

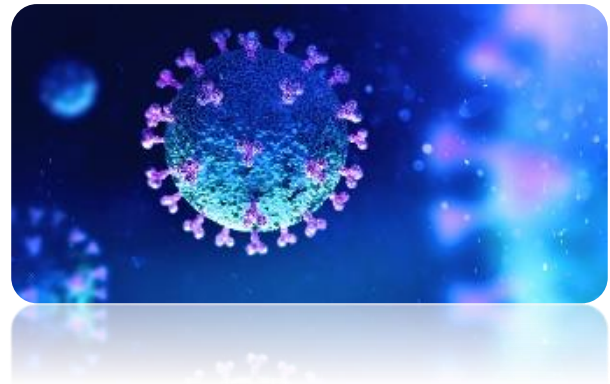
COVID Treatment and Vaccination Frequency in Immune-Compromised Patients

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Objectives

1) COVID-19 and Lupus

- Which patients with SLE will be more affected by COVID (GRA Data)

2) COVID-19 Vaccine

- 1,2,3 or 4 vaccines
- Will SLE patients mount a response to the vaccine?
- If I've already had COVID do I need the vaccine?

3) Paxlovid

- What is this medication?
- Where can patients access this medication
- Do I qualify for this medication?

4) Evusheld – is this available for lupus patients?

5) Rheumatic long COVID symptoms

6) Safety of COVID vaccines in SLE



Results of COVID-19 vaccination in patients with immune diseases on treatment

Alfred Kim , MD

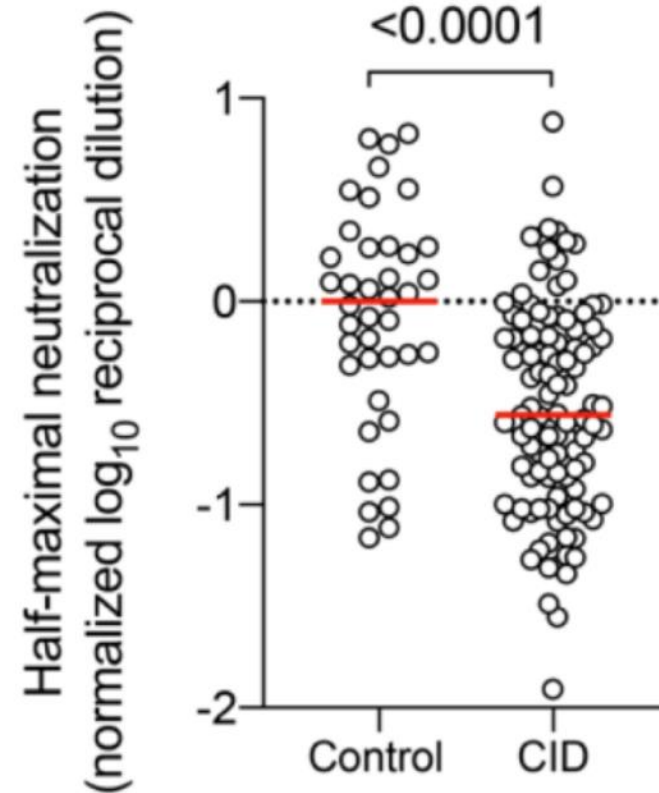
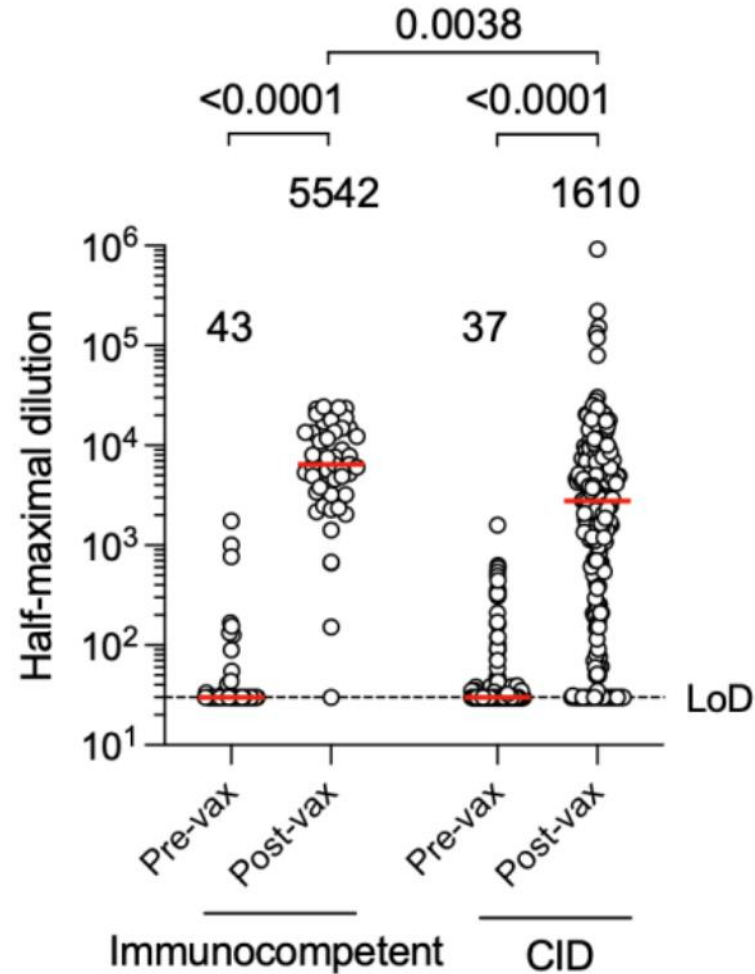
COVaRiPAD study design

