



Updates from DDW: Updates in IBD

SARA LEWIN, MD

ASSISTANT PROFESSOR | UCSF GASTROENTEROLOGY

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Questions answered at DDW 2021

1. What's in the drug development pipeline for IBD?
2. What agent should I choose for my patient with Crohn's disease?
3. Does switching biosimilars affect clinical outcomes?
4. Does ustekinumab treat extra-intestinal manifestations of Crohn's disease?
5. Does steroid use in pregnancy affect pregnancy and neonatal outcomes?
6. What should I tell my Crohn's patients to eat?

Biologic and Small Molecules for IBD

Anti-TNF- α	Anti-integrin	Anti-IL-12/23
Infliximab Adalimumab Golimumab Certolizumab	Vedolizumab Natalizumab Etrolizumab Ontamalimab Abrilumab	Ustekinumab
JAK inhibitor	S1P Modulator	Selective IL-23
Tofacitinib <i>Filgotinib</i> Upatacitinib TD-1473	Ozanimod Fingolimod Etrasimod Amiselimod	Risankizumab Guselkumab <i>Mirikizumab</i> Brazikumab

What agent should I choose for Crohn's?

What agent should I choose for Crohn's?

Adalimumab vs Vedolizumab

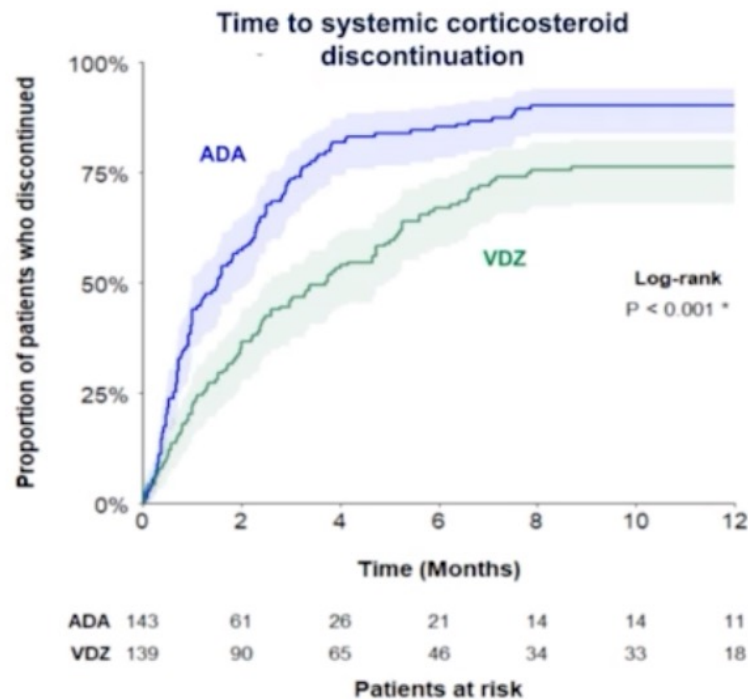
Adalimumab vs Vedolizumab for Crohn's Disease

- ▶ Adalimumab vs Vedolizumab for Crohn's Disease 1st line
 - ▶ IBM®MarketScan® Commercial Claims Database Study
 - ▶ Propensity Score Matching Design
- ▶ Adalimumab associated with less healthcare utilization:
 - ▶ Less likely to visit ER or be hospitalized after induction
 - ▶ Discontinued steroids earlier and more often

What agent should I choose for Crohn's?

Adalimumab vs Vedolizumab

ADA-Treated Patients Discontinued Systemic Corticosteroids Significantly Faster Than VDZ-Treated Patients

