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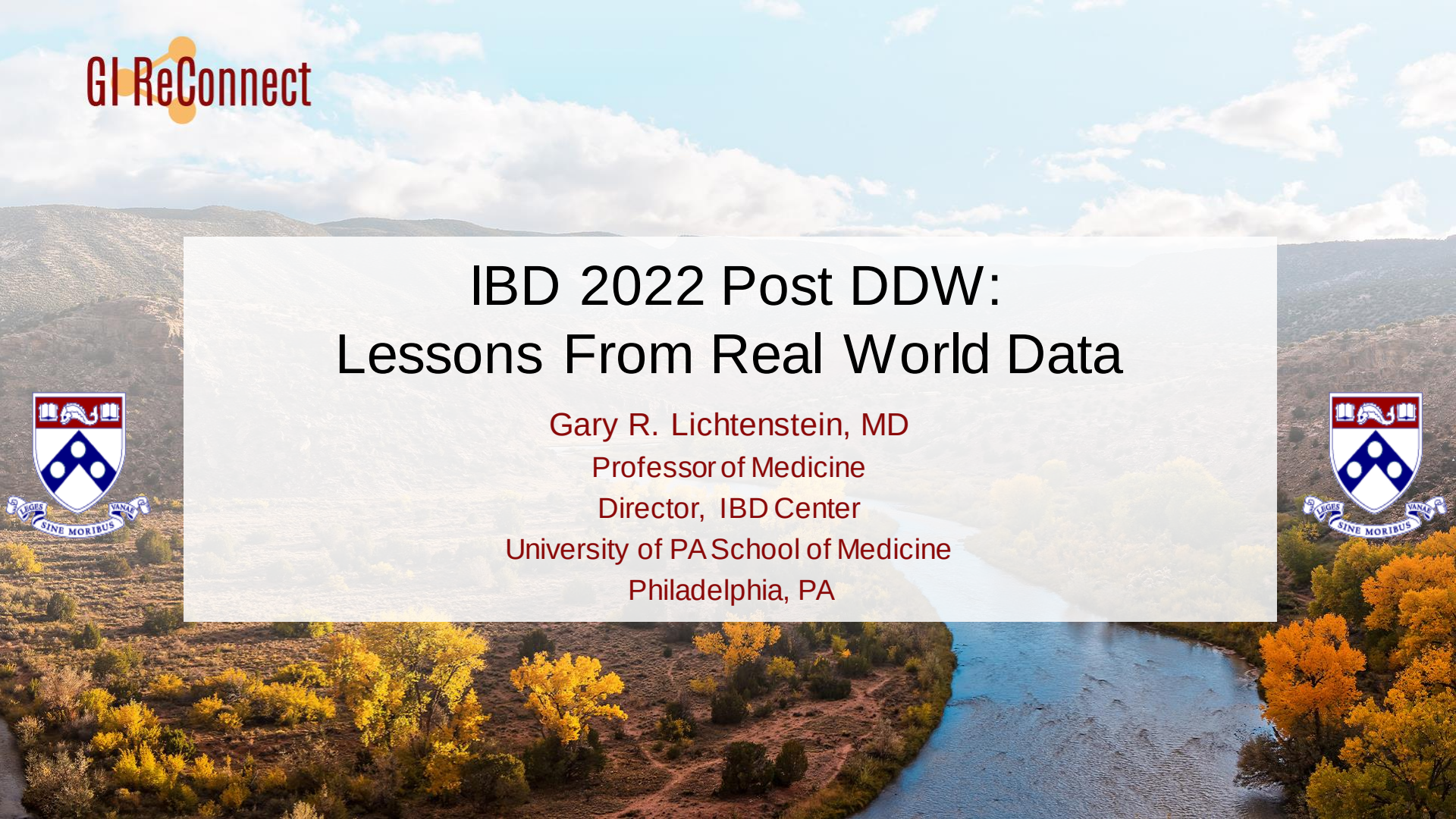

IBD 2022 Post DDW: Lessons From Real World Data

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Disclosures

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Learning Objectives

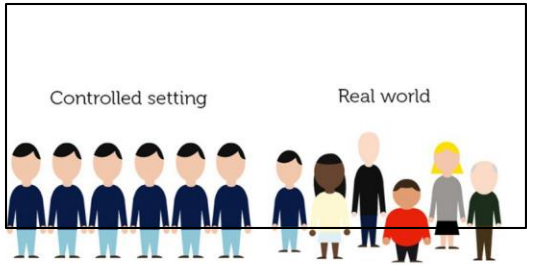
1) Define what is meant by the term “Real world data”
2) Contrast and compare Real world data to randomized controlled clinical trials
3) Discuss the potential advantages / disadvantages of use of real world data
4) Review select Published Real World Data in studies from DDW 2022