- Prospective observational study (pre-vaccination to 5 months post-mRNA vaccination) at Washington University and UCSF
 - Plasma, serum, PBMCs, and PROs are collected at each visit (total 7)
- 274 patients with physician-confirmed CID and 53 immunocompetent controls (confirmed not to have CID nor be on immunosuppression)
 - IBD, RA, SLE, SpA, MS/NMO, SS, Vasculitis
- Anti-S antibodies measured by homebrew ELISA (Ellebody)
- Neutralizing antibodies: fluorescence or focus reduction neutralization test
 - Chimeric VSV pseudotyped with D614G Spike expressing GFP (Whelan)
 - SARS-CoV-2 B.1.617.2 clinical isolate (Diamond)

Turner *et al*, *Nature*, 2021
Case *et al*, *Cell Host Microbe*, 2020
Chen *et al*, *medRxiv*, 2021

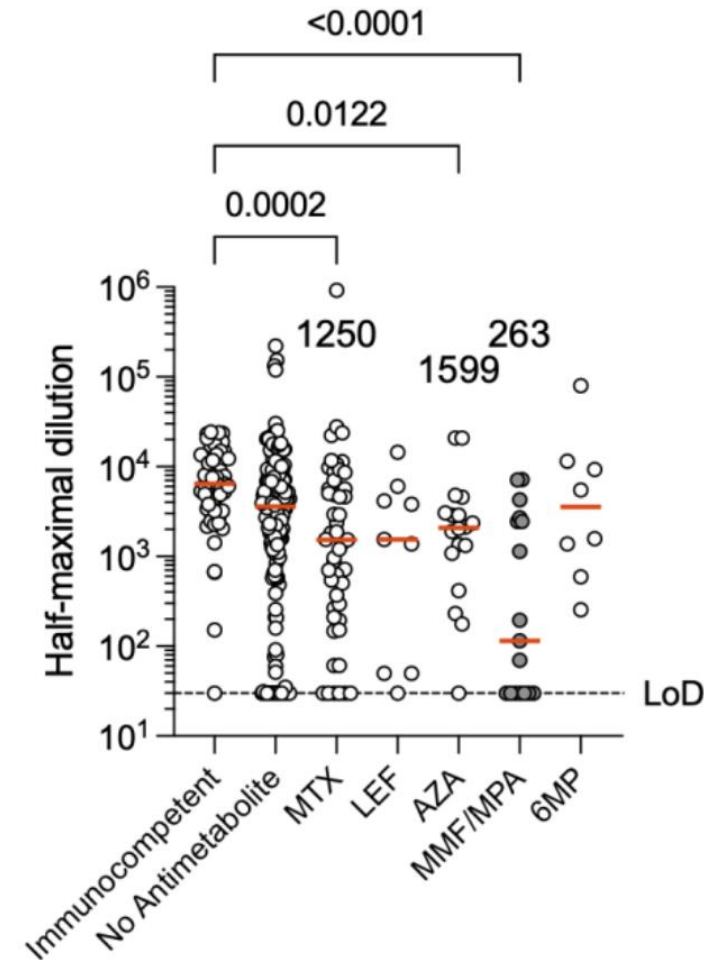
Overall immunogenicity

Most (~90%) of participants with CID will make Ab responses, albeit with reduced (3.4-fold) titers