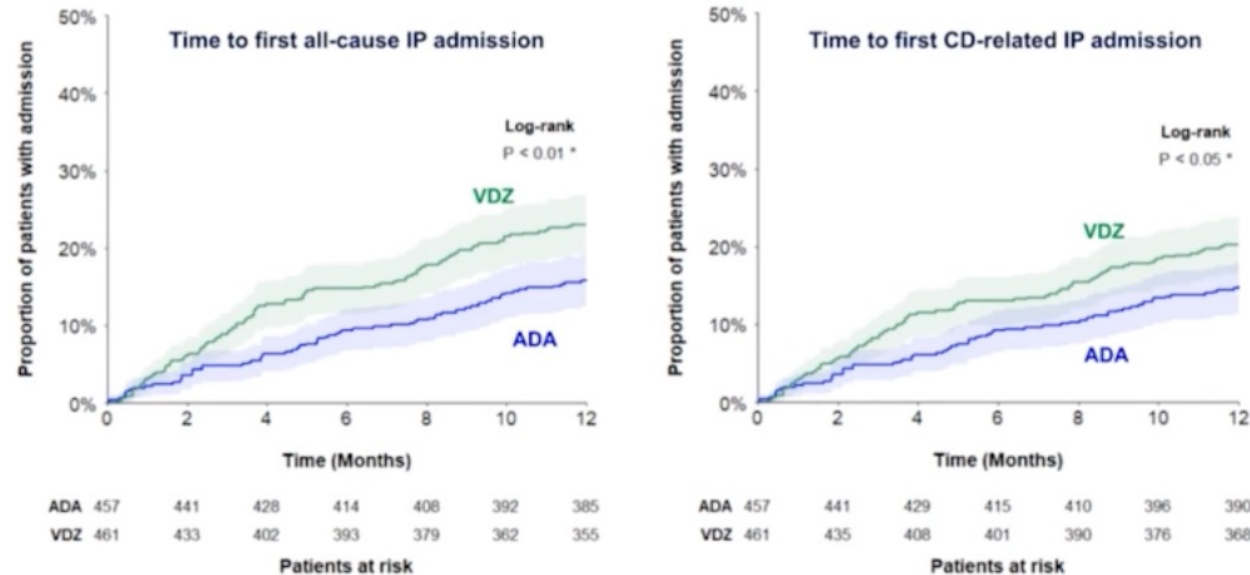


- Systemic corticosteroid discontinuation was only evaluated among patients with concomitant systemic corticosteroid use at index
- A significantly higher proportion of ADA-treated patients discontinued corticosteroids over the course of the 12-month follow-up compared with VDZ-treated patients ($P < 0.001$; proportion at 12 months: 90.2% vs 76.3%)
- Time to discontinuation was significantly shorter among ADA-treated than VDZ-treated patients ($P < 0.001$; median 1.53 months vs 3.70 months)

What agent should I choose for Crohn's?

Adalimumab vs Vedolizumab

IP Admissions Occurred Significantly Faster after Index among VDZ-Treated Than ADA-Treated Patients



- Compared to VDZ-treated patients during follow-up, a significantly lower proportion of ADA-treated patients experienced
 - An all-cause IP admission ($P < 0.01$; proportion at 12 months: 16.0% vs 23.0%), and
 - A CD-related IP admission ($P < 0.05$; proportion at 12 months: 14.9% vs 20.2%)

What agent should I choose for Crohn's?