Outline: IBD 2022: Lessons From Real World Data

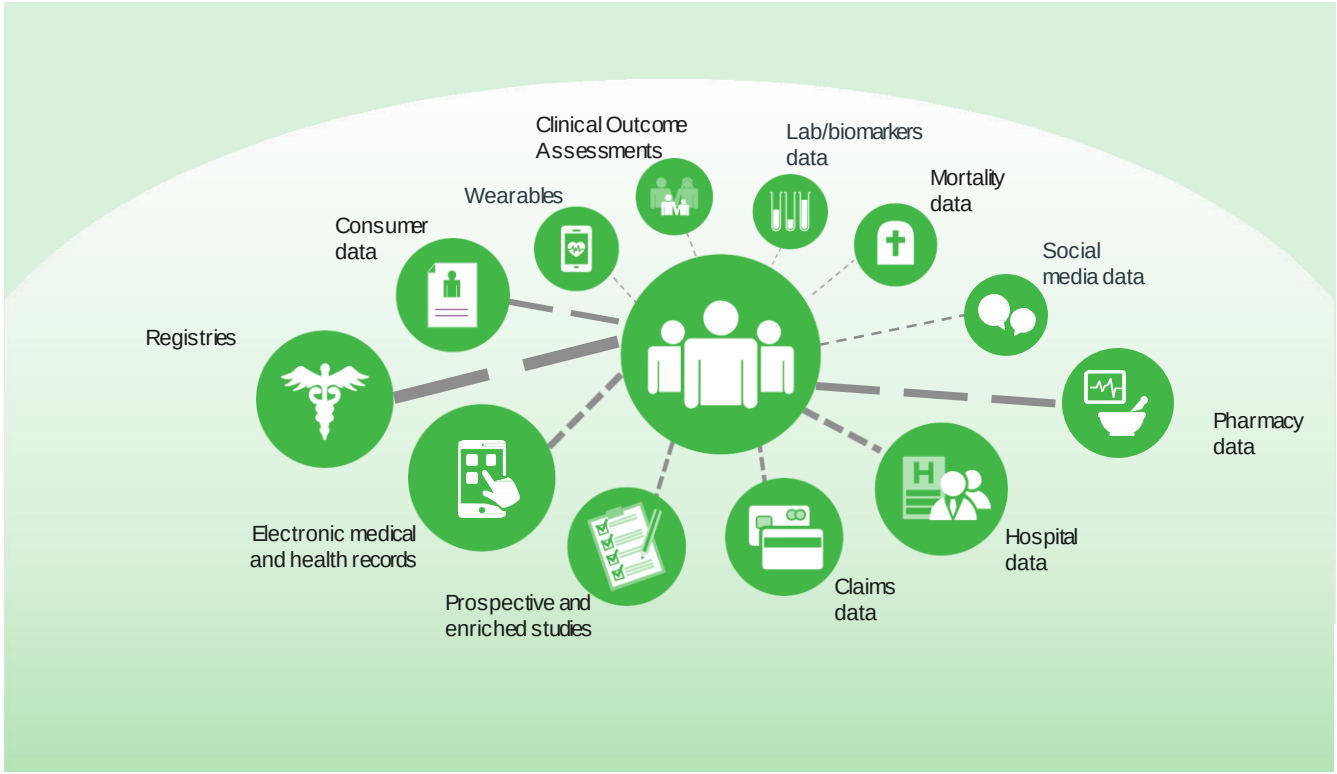
- What is “real-world data”?
  - Differences in RCTs vs. Real World Data
  - What is it best for?
- IBD Publication from Real World Data: 2022 in Review
  - Upadacitinib
  - Ozanimod
  - Ustekinumab
  - Tofacitinib
  - Vedolizumab
  - Crohn’s Disease Exclusion Diet

RCTs vs Observational “Real World” Data

- RCTs provide a benchmark as a treatment goes through development, testing and validation by regulators (short term efficacy)
- Real world data are used to understand post-approval performance of a drug
- Real world data include a variety of information sources: from EMR data to smartphone apps to medical insurance claims
  - None of these data are collected for the purpose of evaluating specific drug safety or efficacy



Real World Data Is PATIENT-Level Data



RCTs vs Observational "Real World" Data

	RCTs*	Observational Study
Population	Strict inclusion criteria	All comers, can be more generalized (children, elderly, pregnant) – can be sicker!
Intervention	Assigned and singular	Can be multifaceted, can also include harmful exposures
Comparison	Placebo or singular active comparator	Other therapies used in practice, often standard of care
Observation period	Short	Long
Sample size	Just enough for power	Larger to overcome population heterogeneity
Outcome	Short-term	Long-term, even death

How observational data can complement RCTs:

- Test external validity of RCTs by expanding to a more representative population
- Formulate hypotheses for RCTs
- Identify appropriate outcomes
- Establish sample sizes
- Determine which patients benefit most from an intervention
- Understand long-term effects of therapy

Problems With RCTs: The 5 S "Shortcomings"

- Too **small**
  - Low power studies can be negative because the intervention was truly not effective, or because of lack of precision (type II error)
  - Small studies can have imbalances in the groups, which can introduce confounding
- Too **short**
  - Follow up time may be too short for outcomes such as death
- Too **selective**
  - May not be generalizable if inclusion/exclusion criteria too rigid
- Too **$$$**
  - A well-designed and conducted RCT is expensive
- Too **shoddy**
  - Just because it's an RCT design, doesn't mean it's high quality
  - Lack of attention to randomization, allocation, blinding, drop out, intention to treat analysis, etc. may introduce bias, undermining study results

Challenges With Use of Real World Data

- Issue with reliability given delivery issues and disparities in how the data are recorded
- Variability in the data – can be associated with potential bias, without quality controls, there is a risk of false conclusions and misinterpretations
- Gaps in data – missing evidence (and how this is handled) can impact the interpretability of the information
- Confounding:

- Selection bias: “Choose or lose”
- Statistical methods such as propensity score matching can help to account for confounding and selection bias, but this does not eliminate it

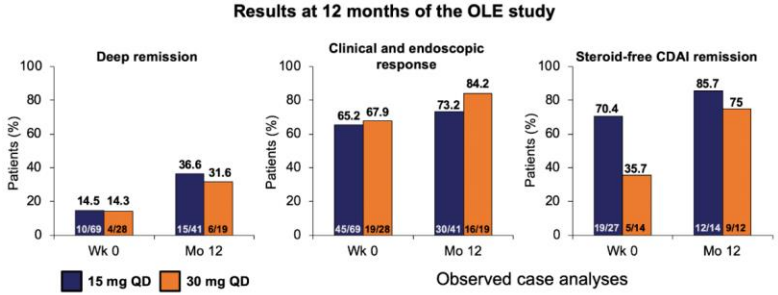
What Is Real World Data Best For?

