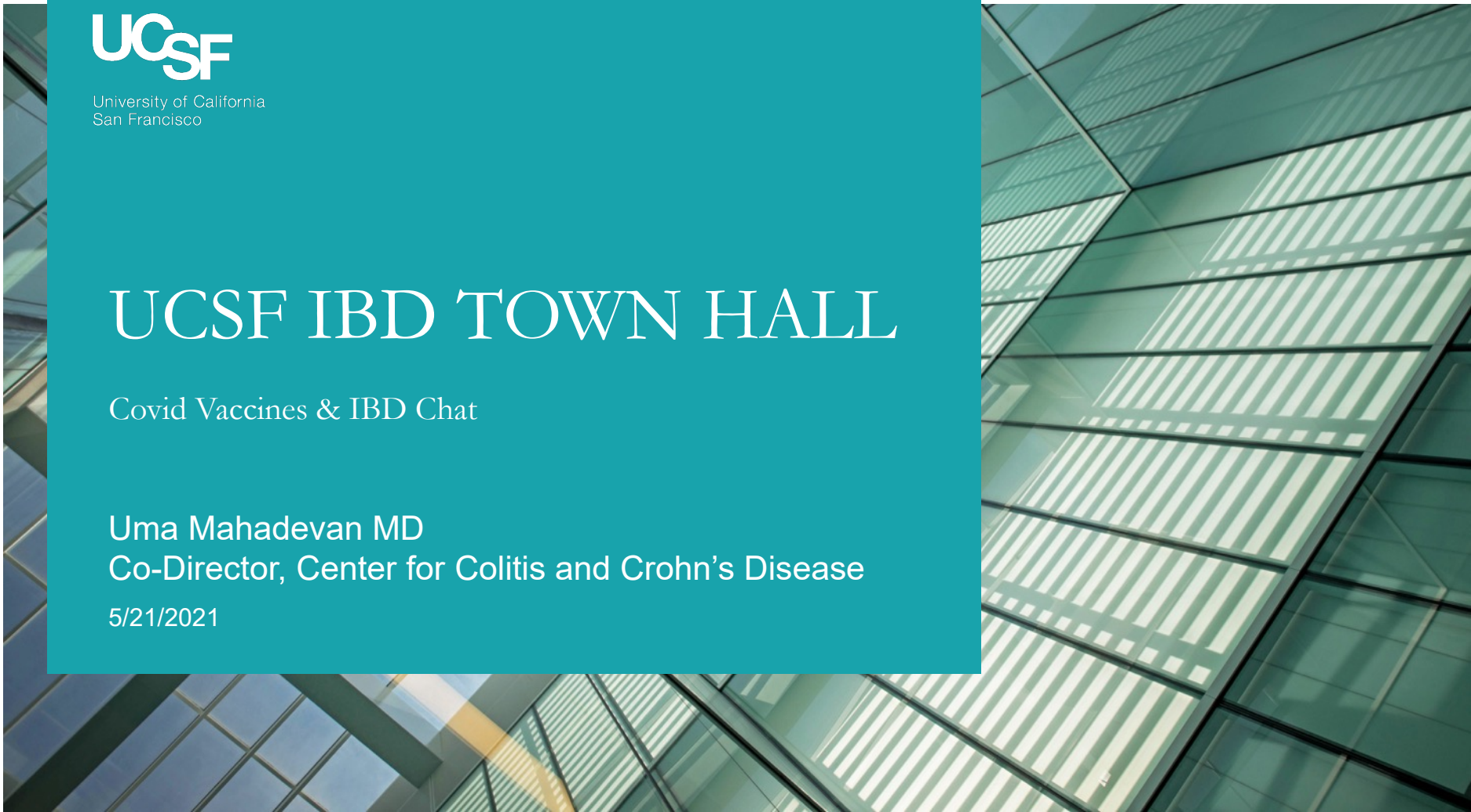

University of California
San Francisco

UCSF IBD TOWN HALL

Covid Vaccines & IBD Chat

Uma Mahadevan MD
Co-Director, Center for Colitis and Crohn's Disease

5/21/2021

Housekeeping

Your microphone will be muted

Ask a question by:

- Typing your question in the Q&A box
- Upvote similar questions you like
- You can choose to ask a question anonymously or by using your name

UCSF Colitis and Crohn's Disease Center

Twitter: @UCSFIBD

Website: *ibd.ucsf.edu*

COVID VACCINE & IBD

U.S. National Database Study: IBD Patients not at increased risk of severe disease or death from COVID-19

- Retrospective cohort utilizing U.S. EHR data (TriNetX): > 40 million patients
  - 232 IBD patients and 19,776 non-IBD patients with COVID-19 PCR or ICD-10 code
- Severe COVID-19 defined as hospitalization or 30 day mortality
- Medication use extracted from encounters in preceding 12 months

Outcomes		Before propensity matching			After propensity matching		
Outcomes		Overall risk n/total (%)	Risk ratio (95% CI)	*P* value	Overall risk n/total (%)	Risk ratio (95% CI)	*P* value
Severe COVID-19	IBD	56/232 (24.14)	1.15 (0.92–1.45)	.23	56/232 (24.14)	0.93 (0.68–1.27)	.66
	Non-IBD	4139/19,776 (20.92)			60/232 (25.86)		
Hospitalizations	IBD	56/232 (24.14)	1.20 (0.96–1.51)	.11	56/232 (24.14)	1.10 (0.74–1.40)	.91
	Non-IBD	3960/19,776 (20.02)			55/232 (23.70)		