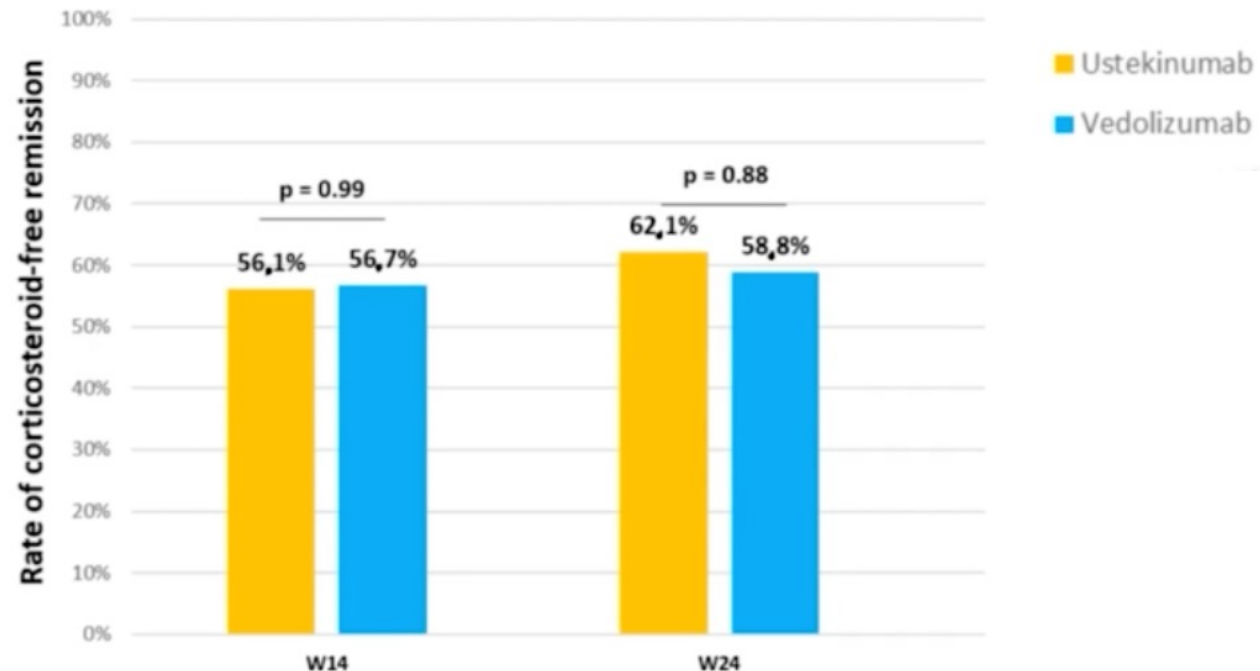
Vedolizumab vs Ustekinumab

- ▶ **VENUS:** Vedolizumab vs Ustekinumab for Crohn's Disease in anti-TNF exposed patients
 - ▶ French Pharmacy Database Study
 - ▶ Matched Propensity Score Design
- ▶ **Corticosteroid-free remission at week 54 greater in ustekinumab**
- ▶ No difference in corticosteroid-free remission at weeks 14, 24
- ▶ Both effective in achieving corticosteroid-free remission (>40%)

What agent should I choose for Crohn's?

Vedolizumab vs Ustekinumab

Corticosteroid-free remission at week 14 and 24

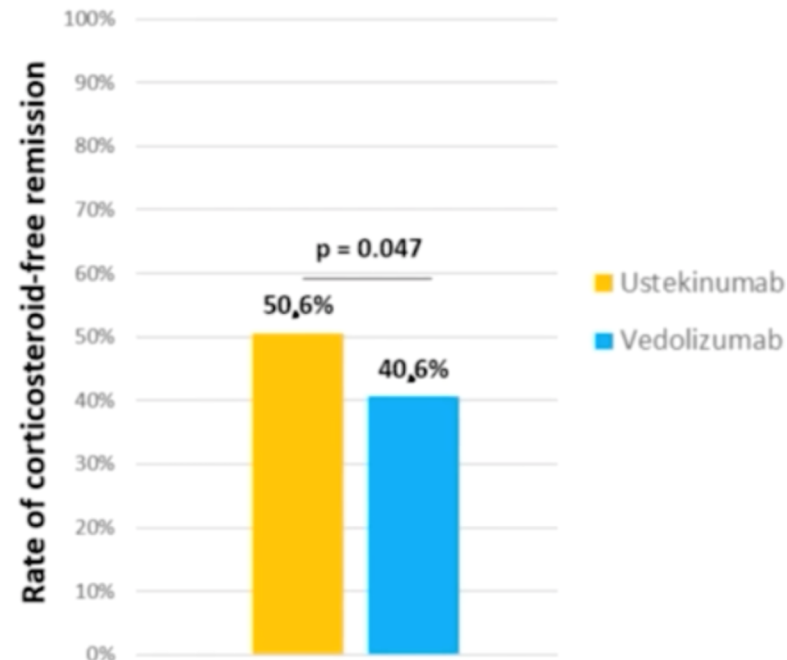


CFREM was defined as CDAI < 150 and no surgery
Results are given after IPTW with adjusted p-values

What agent should I choose for Crohn's?

Vedolizumab vs Ustekinumab

Corticosteroid-free remission at week 54



CFREM was defined as CDAI < 150 and no surgery
Results are given after IPTW with adjusted p-values

What agent should I choose for Crohn's?

