher Kornbluth, MD

SAB, Speaker's Bureau: Abbvie, Janssen, Takeda, Pfizer, BMS

Conceptual Rationale for Different Combinations



Staglis, et al CGH 2021 in press

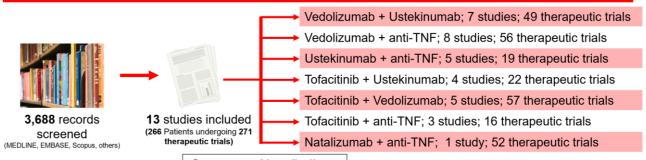
Rationales for Combination Therapy: Different Clinical Scenarios (and Considerations)

- Combination because of suboptimal response with each drug
 - Has each drug been optimized?
- Combination to address 2 different indications, ie luminal disease and perianal disease
 - Can the drug have preferential benefit in luminal vs perianal disease?
- Combination because of dose dependent toxicity with one of the agents
 - e.g dose dependent AEs with tofa; not generally seen with biologics



Effectiveness and Safety of Combining Biologics and/or Small Molecules in Inflammatory Bowel Diseases: Systematic Review With Meta-Analysis

Safety and Effectiveness of Combining Biologics and Small Molecules in IBD: Systematic Review with Meta-Analysis

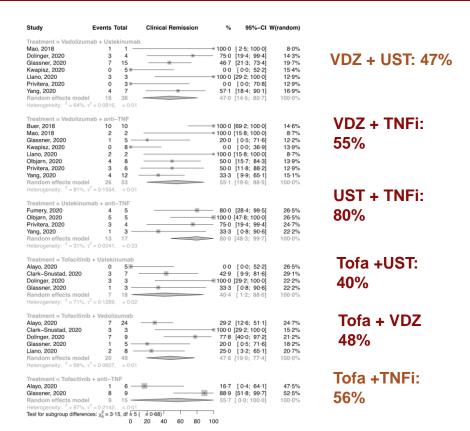


Summary of key findings

Combination therapy	Serious Adverse Events		Clinical remission		Endoscopic remission	
	n/N	ES [95% CI] (%)	n/N	ES [95% CI] (%)	n/N	ES [95% CI] (%)
Vedolizumab + Ustekinumab	49/7	12. [2.0 - 26.8]	38/7	47.0 [14.5 - 80.7]	20/3	25.6 [4.2 - 53.3]
Vedolizumab + anti-TNF	56/8	9.6 [1.5 – 21.4]	53/8	55.1 [19.6 - 88.5]	35/9	18.0 [1.6 - 41.8]
Ustekinumab + anti-TNF	19/5	0.0 [0.0 - 11.1]	17/4	80.0 [48.3 - 99.7]	10/3	35.9 [4.2 - 74.6]
Tofacitinib + Ustekinumab	22/4	0.0 [0.0 - 8.0]	18/4	40.4 [1.2 - 88.0]	13/5	37.4 [9.5 - 69.4]
Tofacitinib + Vedolizumab	57/5	1.0 [0.0 - 7.6]	49/20	47.8 [19.0 - 77.4]	31/4	24.6 [6.4 - 47.6]
Tofacitinib + anti-TNF	16/3	0.0 [0.0 - 17.5]	15/2	55.7 [0.0 - 100.0]	10/2	33.4 [0.0 - 100.0]
Natalizumab + anti-TNF	52/1	0.0 [0.0 - 3.3]	N/A	N/A	N/A	N/A

CI, Confidence interval; ES, Effect size; N/A, No available, Number of patients/Number of studies in each combination pooled estimate. Alayo Q...Colombel JF, Deepak P. Submitted.

Clinical Remission Rates With Combination Therapy



Summary: Combination of Biologic Therapies or with Tofacitinib

- Low quality evidence:
 - Very heterogeneous populations
 - Sequence of failed medication
 - Dose escalation and drug levels not described pre or post combination
 - Indication for drug addition
 - Study design
 - Uncontrolled, retrospective
 - Variable endpoints and duration of treatments
 - Multiple sites each with small number of patients
 - Negative outcome publication bias

Summary: Clinical Considerations

Different MOAs offer potential additive clinical benefits, but without significant toxicity (but data very limited to date)

Biologic agents with favorable safety profile, i.e., vedolizumab and ustekinumab, may allow safe combinations without incremental toxicity

Different MOAs may allow targeting of different disease behaviors, e.g., anti-TNFs for penetrating disease and alternative agents for luminal disease

Cost remains prohibitive, and in some cases an insurmountable limitation