- Identify *exposures* or risk factors that increase or decrease the risk of a disease (incidence)
- Study *natural history* of disease
  - Factors that increase the risk of a disease can be very different than those that affect prognosis
- Investigate the *effect of a treatment on a disease or condition*
  - Particularly useful when studying something where patients would not want to participate in a RCT
  - May be susceptible to **confounding or selection bias**
- Understanding *safety associated with a therapy* (need very large numbers to assess rare complications)
  - Some complications are only recognized after decades of use

Real World Data

Composite and Individual Measures of Efficacy and Safety After 2 Years of Upadacitinib Treatment for Crohn's Disease

- Patients completing the 52-week CELEST study were enrolled in the CELEST OLE study
  - 76 patients received 15 mg daily
  - 31 patients received 30 mg daily
- In an as-treated analysis, steroid-free CDAI remission rates were similar between groups
- The incidence of AEs, serious AEs, and severe AEs was similar between groups
  - VTE: 0 in active treatment group
  - Herpes zoster: 1 (1.3%) UPA 15 mg, 2 (6.5%) UPA 30 mg



IBDQ domain score, mean	UPA 15 mg QD			UPA 30 mg QD		
	Baseline	Wk 0 (n=75)	Mo 12 (n=61)	Baseline	Wk 0 (n=31)	Mo 12 (n=30)
Bowel	37	54.4	56.2	35.9	55.2	54.3
Emotional	46.7	63.5	64.2	42.9	59.5	60
Social	20.1	28.8	29.4	19	27.7[b]	28.7
Systemic	16	23.1	23.9	13.6	22.2[d]	21.1[c]
Total	119.8	169.8	173.6	112.9	163.7[a]	163.1[c]

[a]n=27. [b]n=28. [c]n=29. [d]n=30.

In patients remaining on therapy up to 2 years, use of UPA was associated with improvements in multiple clinical outcomes and quality of life.

AE, adverse event; CDAI, Crohn's Disease Activity Index; IBDQ, IBD Questionnaire; OLE, open-label extension; UPA, upadacitinib; VTE, venous thromboembolism.

D'Haens GR et al. *UEG*. 2020. OP088.

Real-World Outcomes for Upadacitinib in Crohn's Disease Patient at a Single Center

- Upadacitinib was given off-label to patients who have failed all appropriate FDA approved medications for CD.
- The goal of this study was to retrospectively assess the efficacy and safety of upadacitinib in this group of medically refractory patients with CD.

RESULTS:

- 15 patients with CD on upadacitinib.
- 14/15 patients were prescribed upadacitinib for IBD management 1 received it through rheumatology for axial spondyloarthritis.
- 11/15 (73%) of patients were started on a dose of 45 milligrams (mg) daily.
- 9/15 (60%) patients received 45 mg daily as their maintenance dose.
- 2/15 patients were started on a dose of 30 mg daily and were later increased to 45 mg daily with symptomatic improvement.
- One patient was initiated on 45 mg daily and achieved clinical remission but with dose decrease to 30 mg daily developed a disease flare.
- Of the 13 patients with follow up, 6 (46%) achieved clinical remission and 9 (69%) had a clinical response.
- There was a single adverse event reported: mild neutropenia with absolute neutrophil count of 1300 on upadacitinib 45 mg daily, which resolved after the dose was decreased to 30 mg daily.

Chugh R et al. *Gastroenterology*. 2022; Abstract Tu 1504.

Real-World Outcomes for Upadacitinib in Crohn's Disease Patient at a Single Center

- **Conclusion:**
  In this small series, clinical remission and response rates with upadacitinib suggest significant efficacy for management of patients with severe refractory Crohn's disease with minimal adverse effects.

Critique:

- Small number of patients
- Single center
- Varied doses
- Not powered for safety assessment

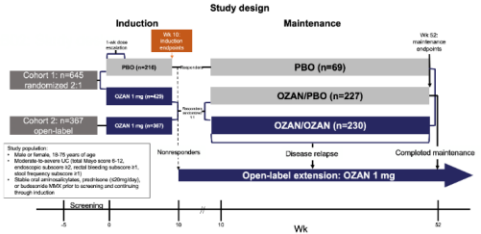
Benefit:

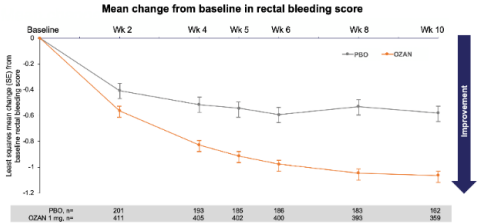
- There is a response similar to initial study- gives us a "flavor" or real-world numbers

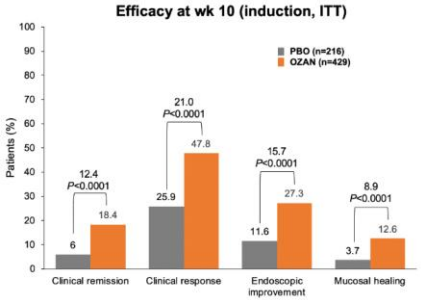
Chugh R et al. *Gastroenterology.* 2022; Abstract Tu 1504.