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Singh S. et al Gastroenterology 2020

SECURE-IBD Data on COVID-19

Slides courtesy of Ryan Ungaro MD

- Large international registry of IBD patients with confirmed COVID-19 infection
- Web-based, voluntary reporting system
- Health care providers report confirmed COVID-19 cases and outcomes with medication exposure data

SECURE-IBD DATABASE
Surveillance Epidemiology of Coronavirus (COVID-19) Under Research Exclusion

https://covidibd.web.unc.edu

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Brenner EJ, Ungaro RC, et al. Gastroenterology 2020

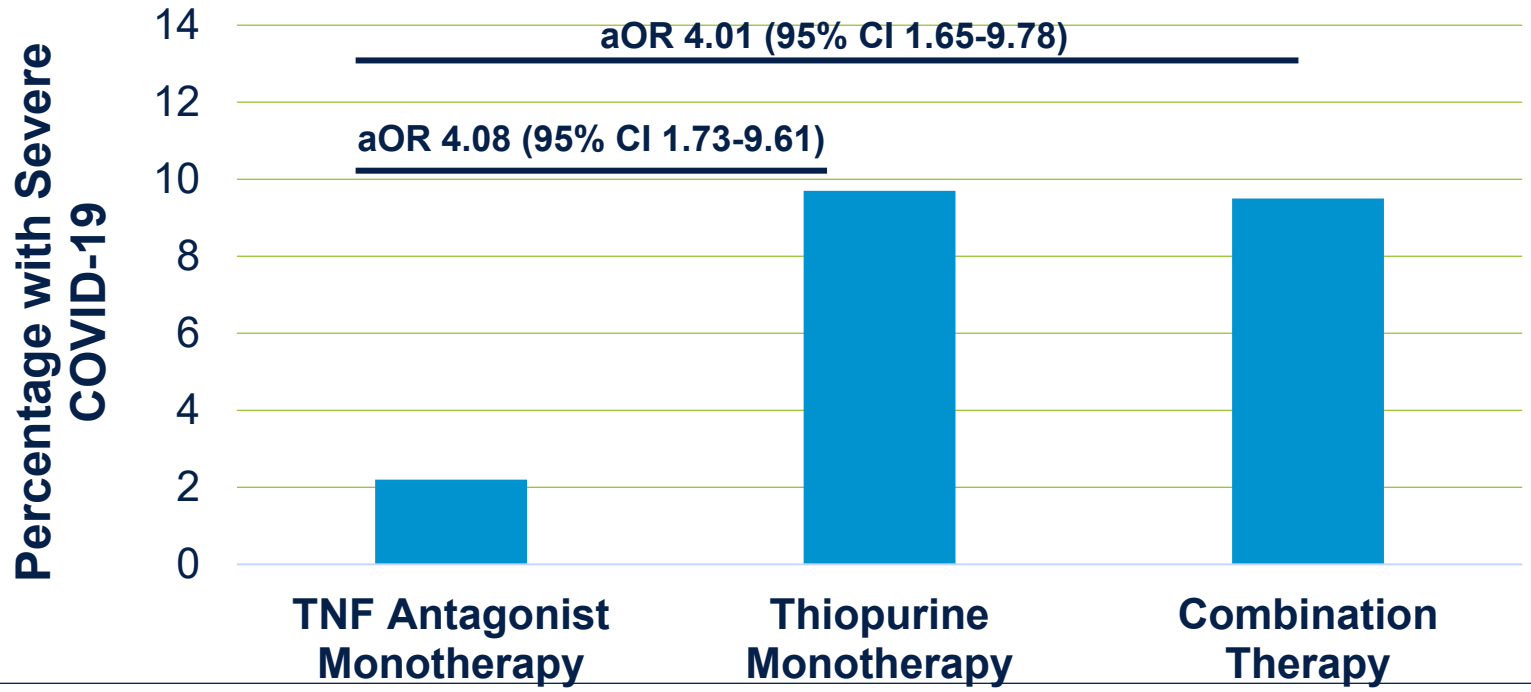
SECURE-IBD Multivariable Regression for Primary and Secondary Outcomes of COVID