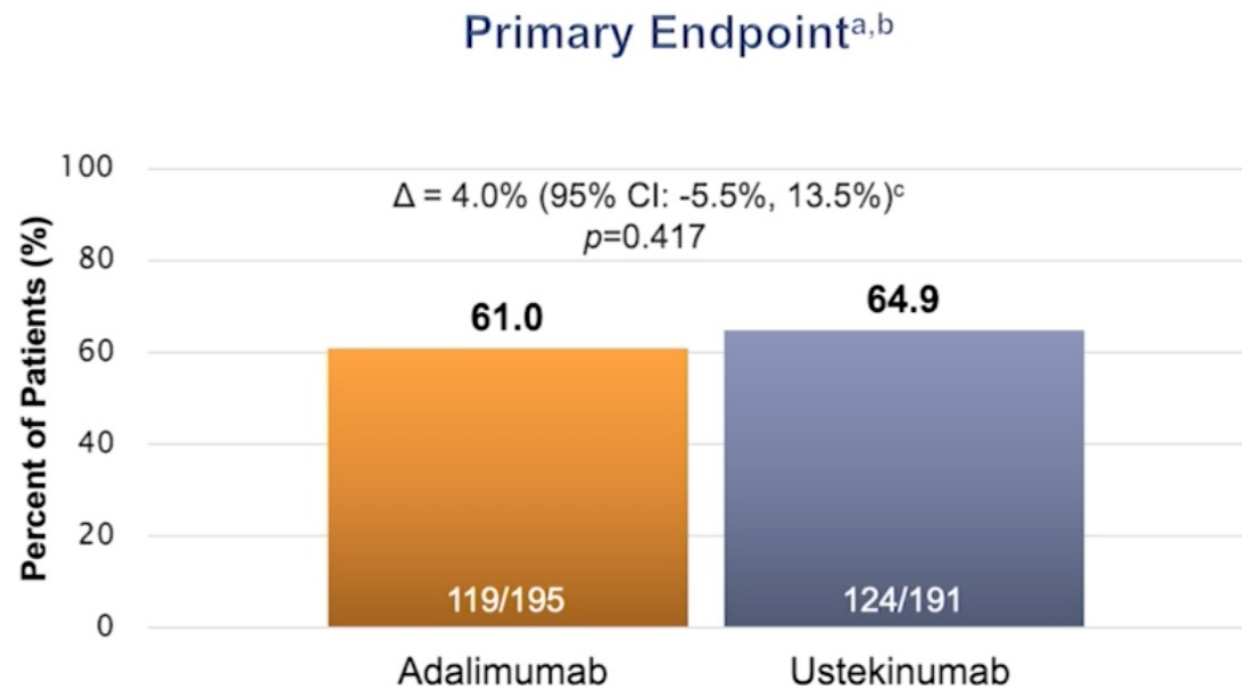
Ustekinumab vs Adalimumab

- ▶ **SEAVUE:** Ustekinumab Versus Adalimumab for Crohn's Disease:
 - ▶ Multi-center randomized, blinded, parallel-group, active-controlled study of **biologic naïve** patients with moderate to severe Crohn's disease
 - ▶ Randomized to ustekinumab with sham injections or adalimumab with sham infusion
- ▶ First head-to-head study of biologics in patients with Crohn's
- ▶ Both ustekinumab and adalimumab were highly effective in this biologic-naïve population

What agent should I choose for Crohn's?