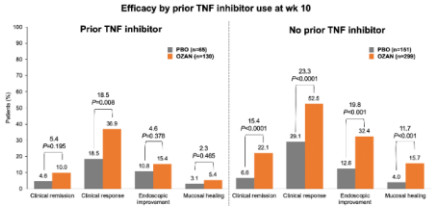
True North: Ozanimod Phase 3 RCT in Ulcerative Colitis Induction Results (Wk 10)

Primary endpoint: Clinical remission (Mayo score excluding PGA); secondary endpoints: clinical response, endoscopic improvement (without friability), mucosal healing (included histology with Geboes score)









	PBO (n=216)	OZAN (n=429)
Any TEAE	82 (38.0)	172 (40.1)
Common TEAEs (≥3% in any group)		
Anemia	12 (5.6)	18 (4.2)
Nasopharyngitis	3 (1.4)	15 (3.5)
Headache	4 (1.9)	14 (3.3)
Serious TEAEs	7 (3.2)	17 (4.0)
UC exacerbation	4 (1.9)	6 (1.4)
Anemia	0	4 (0.9)
Infection	1 (0.5)	4 (0.9)
Severe TEAEs	4 (1.9)	14 (3.3)
TEAEs leading to treatment discontinuation	7 (3.2)	14 (3.3)

OZAN induction therapy for UC demonstrated significant efficacy in all endpoints, with numerical improvements for TNF inhibitor–exposed patients. No new safety signals were observed.

OZAN, ozanimod; PGA, physician's global assessment; SE, standard error; TEAE, treatment-emergent adverse event; TNF, tumor necrosis factor.

Sandborn WJ et al. *UEG*. 2020, LB02.

Real World Effectiveness and Safety of Ozanimod: Initial Results From a Large Tertiary Center

Methods:

- Prospective, observational cohort study includes consecutive patients who initiated ozanimod following FDA approval in May 2021.
- Clinical disease activity was assessed using the Simple Clinical Colitis Activity Index (SCCAI).
- Clinical response was defined as a decrease in ≥3 points in SCCAI from baseline, and clinical remission was defined as an SCCAI score of ≤ 2.
- Adverse events were extracted from the electronic medical records (EMR) and regular clinical pharmacist follow up.

Results

- 21 patients have initiated ozanimod :,
  - 18 -UC,
  - 1 - indeterminate colitis (IC),
  - 1- Crohn's colitis, and
  - 1 - lymphocytic colitis.
- The median age was 35 (interquartile range (IQR) 29-58), with a median disease duration of 5 (IQR 2-14).

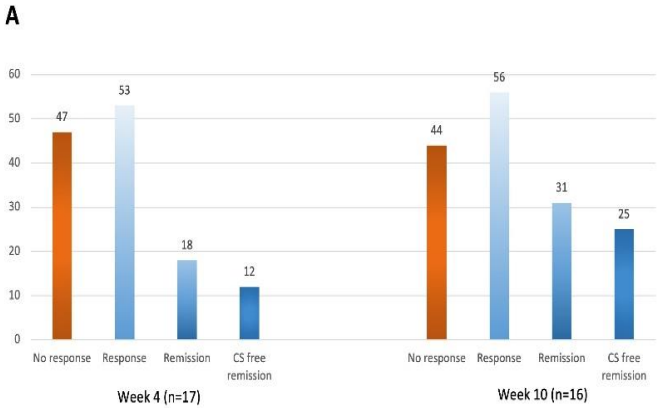
Cohen N et al. DDW 2022, Abstract Mo1567.

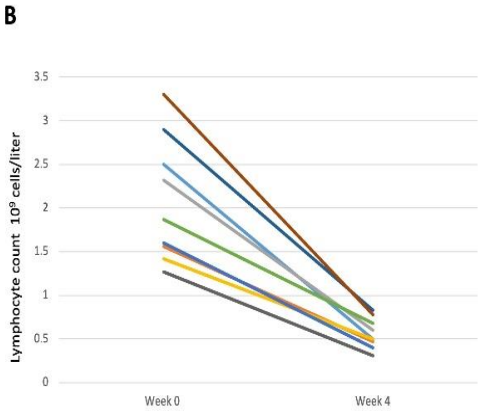
Real World Effectiveness and Safety of Ozanimod: Initial Results from a Large Tertiary Center

Results:

- Week 4: Follow up was available for 17 patients. Among these, 9 patients (53%) demonstrated clinical response, 3 (18%) were in clinical remission, and 2 patients (12%) achieved corticosteroid free remission (CSFR).
- Week 10: Follow up data were available for 16 patients; 9 patients (56%) had a clinical response, 5 (31%) were in clinical remission and 4 patients (25%) achieved CSFR

Conclusion: We present the first real world data of ozanimod in treatment refractory cohort of patients with UC and describe excellent effectiveness, and in a larger cohort of treated patients, a safety profile that is not different from that described in the clinical trials.





Graph B – reduction in absolute lymphocyte counts.
Cohen N et al. DDW 2022. Abstract Mo1567.

Ustekinumab Exposure Affects Real-World Endoscopic and Histologic Outcomes in Ulcerative Colitis

- **Background:** Very little is known about the Pk-PD relationship of ustekinumab in UC patients, and especially whether serum UST concentrations correlate well with colonic tissue drug exposure and with histologic healing.
- **Aim:** To provide real-world data including histology, and to study UST serum levels and its relation to tissue levels and drug efficacy.
- **Methods:** Prospective assessment of UC patients starting UST in standard dosage followed by clinical and endoscopic assessments at week 16 or week 24, and colonic biopsies were taken for histopathologic scoring.
- **Definitions**
  - **Histologic remission** – Nancy histology index of 0
  - **Clinical response** – Decrease in partial Mayo score [PMS] of ≥2 points, plus a decrease in rectal bleeding subscore [RBS] of ≥1 point or an absolute RBS of 0 or 1)
  - **Clinical remission** – PMS of ≤2 with no individual subscore >1, and a RBS of 0)
  - **Endoscopic improvement** – Mayo endoscopic sub-score [MES] of ≤1
  - **Endoscopic remission** – MES of 0
  - **Mucosal healing** – Combination of endoscopic and histologic remission.

Alsoud D et al. DDW 2022. Abstract Mo 1559.

Ustekinumab Exposure Affects Real-World Endoscopic and Histologic Outcomes in Ulcerative Colitis

- Paired trough serum sample and colonic mucosal biopsy were collected for UST levels measurement.