Variable (Referent Group)[a]	ICU/Vent/Death OR (95%CI) N = 517	P-value	Hospitalization or Death OR (95%CI) N = 517	P-value	Death OR 95% CI N= 513	P-value
Age	1.04 (1.01-1.06)	0.002	1.03 (1.01-1.04)	<0.001*	1.07 (1.03-1.11)	<0.001*
Male (Female)[b]	1.20 (0.55-2.60)	0.65	1.38 (0.89-2.15)	0.15	2.78 (0.76-10.14)	0.12
Diagnosis CD (UC/unspecified)	0.76 (0.31-1.85)	0.54	0.84 (0.51-1.38)	0.49	1.64 (0.42-6.43)	0.48
Disease severity[c] Active disease (remission)	1.14 (0.49-2.66)	0.76	1.96 (1.23-3.11)	0.005*	0.97 (0.26-3.62)	0.96
Systemic corticosteroid (none)	6.87 (2.30-20.51)	<0.001*	6.46 (2.74-15.23)	<0.001*	11.62 (2.09-64.74)	0.005*
TNF antagonist (none)	0.90 (0.37-2.17)	0.81	0.60 (0.38-0.96)	0.03*	0.99 (0.23-4.23)	0.99
Current smoker	0.55 (0.06-4.94)	0.59	2.38 (0.92-6.16)	0.07	1.47 (0.12-17.53)	0.76
BMI ≧30	2.00 (0.72-5.51)	0.18	1.18 (0.61-2.31)	0.63	1.58 (0.28-8.80)	0.60
Comorbidities (none) 1 ≧2	 1.22 (0.45-3.26) 2.87 (1.05-7.85)	 0.70 0.04*	 1.29 (0.76-2.20) 4.42 (2.16-9.06)	 0.34 <0.001*	 1.64 (0.35-7.67) 2.51 (0.56-11.24)	 0.53 0.23
5-ASA/Sulfasalazine (none)	3.14 (1.28-7.71)	0.01*	1.77 (1.00-3.12)	0.05*	1.71 (0.46-6.38)	0.43

Brenner E and Ungaro R, et al. *Gastroenterology*. 2020; 159(2): 481–491.e3.

Thiopurines, Anti-TNF, and Combination Therapy

(updated analysis in >1400 cases)



Ungaro R et al. Gut 2020

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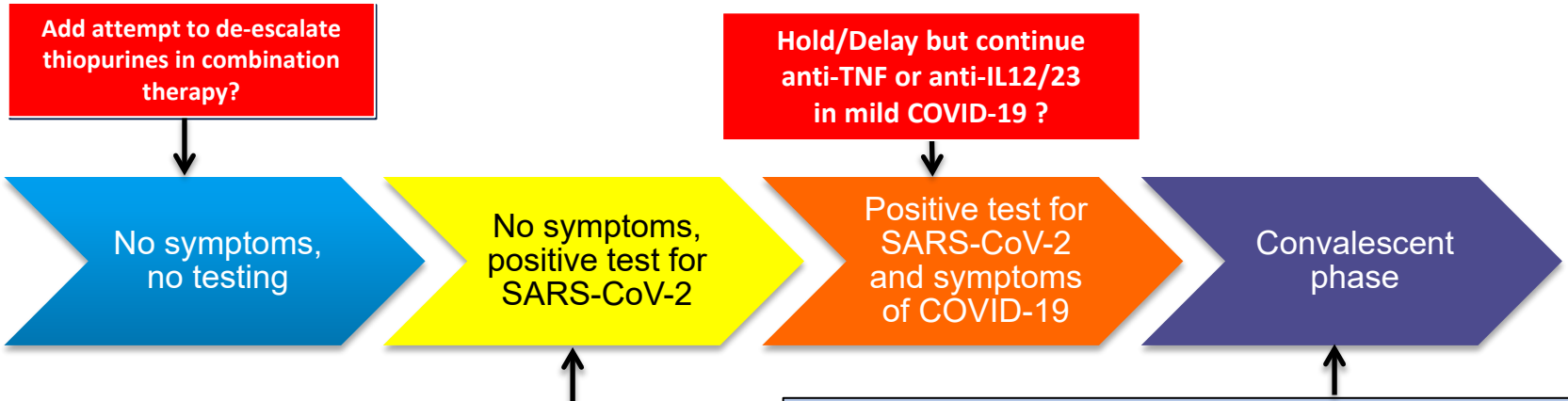
Impact of Disease Activity in SECURE-IBD

	≤50 years				>50 years			
	ICU/vent/death OR (95% CI)	P-value	Hospitalization OR (95% CI)	P-value	ICU/vent/death OR (95% CI)	P-value	Hospitalization OR (95% CI)	P-value
PGA								
Remission/mild	Reference		Reference		Reference		Reference	
Moderate	**1.83 (0.82-4.08)**	0.14	**1.43 (1.03-1.98)**	0.032	1.07 (0.82-1.38)	0.63	1.61 (1.09-2.37)	0.016
Severe	**3.67 (1.47-3.36)**	0.0052	**3.66 (2.11-6.35)**	<0.001	0.92 (0.39-2.19)	0.86	0.89 (0.32-2.48)	0.82

Associations between disease activity and COVID-19 outcomes stratified by age (multivariable GEE models)

Medication Management

IOIBD Rand Panel: Management of IBD Therapies



WHEN TO RESTART THERAPY

Symptom-based strategy:

1. At least 10 days have passed since COVID-19 symptom *onset* **and**
2. At least 3 days (72 hours) have passed *since recovery* - defined as resolution of fever without the use of fever-reducing medications **and** improvement in respiratory symptoms (e.g., cough, shortness of breath)
3. In severe COVID-19, a greater time frame from recovery may be appropriate depending on severity of IBD and need to re-start medication.