Ustekinumab vs Adalimumab

CLINICAL REMISSION (CDAI <150) AT WEEK 52

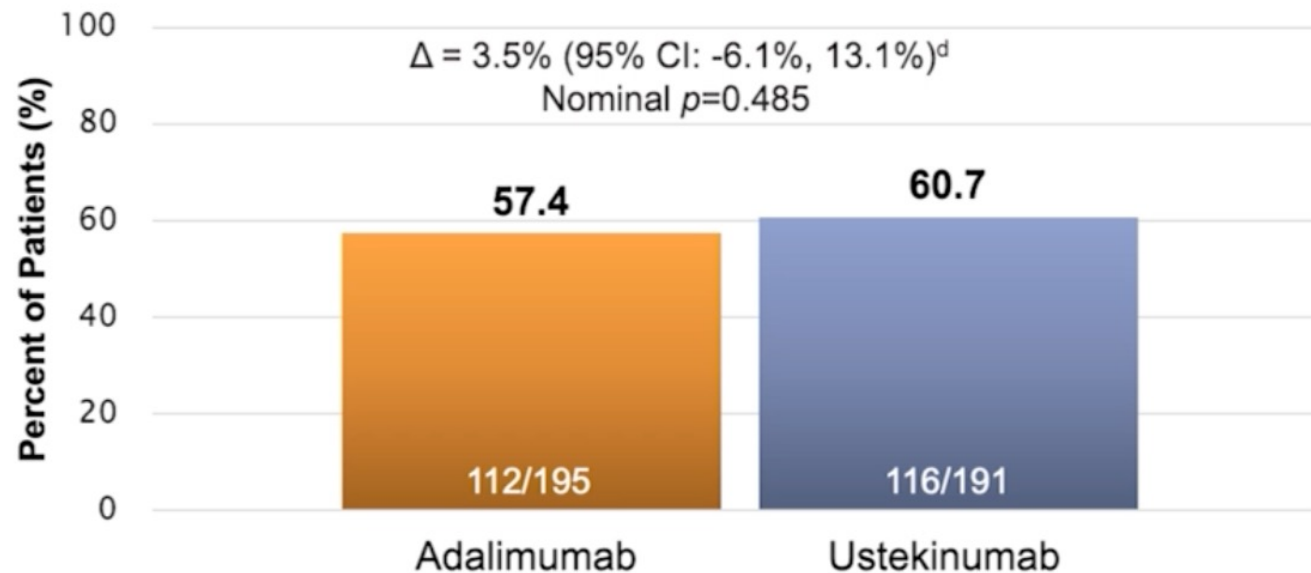


What agent should I choose for Crohn's?

Ustekinumab vs Adalimumab

CORTICOSTEROID-FREE CLINICAL REMISSION AT WEEK 52

Major Secondary Endpoint^{a,b,c}



Sands BE, et al. Presented at DDW May 2021, Abstract 775d

What agent should I choose for Crohn's?

Ustekinumab vs Adalimumab

	Adalimumab	Ustekinumab
Serious Adverse Events	16.4%	13.1 %
Infections	40.5%	34.0%
Similar safety profile as seen in previous studies		

What agent should I choose for Crohn's?

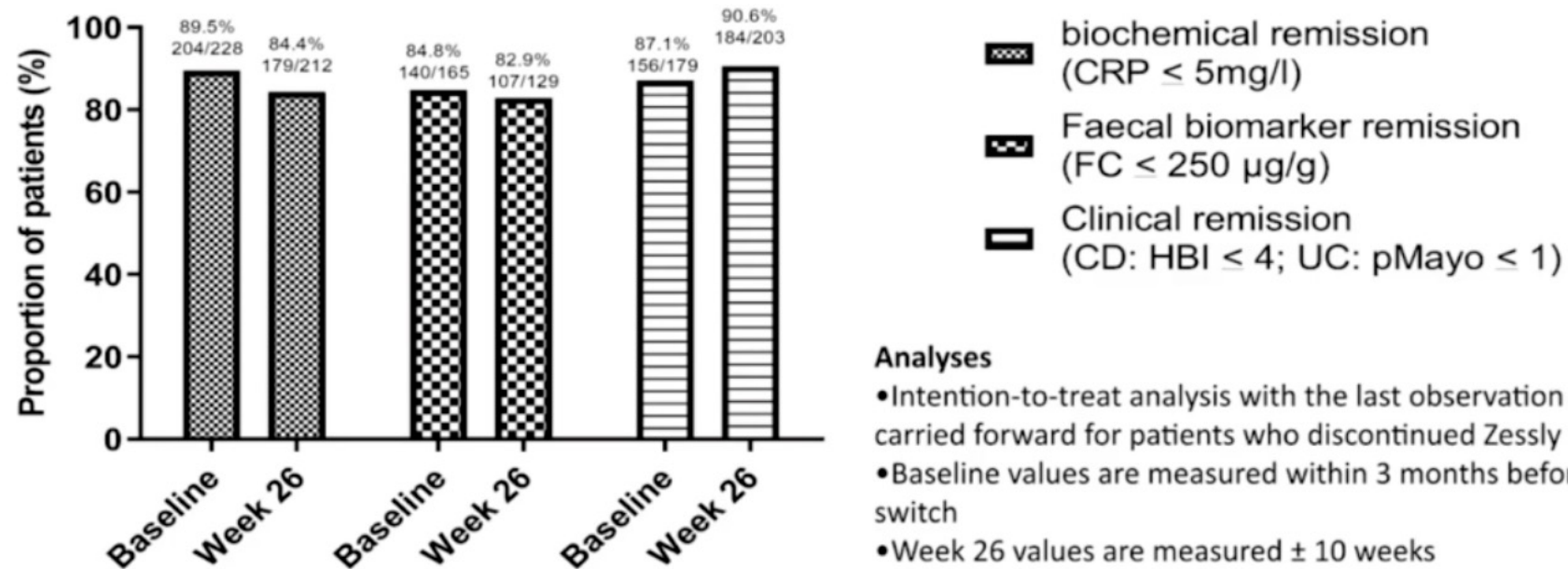
- ▶ Adalimumab and ustekinumab are both good choices for biologic-naïve
- ▶ Adalimumab and ustekinumab are associated with improved outcomes compared to vedolizumab