Results:

- 42 UC patients started UST between June 2019 and May 2021, allowing a follow-up of at least 6 months.
- By week 24, histologic remission, clinical response, clinical remission, endoscopic improvement, endoscopic remission, and mucosal healing were observed in 19 (45%), 31 (74%), 24 (57%), 22 (52%), 11 (26%) and 10 (24%) patients, respectively.
- Multivariate analysis identified clinical response at week 8 as a predictor for histologic remission at week 24 [OR 8.84, p = 0.024], and inversely correlated with therapy discontinuation [OR 0.10, p = 0.006].

Alsoud D et al. DDW 2022. Abstract Mo 1559.

Ustekinumab Exposure Affects Real-World Endoscopic and Histologic Outcomes in Ulcerative Colitis

- A trend of higher UST serum trough levels was observed in patients achieving histologic and endoscopic outcomes in comparison with patients who did not reach these outcomes, with a significant statistical difference at week 8 for endoscopic outcomes
- UST concentrations from paired serum and biopsy samples revealed a strong positive correlation (Spearman r=0.88, p<0.001, n=17), both in inflamed (mayo endoscopic score >1) (r=0.89, p<0.001, n=10) and uninflamed (mayo endoscopic score ≤ 1) tissue (r=0.88, p<0.008, n=7).

Conclusion: In this real-word cohort of UC patients initiating UST, more than a third of the patients achieved histologic remission. Serum UST levels were furthermore strongly correlated with tissue levels of UST. A drug exposure-response relationship was observed for histologic and endoscopic outcomes

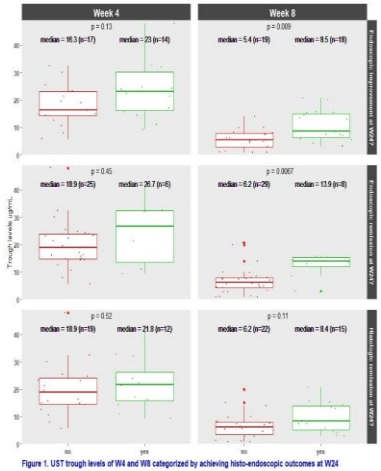


Figure 1. UST trough levels of W4 and W8 categorized by achieving histo-endoscopic outcomes at W24

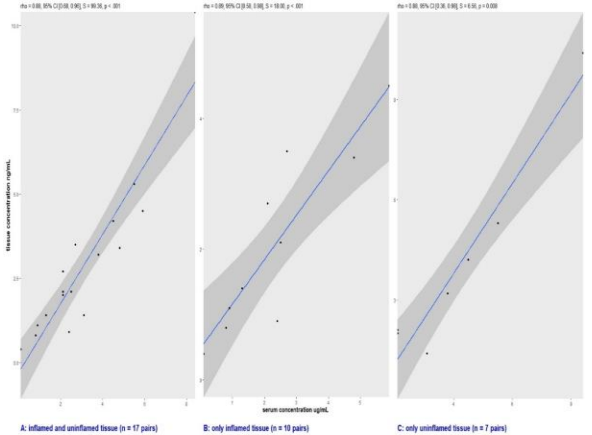


Figure 2. Correlation between tissue and serum ustekinumab concentrations at week 16

Alsoud D et al. DDW 2022. Abstract Mo 1559.

Real-World Multicenter Comparison of Effectiveness Between Tofacitinib and Vedolizumab in Patients With Ulcerative Colitis After Failure to at Least One Anti-TNF Agent

Background:

- Several therapeutic options are now available in ulcerative colitis after anti-TNF failure, but no data compared tofacitinib and vedolizumab.
- This study compared the effectiveness of tofacitinib and vedolizumab in UC patients with prior exposure ≥ 1 anti-TNF.

Methods:

- Design: Multicenter retrospective cohort study [January 2019 to June 2021].
- Inclusion: All adult UC patients with partial Mayo score > 2, who previously received ≥ 1 anti-TNF agent and started either tofacitinib (10mg b.i.d ± decreased to 5 mg b.i.d from W8) or vedolizumab (300 mg IV at W0-W2-W6 -W14 [± additional W10] and every 4 to 8 weeks based on physician judgement).
- Primary endpoint: Corticosteroid-free clinical remission or CFREM (partial Mayo score ≤ 2) at week 16.
- Secondary endpoints: Endoscopic improvement (CFREM + endoscopic Mayo score ≤ 1) and mucosal healing (CFREM + endoscopic and histological remission defined as Nancy index ≤ 1).
- Comparisons were performed using propensity score analyses (IPTW method) adjusted on gender, smoking, UC duration, UC extent, number of prior biologics classes, number of prior primary failure to biologics, concomitant 5-ASA, steroids or immunosuppressive agents, and disease severity.

Buisson A et al. DDW 2022. Abstract Su 1503.

Real-World Multicenter Comparison of Effectiveness Between Tofacitinib and Vedolizumab in Patients With Ulcerative Colitis After Failure to at Least One Anti-TNF Agent