If test-based strategy is required, the above clinical parameters must be met **PLUS** two consecutive negative NP or OP COVID-19 molecular assays (RT-PCR or NAAT swab specimens) collected ≥24 hours apart.

IBD = inflammatory bowel disease
COVID-19 = coronavirus disease 2019
SARS-Co-V-2 = severe acute respiratory syndrome coronavirus 2
NP = nasopharyngeal
OP = oropharyngeal
RT-PCR = reverse transcription-polymerase chain reaction
NAAT = nucleic acid amplification test

IOIBD COVID-19 Task Force. Siegel CA et al JCC 2020

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Conclusions

- IBD patients do not appear to be at increased risk of contracting COVID-19
- Certain IBD patients with COVID-19 may be at increased risk of adverse events
  - Risk primarily driven by older age, co-morbidities, and steroid use
  - Thiopurines and combination therapy may increase risk as well
- Anti-TNFs and other biologics appear to be low risk and should be continued in the COVID-19 era
- IBD patients who develop COVID-19 should be managed on a case by case basis
  - Another reason to de-escalate combination therapy / taper steroids
  - In difficult to control patients, can consider not delaying/stopping biologics if asymptomatic / mild disease

Vaccines

Company	Platform	Doses	Non-clinical results	# with vaccine (same placebo)	Protection from COVID-19 hospitalization	Protection from COVID severe dz (some at home)	Efficacy against milder COVID
moderna	mRNA-1273 mRNA in lipid nanoparticle	2	Neutralizing Abs; Strong Th1 CD4+ protection from challenge (macaques)	~15,000	90% (1 in vaccine arm after 2nd dose hospitalized)	97% (30 cases in placebo arm; 0 in vaccine reported but 1 severe per FDA)	94.1%
Pfizer	BNT162b2 mRNA in lipid nanoparticle	2	Neutralizing Abs; Strong Th1 CD4+, CD8+; protection from challenge (macaques)	~18,600	100%	100% (9 cases in placebo arm; 0 in vaccine- 1 initially severe but not)	95%
Johnson & Johnson	JNJ-78436725 Non-replicating human adenovirus/DNA	1	Neutralizing Abs; Strong Th1 CD4+ > Th2; CD8+; challenge protection (macaque)	~22,000 US, Latin America, S. Africa	100%	85.4% across 3 sites (7 deaths, 16 hospitalizations, all in placebo arm)	72% US; 61% Latin America; 64% S. Africa (95% B1.351)
AstraZeneca	AZD 1222 Non-replicating Chimp Adenovirus-DNA	2	Neutralizing Abs; Strong Th1 CD4+ > Th2; CD8+; protection from challenge (macaques)	~28,588 (UK, SA, US/Peru/ Chili)	100%	100% (UK, 15 placebo arm hospitalized, 0 in vaccine; US, 8 severe in placebo, 0 vaccine)	76% US (85% in >65 yrs); 70% UK; S. Africa halted for mild
BHARAT	Inactivated whole virus	2	Neutralizing Abs; Strong Th1 CD4 responses in phase II trial (Lancet)	11,000 (press release 4/21)	100%	100%	78%
Sputnik V	Ad26 and Ad5 adenovirus/DNA	2	NAbs; IFN-γ secretion PMBCs, cellular response	~14964	100%	100% (20 in placebo; 0 vaccine)	91.6%

Slide @MonicaGandhi9

Studies to date that showed COVID-19 vaccines reduce asymptomatic infection (transmission)

Setting	% reduction in asymptomatic infection or transmission	Reference
Healthcare workers in England	85%	Hall Lancet, April 23, 2021
Healthcare workers in Israel	75% and 86%	Amit, Lancet, March 6; Angel JAMA May 6
Patients in Mayo Clinic health system	88.7%	Pawlowski medRxiv, February 27, 2021
Israel Ministry of Health (nationwide)	94% (largest study)	Pfizer press release, March 11, 2021 (and Goldberg Medrxiv, April 24, 2021)
Israel general population (Pfizer)	90%	Dagan NEJM, February 24, 2021
Pre-surgical patients in Mayo Clinic system swabbed asymptomatically	80%	Tande Clin Inf Dis, March 10, 2021
Healthcare workers in Cambridge University Hospitals	75%	Weekes Authorea, February 24, 2021
First-line responders and HCWs in US	90%	Thompson A. MMWR, March 30, 2021
Israel population (>16) with children unvaccinated	For every 20-point increase in adult vaccination, rates of kids testing positive halves	Milman O. Medrxiv. March 31, 2021
Long-term care facility, Spain	90%	Salazar P. Medrxiv. April 13, 2021
Nursing homes, U.S. (two studies)	100%	Cavanaugh MMWR, April 21 and Terran MMWR, April 30

Nasal viral load values most important determinant of transmissibility (Lancet study, Spain); Viral loads from post-vaccination exposures are low and likely noninfectious per CT values (use rapid antigen tests after vaccination if test symptomatic or incorporate CT)

Slide: @MonicaGandhi

COVID-19 Vaccines: IOIBD Guidance

- Consensus statements from the International Organization for the Study of Inflammatory Bowel Disease (IOIBD)
- Iterative Delphi method to develop consensus expert opinion statements

Highlighted themes of accepted statements related to SARS-CoV-2 vaccination for patients with IBD by the International Organization for the Study of Inflammatory Bowel Disease (IOIBD)
Patients with IBD should be vaccinated against SARS-CoV-2.
The best time to administer SARSCoV-2 vaccination in patients with IBD is at the earliest opportunity to do so.
SARS-CoV-2 vaccines including messenger RNA vaccines, replication incompetent vector vaccines, inactivated vaccines and recombinant vaccines are safe to administer to patients with IBD.
SARS-CoV-2 vaccination should not be deferred because a patient with IBD is receiving immune-modifying therapies.
Patients with IBD vaccinated with SARS-CoV-2 should be counselled that vaccine efficacy may be decreased when receiving systemic corticosteroids.