Switching Infliximab Biosimilars Does Not Affect Clinical Outcomes

- ▶ Prospective observational study of switch from infliximab biosimilar CT-P13 (Inflectra) to another infliximab biosimilar (Zessly/Ixifi)
- ▶ No difference in clinical and biochemical remission between baseline and at week 26
- ▶ Both single switch (Inflectra to Zessly/Ixifi) and Double switch (Infliximab to Inflectra to Zessly/Ixifi) did not impact clinical outcomes

Switching Infliximab Biosimilars Does Not Affect Clinical Outcomes

Biochemical/clinical outcomes - remission



Does ustekinumab treat extra-intestinal manifestations of Crohn's?

- ▶ Ustekinumab therapy for Crohn's disease resulted in improvement or resolution of active Extraintestinal manifestations in approximately 2/3 of patients

How does steroid use affect pregnancy?

- ▶ Pregnancy in Inflammatory Bowel Disease And Neonatal Outcomes (PIANO) registry is a prospective, multicenter, observational cohort study
- ▶ Corticosteroid use among pregnant women with IBD associated with increased risk of:
 - ▶ Low birth weight
 - ▶ Preterm birth
 - ▶ NICU stay at birth
 - ▶ Congenital malformations (1st trimester exposure)

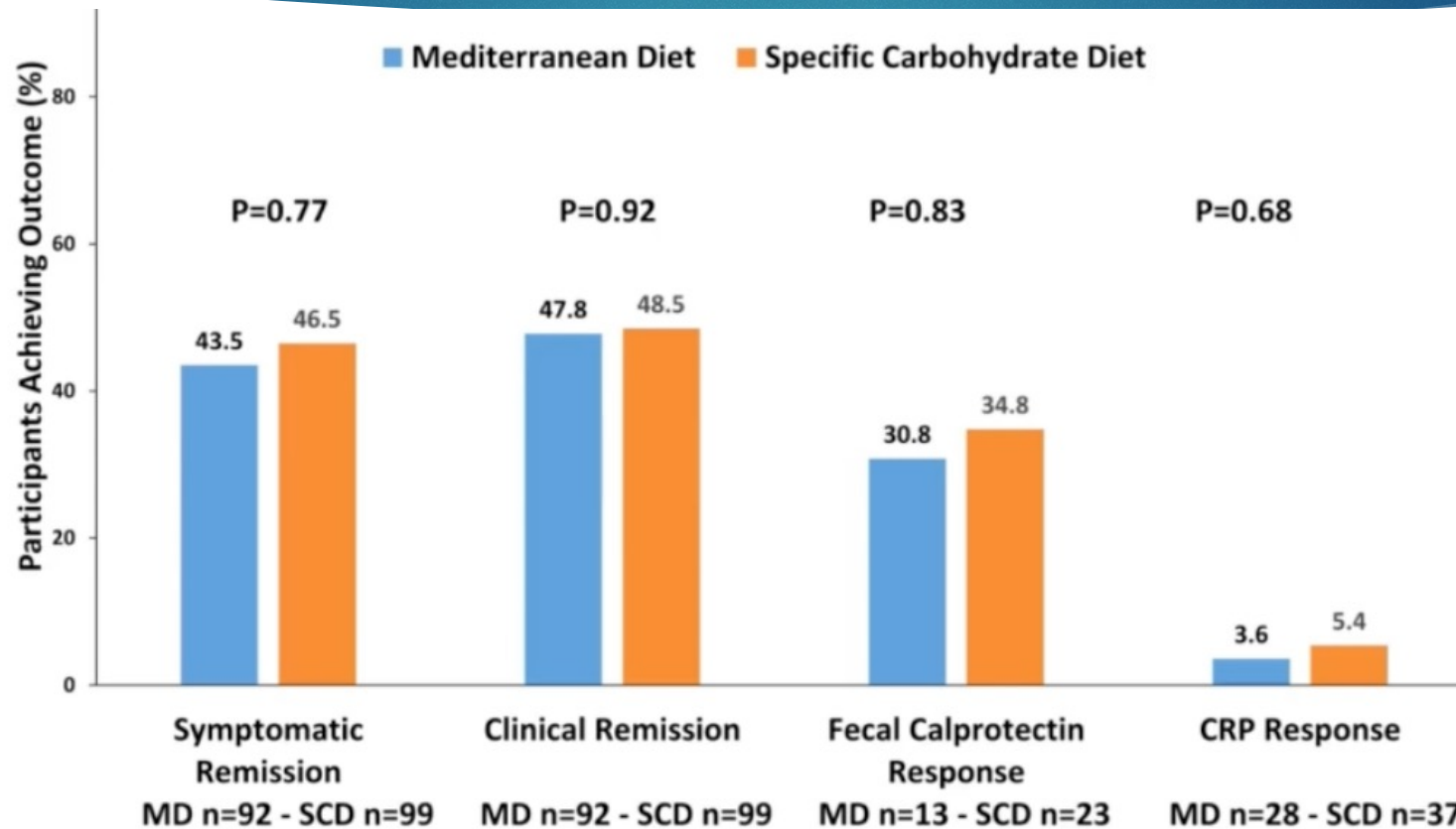
How does steroid use affect pregnancy?

- ▶ Well-controlled disease prior to conception and increased use of steroid-sparing agents for flares during pregnancy should be encouraged

What should I tell my Crohn's patients to eat?