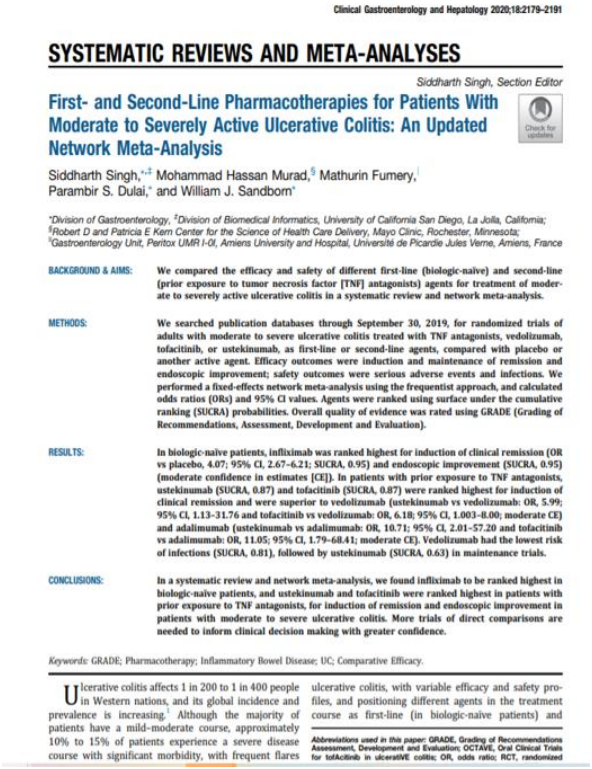
Results:

- CFREM was achieved in
  - 54.2% : tofacitinib and
  - 42.5% vedolizumab, respectively (p=0.089).
- The rate of CFREM at W16 was
  - 57.4% vs 51.1% (p=0.77): After one biologic,
  - 55.4% vs 41.8% (p=0.61): After 2 biologics,
  - 56.9% vs 6.3% (p=0.007): After at least 3 biologics,
  - 59.0% vs 33.3% (p=0.17): Partial Mayo score ≥ 6, in tofacitinib and vedolizumab groups, respectively.
- Tofacitinib was more effective than vedolizumab to achieve CFREM at W16 in patients with primary failure to at least biologic (71.6% vs 30.8%, p=0.049).
- Among 177 patients, endoscopic improvement was higher in patients treated with tofacitinib (33.6 % vs 7.1%, p=0.048).
- Mucosal healing was observed in 6.4% vs 3.8% in tofacitinib and vedolizumab arms, respectively (p=0.27).

Tofacitinib and vedolizumab are effective after failure to anti-TNF agents. Tofacitinib seems to be more effective in case of primary failure to biologics and multiple therapeutic failures.

Buisson A et al. DDW 2022. Abstract Su 1503.

Network Meta-Analysis in UC



Clinical Gastroenterology and Hepatology 2020;18:2179–2191

SYSTEMATIC REVIEWS AND META-ANALYSES

Siddharth Singh, Section Editor

First- and Second-Line Pharmacotherapies for Patients With Moderate to Severely Active Ulcerative Colitis: An Updated Network Meta-Analysis

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BACKGROUND & AIMS: We compared the efficacy and safety of different first-line (biologic-naive) and second-line (prior exposure to tumor necrosis factor [TNF] antagonists) agents for treatment of moderate to severely active ulcerative colitis in a systematic review and network meta-analysis.

METHODS: We searched publication databases through September 30, 2019, for randomized trials of adults with moderate to severe ulcerative colitis treated with TNF antagonists, vedolizumab, tofacitinib, or ustekinumab, as first-line or second-line agents, compared with placebo or another active agent. Efficacy outcomes were induction and maintenance of remission and endoscopic improvement; safety outcomes were serious adverse events and infections. We performed a fixed-effects network meta-analysis using the frequentist approach, and calculated odds ratios (ORs) and 95% CI values. Agents were ranked using surface under the cumulative ranking (SUCRA) probabilities. Overall quality of evidence was rated using GRADE (Grading of Recommendations, Assessment, Development and Evaluation).

RESULTS: In biologic-naive patients, infliximab was ranked highest for induction of clinical remission (OR vs placebo, 4.07; 95% CI, 2.67–6.21; SUCRA, 0.95) and endoscopic improvement (SUCRA, 0.95) (moderate confidence in estimates [CE]). In patients with prior exposure to TNF antagonists, ustekinumab (SUCRA, 0.87) and tofacitinib (SUCRA, 0.87) were ranked highest for induction of clinical remission and were superior to vedolizumab (ustekinumab vs vedolizumab: OR, 5.99; 95% CI, 1.13–31.76 and tofacitinib vs vedolizumab: OR, 6.18; 95% CI, 1.003–8.00; moderate CE) and adalimumab (ustekinumab vs adalimumab: OR, 10.71; 95% CI, 2.01–57.20 and tofacitinib vs adalimumab: OR, 11.05; 95% CI, 1.79–68.41; moderate CE). Vedolizumab had the lowest risk of infections (SUCRA, 0.81), followed by ustekinumab (SUCRA, 0.63) in maintenance trials.

CONCLUSIONS: In a systematic review and network meta-analysis, we found infliximab to be ranked highest in biologic-naive patients, and ustekinumab and tofacitinib were ranked highest in patients with prior exposure to TNF antagonists, for induction of remission and endoscopic improvement in patients with moderate to severe ulcerative colitis. More trials of direct comparisons are needed to inform clinical decision making with greater confidence.

Keywords: GRADE; Pharmacotherapy; Inflammatory Bowel Disease; UC; Comparative Efficacy.

Ulcerative colitis affects 1 in 200 to 1 in 400 people in Western nations, and its global incidence and prevalence is increasing.[1] Although the majority of patients have a mild-moderate course, approximately 10% to 15% of patients experience a severe disease course with significant morbidity, with frequent flares ulcerative colitis, with variable efficacy and safety profiles, and positioning different agents in the treatment course as first-line (in biologic-naive patients) and

Abbreviations used in this paper: GRADE, Grading of Recommendations Assessment, Development and Evaluation; OCTAVE, Oral Clinical Trials for tofAcitinib in ulceratIVE colitis; OR, odds ratio; RCT, randomized

Singh S et al. *Clin Gastroenterol Hepatol*. 2020; 18;10:2179-2191.