Siegel et al Gut 2021

Should you vaccinate pregnant women?

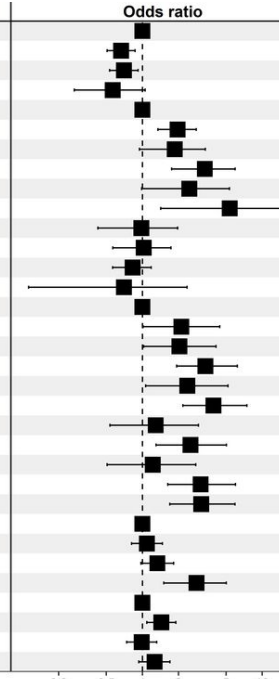
- **Pregnant women were not part of the trials**
  - mRNA vaccines do not interact with genetic material DNA because mRNA does not enter the nucleus of the cell.
  - Inactive vaccine so no risk of getting COVID
- **ACOG:**
  - COVID-19 vaccines should not be withheld from pregnant individuals who meet criteria for vaccination based on ACIP-recommended priority groups.
  - COVID-19 vaccines should be offered to lactating individuals similar to non-lactating individuals when they meet criteria for receipt of the vaccine based on prioritization groups outlined by the ACIP.
- **ACIP/CDC:**
  - If a pregnant woman is part of a group (e.g. healthcare personnel) who is recommended to receive a COVID vaccine, she may choose to be vaccinated.
  - V-safe: 275 vaccinated pregnant women: no evidence of harm
- **WHO:**
  - Pregnant women at high risk of exposure to SARS-CoV-2 (e.g., health workers) or who have comorbidities which add to their risk of severe disease may be vaccinated in consultation with their health care provider
  - WHO does not recommend discontinuing breastfeeding after vaccination

Anti-SARS-CoV-2 Antibody Responses are Attenuated in Patients with IBD Treated with Infliximab and Immunomodulators (INFECTION)

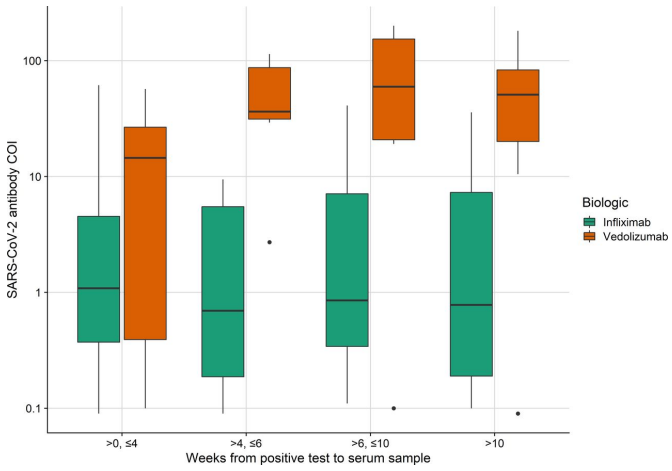
N=6935
67.6% infliximab and 32.4% vedolizumab

Multivariable logistic regression model of associations with a positive anti-SARS-CoV-2 antibody

Variable		N	OR (95% CI)	p
Biologic	Vedolizumab	2245	Reference	
	Infliximab	4675	0.66 (0.51, 0.87)	0.0027
Immunomodulator		3059	0.70 (0.53, 0.92)	0.012
Age > 70		387	0.56 (0.27, 1.06)	0.097
Ethnicity	White	6116	Reference	
	Asian	479	1.97 (1.35, 2.81)	0.00031
	Mixed	154	1.86 (0.95, 3.36)	0.052
	Black	108	3.32 (1.75, 5.94)	0.00011
	Other	63	2.47 (0.98, 5.33)	0.034
Income deprivation score		6920	5.36 (1.42, 19.55)	0.012
Heart disease		210	0.98 (0.43, 1.97)	0.96
Diabetes		311	1.03 (0.57, 1.73)	0.93
Lung disease		963	0.83 (0.56, 1.18)	0.32
Cancer		50	0.70 (0.11, 2.36)	0.63
Region	South West	958	Reference	
	East Midlands	467	2.12 (1.01, 4.42)	0.044
	East of England	644	2.04 (1.03, 4.12)	0.043
	London	1188	3.35 (1.93, 6.20)	<0.0001
	North East	284	2.37 (1.06, 5.18)	0.031
	North West	630	3.92 (2.18, 7.44)	<0.0001
	Scotland	423	1.29 (0.54, 2.94)	0.55
	South East	654	2.52 (1.30, 5.03)	0.0069
	Wales	451	1.22 (0.51, 2.79)	0.64
	West Midlands	527	3.06 (1.63, 5.98)	0.00067
	Yorkshire and the Humber	694	3.10 (1.69, 5.94)	0.00038
Shielding Apr-Jul	Remained at home	2391	Reference	
	Exercise w/ own household	2699	1.09 (0.81, 1.47)	0.57
	Met others, social distancing	1694	1.33 (0.97, 1.83)	0.072
	No social distancing	136	2.83 (1.51, 5.01)	0.00062
Diagnosis	Crohn's disease	3941	Reference	
	UC/IBDU	2979	1.44 (1.09, 1.90)	0.011
5-ASA		1825	0.99 (0.74, 1.32)	0.94
Steroid use at any point in 2020		1154	1.27 (0.93, 1.70)	0.12