- ▶ Multicenter randomized comparative effectiveness trial of Specific Carbohydrate Diet vs Mediterranean Diet (DINE CD)
- ▶ Specific carbohydrate Diet
 - ▶ Avoid grains, most dairy, sweeteners other than honey
- ▶ Mediterranean Diet:
 - ▶ Limit intake of red and processed meats and sweets

What should I tell my Crohn's patients to eat?



What should I tell my Crohn's patients to eat?

- ▶ Specific Carbohydrate Diet was not superior to Mediterranean Diet
- ▶ Both diets well tolerated despite increased fruit and vegetable intake

Questions Answered at DDW 2021

1. What's in the drug development pipeline for IBD?

Phase 2 Efficacy for Risankizumab and Guselkumab (IL-23)

Phase 2 Safety for Filgotinib (JAK) and Mirikizumab (IL-23)

2. What agent should I choose for my patient with Crohn's?

Adalimumab=Ustekinumab>Vedolizumab*

*head to head VDZ trials needed

3. Does switching biosimilars affect clinical outcomes?

No.

Questions Answered at DDW 2021

4. Does ustekinumab treat extra-intestinal manifestations of Crohn's?

Yes.

5. Does steroid use in pregnancy affect pregnancy and neonatal outcomes?

Yes. Control the disease before pregnancy and with steroid-sparing agents during flares in pregnancy.

6. What should I tell my Crohn's patients to eat?

Mediterranean Diet and SCD were equivalent. Veggies and Fruits well tolerated.

Sample Chart

■ Series 1 ■ Series 2 ■ Series 3 ■ Series 4 ■ Series 5