NMA Data on Clinical Remission: End of Induction for Bio-Naïve

Induction of clinical remission[1]						
Ustekinumab 6mg/kg	0.96 (0.38-2.45)	0.80 (0.35-1.83)	0.73 (0.31-1.74)	1.05 (0.48-2.32)	0.50 (0.22-1.12)	**2.04 (1.03-4.05)**
	Tofacitinib 10mg BID	0.84 (0.39 - 1.82)	0.76 (0.33-1.76)	1.10 (0.51-2.34)	0.52 (0.24-1.12)	**2.12 (1.12-4.02)**
		Vedolizumab	0.91 (0.44-1.86)	1.31 (0.88-1.95)	0.62 (0.34-1.15)	**2.54 (1.60-4.02)**
			Golimumab	1.44 (0.76-2.75)	0.69 (0.35-1.36)	**2.79 (1.64-4.02)**
				Adalimumab	**0.48 (0.26-0.86)**	**1.94 (1.30-2.88)**
					Infliximab	**4.07 (2.67-6.21)**
						Placebo

No significant differences between most products for induction of remission

Only significant differences in odds ratios observed for ADA vs IFX for both clinical remission

2a. In adults with moderate to severe UC who are naïve to biologic agents, the AGA suggests using infliximab or vedolizumab rather than adalimumab for induction of remission.[2]

- Only IFX or VDZ recommended as first-line therapy although NMA showed ustekinumab was not significantly different from these recommended therapies at induction
- UST and GLM could be recommended as a "convenient" option since they are also subcutaneously administered
- Clinical response and delayed responders not included in analysis

NMA, network meta-analysis.

1. Singh S et al. *Gastroenterology*. 2020;158:1465-1496; 2. Feuerestein JD et al. *Gastroenterology*. 2020;158:1450-1461.

AGA Recommendation for Induction of Remission

2c. In adult outpatients with moderate-severe UC who have previously been exposed to IFX, particularly those with primary non-response, the AGA suggests using UST or TOF, rather than VDZ or ADA for induction of remission.[1]

Conditional recommendation, low quality evidence

- In VARSITY, TNF-IR patients ... "no significant differences in ... achieving clinical remission at week 52" → overall quality of evidence was low
- A separate NMA was performed in TNF-IRs
  - Low confidence in supporting higher efficacy of TOF and UST over ADA for induction of clinical remission in TNF-IRs (only for patients with prior IFX exposure)
  - Data for maintenance of remission could not be reliably synthesized using NMA
- Singh NMA suggested that UST and TOF are best after IFX failure for inducing remission[2]

1. Feuerestein JD et al. *Gastroenterology*. 2020;158:1450-1461; 2. Singh S et al. *Gastroenterology*. 2020;158:1465-1496.

Singh NMA Data on Clinical Remission: End of Induction for Prior Biologic Experience

Induction of clinical remission[1]

Ustekinumab 6mg/kg	0.97 (0.11-8.72)	**5.99 (1.13-31.76)**	**10.71 (2.01-57.20)**	**11.51 (2.65-49.96)**
	Tofacitinib 10mg BID	**6.18 (1.00-38.00)**	**11.05 (1.79-68.41)**	**11.88 (2.32-60.89)**
		Vedolizumab	1.79 (0.86-3.70)	1.92 (0.87-4.25)
			Adalimumab	1.07 (0.48-2.41)
				Placebo

No significant differences between ustekinumab and tofacitinib

Significant differences in ORs observed for ustekinumab and tofacitinib vs other comparators in bio-experienced for remission

2c. In adult outpatients with moderate to severe UC who have previously been exposed to infliximab, particularly those with primary nonresponse, the AGA suggests using ustekinumab or tofacitinib rather than vedolizumab or adalimumab for induction of remission.[2]

- TNF failure patients in VARSITY could have failed IFX or golimumab, but only IFX is mentioned
- Difference for ustekinumab vs vedolizumab, adalimumab, and placebo are all significant for clinical remission, which is particularly noteworthy given that UNIFI is the only trial to include patients with prior failure to vedolizumab as well as anti-TNFs

NMA, network meta-analysis.

Singh S et al. *Gastroenterology*. 2020;158:1465-1496.
Feuerestein JD et al. *Gastroenterology*. 2020;158:1450-1461.

Crohn's Disease Exclusion Diet

- The CD exclusion diet (CDED), is a whole-food diet coupled with Partial Enteral Nutrition (PEN), designed to reduce exposure to dietary components, hypothesized to negatively affect the microbiome (dysbiosis), intestinal barrier, and intestinal immunity.
- It has shown promising ability to induce remission and decrease inflammation in case series in both children and adults with CD, including in patients with secondary loss of response to anti–tumor necrosis factor therapy.
- In this multinational randomized clinical trial, we aimed to compare the tolerability and efficacy of CDED coupled with PEN with the current gold standard for induction of remission, EEN, in inducing and sustaining corticosteroid-free remission.

Crohn's Disease Exclusion Diet Plus Partial Enteral Nutrition Induces Sustained Remission in a Randomized Controlled Trial

CLINICAL AT

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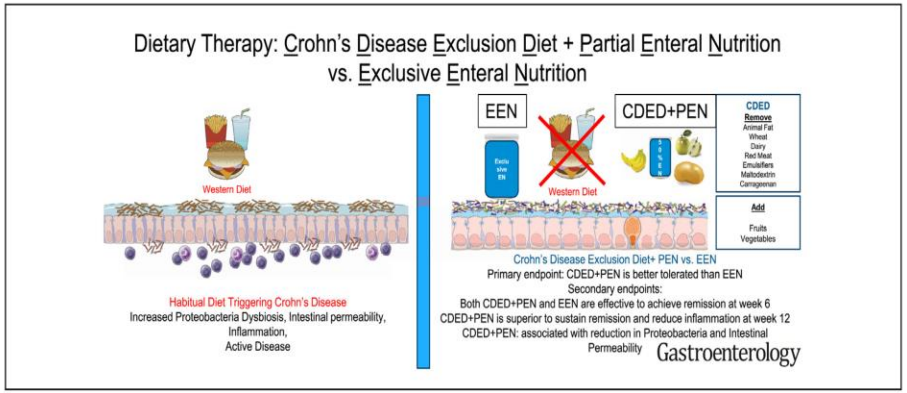
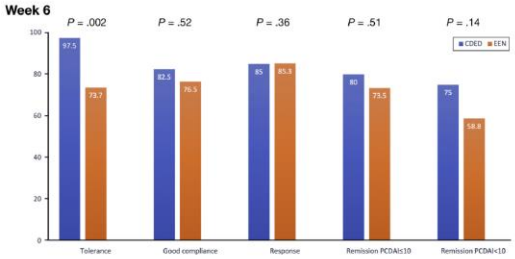