Magnitude of anti-SARS-CoV-2 antibody reactivity stratified by biological therapy and time since prior positive PCR test

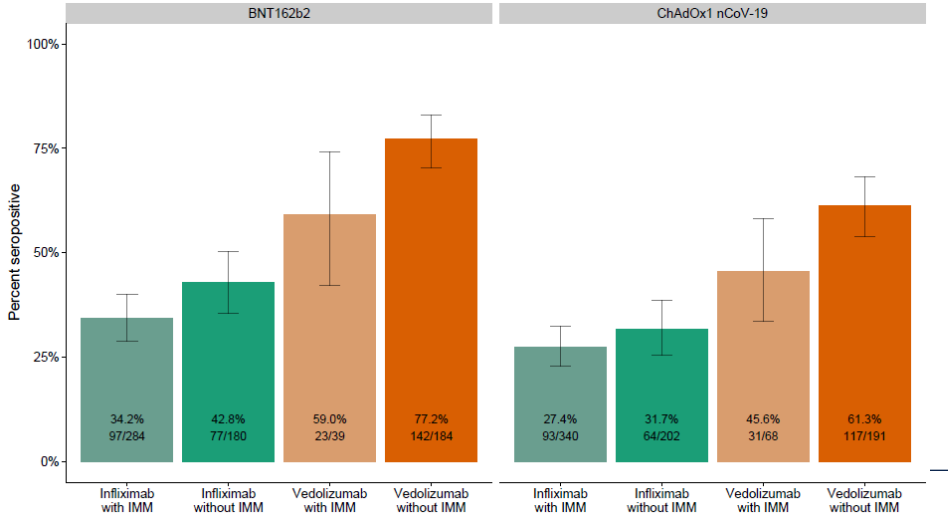


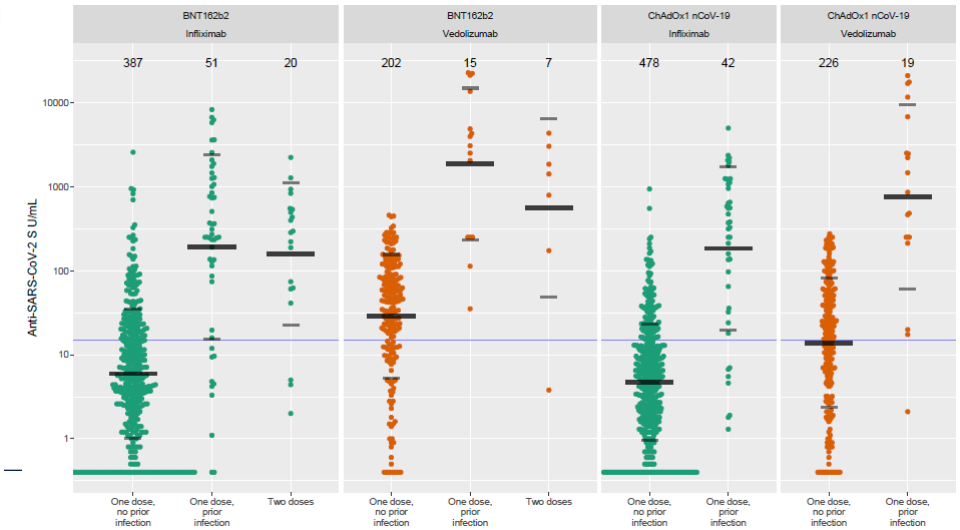
Kennedy NA, et al. *Gut*. 2021. [Epub ahead of print].

Immunogenicity to BNT162b2 (Pfizer/BioNTech) and ChAdOx1 (AstraZeneca) nCoV-19 SARS-CoV-2 vaccines

Infliximab n=865; Vedolizumab n=428

- Age >59, immunomodulator use, CD, and smoking were associated with lower, while non-white ethnicity was associated with higher, anti-SARS-CoV-2 antibody concentrations.
- Infliximab was associated **with attenuated immunogenicity to a single-dose** of the BNT162b2 and ChAdOx1 nCoV-19 SARS-CoV-2 vaccines **BUT** vaccination after SARS-CoV-2 infection or a **second dose of vaccine led to seroconversion in most patients**
- **Delayed second dosing should be avoided in patients treated with infliximab**