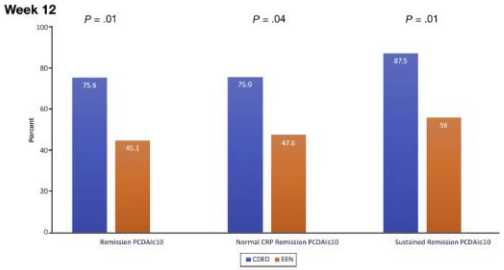
Levine A et al. *Gastroenterology*. 2019;157:440–450.

Crohn's Disease Exclusion Diet

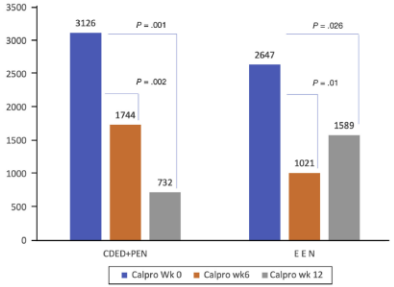
Primary and secondary endpoints CDED vs Exclusive Enteral Nutrition (EEN)-tolerance, compliance and ITTresponse and ITTremission



Week 12 remission, normal CRP remission, and sustained remission.



Change in median calprotectin during CDED study.



CONCLUSION:

- CDED plus PEN was better tolerated than EEN in children with mild to moderate CD.
- Both diets were effective in inducing remission by week 6.
- The combination CDED plus PEN induced sustained remission in a significantly higher proportion of patients than EEN, and produced changes in the fecal microbiome associated with remission.
- These data support use of CDED plus PEN to induce remission in children with CD.

Levine A et al. *Gastroenterology*. 2019;157:440–450.

Real World Experience With the Crohn's Disease Exclusion Diet (CDED) in a Tertiary IBD Clinic

Aim: To describe our real-world experience with the CDED, in a clinically diverse CD population.

Methods: Single center, retrospective cohort study of CD patients prescribed with the CDED, between 01/2018 and 11/2021.

Results:

- The CDED was initiated in 155 patients (age 37.7±16.3, 66% men, disease duration 7.8±9.6), 35.3% had colonic/ileo-colonic disease, 23.7% and 25% had a stricturing and penetrating disease respectively, 27.5% had a history of intestinal resection, 19.9% had extra-intestinal involvement, and 7.7% had a severe endoscopic disease at diet initiation.
- **Indications for therapy** included patient's will (44.7%), adjunctive therapy (23.7%), bridge with biologic induction (20.4%), rescue therapy (3.9%), exhaustion/contraindication of other advanced therapy options (1.4%), de-escalation of biologics (0.7%), preparation for surgery (0.7%), and others (3.9%).
- Upon initiation:
  - **Active disease** – 67.3% (n=105) [Harvey Bradshaw index (HBI) ≥5 / Calprotectin ≥250 g/l]
  - **Remission** – 32.7%

Isakov NF et al. *Gastroenterology*. 2022; abstract Tu 1422.

Real World Experience With the Crohn's Disease Exclusion Diet (CDED) In a Tertiary IBD Clinic

Results (continued):

- Physician and dietician follow-up at the end of phase 1 was documented in 89 (57.4%) and 74 (47.7%) of patients with an active disease (mean follow-up period 14.6±9.3 weeks).
- Fifty-eight percent of patients with dietary follow-up (n=43) were fairly-fully compliant to the CDED.
- Clinical response (drop in HBI>2 points) and remission (HBI<5) at the end of phase 1, were achieved by 58.9% (n=62) and 57.5% (n=60) of patients who were treated for an active disease (n=105). Clinical remission rate at the end of phase 1 was lower among patients with higher baseline HBI score (P for trend=0.028), lower dietary adherence (P for trend<0.001) and a surgical history (P=0.033).
- **Conclusions:**
  - The CDED may have efficacy across different clinical scenarios.
  - Adherence is reasonable, and is associated with higher remission rates among patients treated for an active disease.

Isakov NF et al. *Gastroenterology*. 2022. abstract Tu 1422.

Conclusion

Real World Evidence has supported —

- Upadacitinib appears safe and effective to treat patients with Crohn's disease with minimal adverse events
- Ozanimod in treatment refractory UC pts had efficacy consistent with the clinical trials and a safety profile that is not different from that described in the clinical trials
- In a prospective assessment of Ustekinumab in UC pts newly initiating UST, more than a third of the patients achieved histologic remission. Serum UST levels were strongly correlated with tissue levels of UST. A drug exposure-response relationship was observed for histologic and endoscopic outcomes
- Despite a NMA suggesting that Vedolizumab is ineffective after TNF failure in UC pts – Tofacitinib and vedolizumab were found to be effective after failure to anti-TNF agents. Tofacitinib seems to be more effective in case of primary failure to biologics and multiple therapeutic failures – similar to the NMA.
- The CDED (Crohn's Disease Exclusion Diet) may work across different clinical scenarios. Adherence is reasonable, and is associated with higher remission rates among patients treated for an active disease.