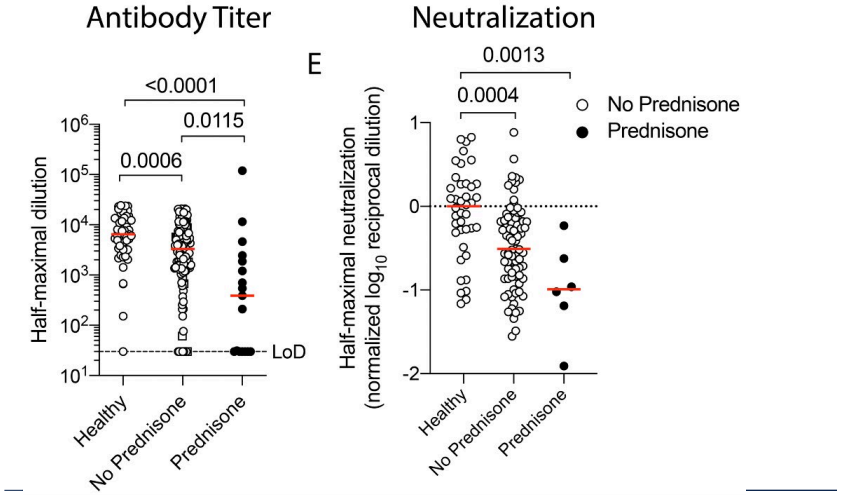


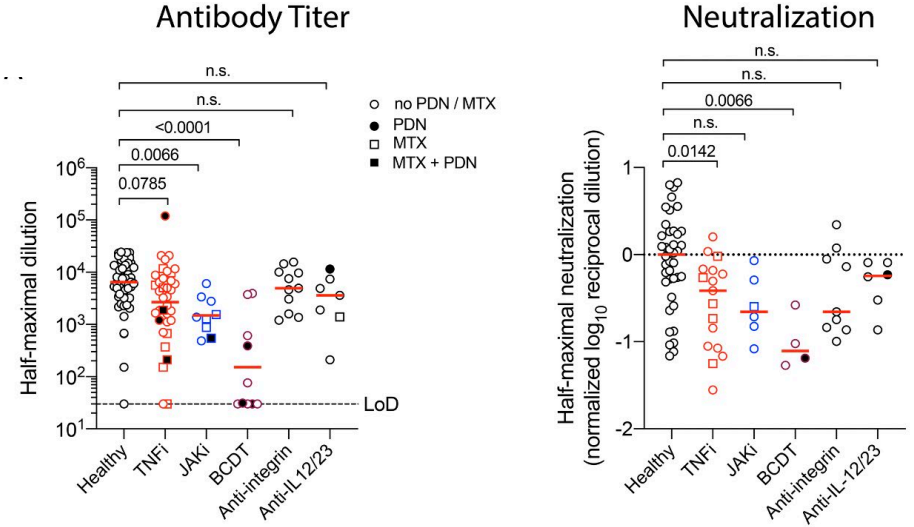


Kennedy NA, et al. *medRxiv*. 2021. [preprint].

COVaRiPAD (**CO**VID-19 **Va**ccine **R**esponses **i**n **P**atients with **A**utoimmune **D**isease) Study

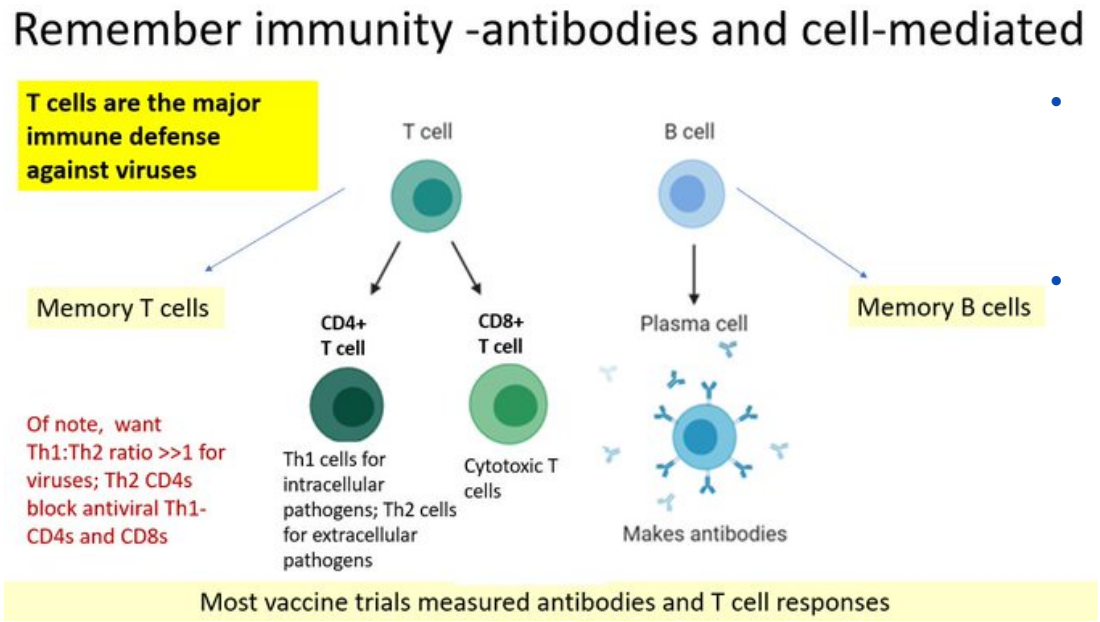
- Prospective assessment of mRNA-based vaccine immunogenicity in 133 adults with chronic inflammatory diseases (CID) and 53 immunocompetent controls
- 31.6% with IBD and 28.6% Rheumatoid Arthritis





Deepak P et al MedRxiv 2021

What if my antibodies are low?



- **Raise T cells after natural infection or vaccines against 57 pieces of the spike protein and receptor binding domain of the virus.**
- **Levels of SARS-CoV-2 neutralization antibodies alone do not determine protection**

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Vaccinated: What now?

- To Mask or Not to Mask?
  - Follow your local ordinance
  - OK to unmask (if you are comfortable) in the following situations
    - Indoors with a small group of vaccinated people outside of your home contacts
    - Outdoors with space
- Do I need to check antibody?
  - No
    - But if you want to, do it the context of a trial
  - Antibody response is not just antibody, but T cell response as well
  - Most IBD medications should not block response

Prevent COVID Vaccine Study

Aim 1: To evaluate the effectiveness of COVID-19 vaccination in preventing COVID-19 infection in patients with IBD

Aim 2: To evaluate safety of COVID-19 vaccination in patients with IBD, including immediate side effects and disease activity

Aim 3: To evaluate antibody response to COVID-19 vaccination in patients with IBD

www.ibdpartners.org/preventcovid

Email: preventcovid@unc.edu

***Will recruit adult and pediatric patients (based on availability of age groups for vaccines; currently 16 and up)*

Prevent COVID Data thus far, over 3000 patients enrolled!

- Mean age 44.4 years
- 75% female
- BMI 26.2
- Mean disease duration 18 years
- 5% with prior COVID infection (infected prior to vaccine)
- Types of vaccine:
- Pfizer 54.1%
- Moderna 37.2%
- J&J 4.4%
- Nearly 30% reported fatigue after vaccine as most common side effect
- Very low rates of worsening GI/IBD symptoms after vaccine (<10%)

University of California
San Francisco

IBD CHAT

Uma Mahadevan MD and Olivia Bigazzi

5/21/2021

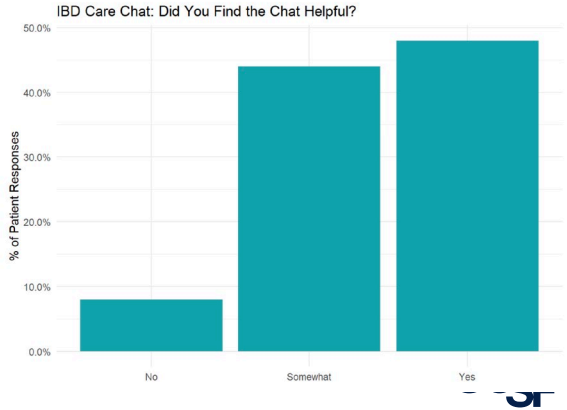
Chat Goals

- Develop a virtual care chat for remote Patient Reported Outcomes in patients with IBD
- Reminder to obtain labs at appropriate time intervals
- Reassurance if doing well without any symptom flares
- Identify symptom flares for clinical escalation to provider

Project Evaluation & Impact

- 53 patients enrolled as initial beta test
  - Only 2 patients opted out
- 33 patients (62.3%) have completed at least one chat module
  - 10 patients have entered responses that generated a clinical escalation, sent to Epic In-Basket Pool
- 91% of patients found the chat at least somewhat helpful

Alert Color	Total Alerts (n)	Alerts per patient
red	10	0.3
yellow	189	5.73



Oliva Bigazzi: Demonstration

What to Expect

- You will receive an email/text asking you to sign up
- You will get prompts to do your questionnaires
- If you have alarm symptoms we will be alerted
- If you are having severe symptoms, call your doctor!

IBD Clinical Trials at UCSF

UCSF Colitis and Crohn's Disease Center
@UCSFIBD
ibd.ucsf.edu

Tigenix Stem Cell Trial

- Phase 3, randomized, double-blind, placebo-controlled, multicenter trial of Cx601 treatment Darvadstrocel
- Treating complex perianal fistulas in patients with Crohn's Disease
- CD in remission or minimally active

Risankizumab

- Phase 3, randomized, double-blind, placebo-controlled, multicenter trial of IL-23 Inhibitor on patients with moderate to severe UC
- Failed at least 1 biologic in the past

MOSAIC: Management **O**f **S**evere UC with **A**mbulatory **I**ntravenous **C**orticosteroids

- Flaring UC patients
- Studying Safety and satisfaction of IV steroid in an outpatient (no hospital admission) setting for patients with severe acute UC

PIANO Registry

- Multicenter national prospective study of pregnancy and neonatal outcomes in women with IBD
- All pregnant women with IBD encouraged to enroll
- PIANO@ucsf.edu

For more information about our clinical trials please visit ibd.ucsf.edu or email karan.bhatia@ucsf.edu

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