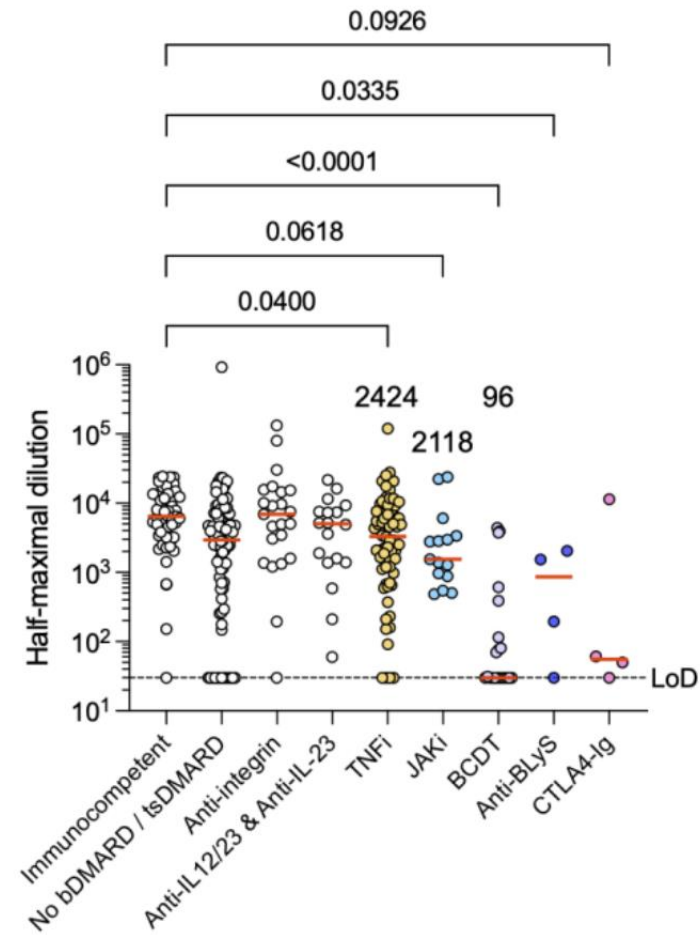
Antimetabolite immunogenicity

- Compared to immunocompetent:
 - MMF/MPA (n=17): 21-fold reduction
 - MTX (n=51): 4.4-fold reduction
 - AZA (n=18): 3.5-fold reduction



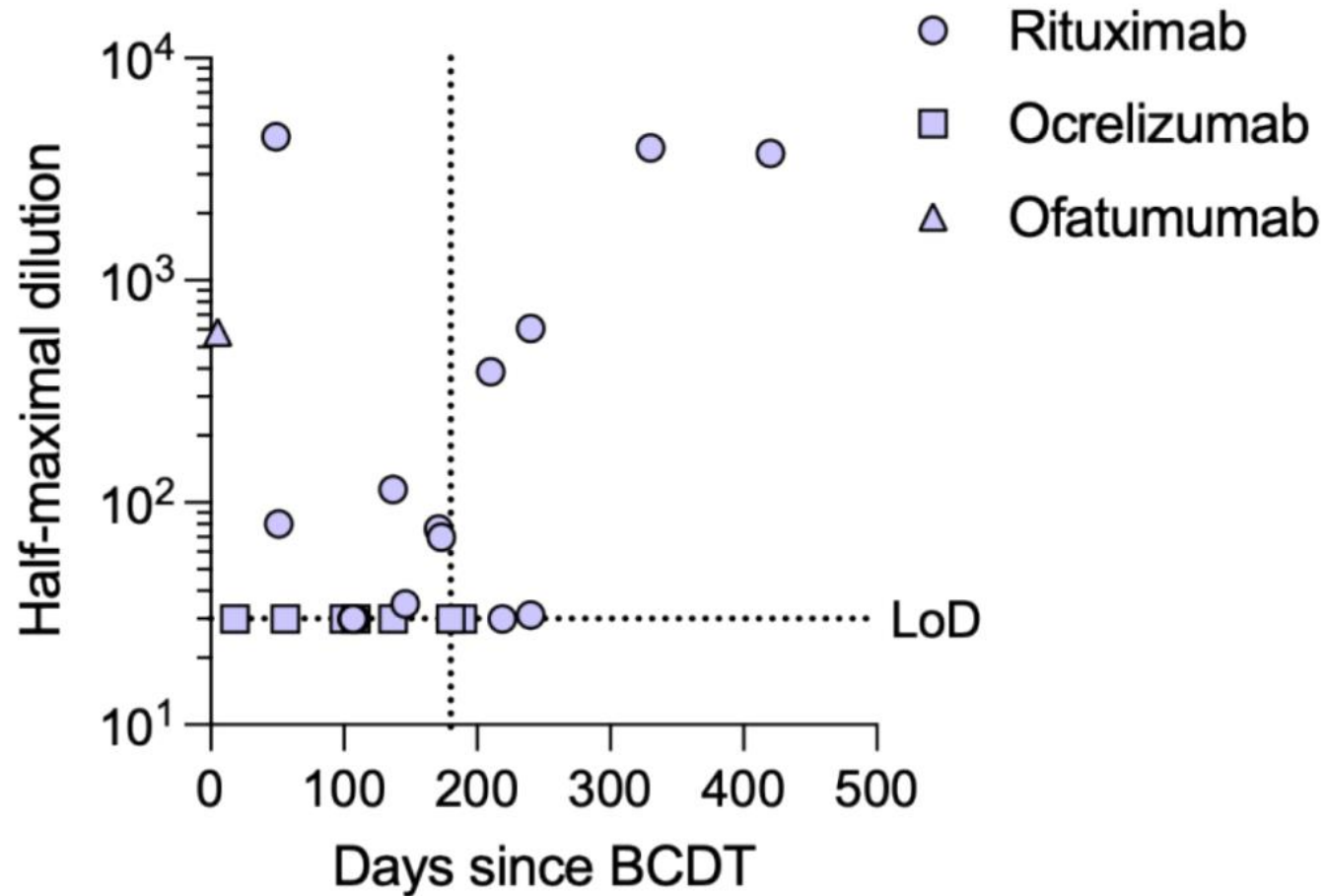
bDMARD/tsDMARD immunogenicity

- Compared to immunocompetent:
 - BCDT (n=21): 57.7-fold reduction
 - JAKi (n=15): 2.6-fold reduction
 - TNFi (n=68): 2.3-fold reduction



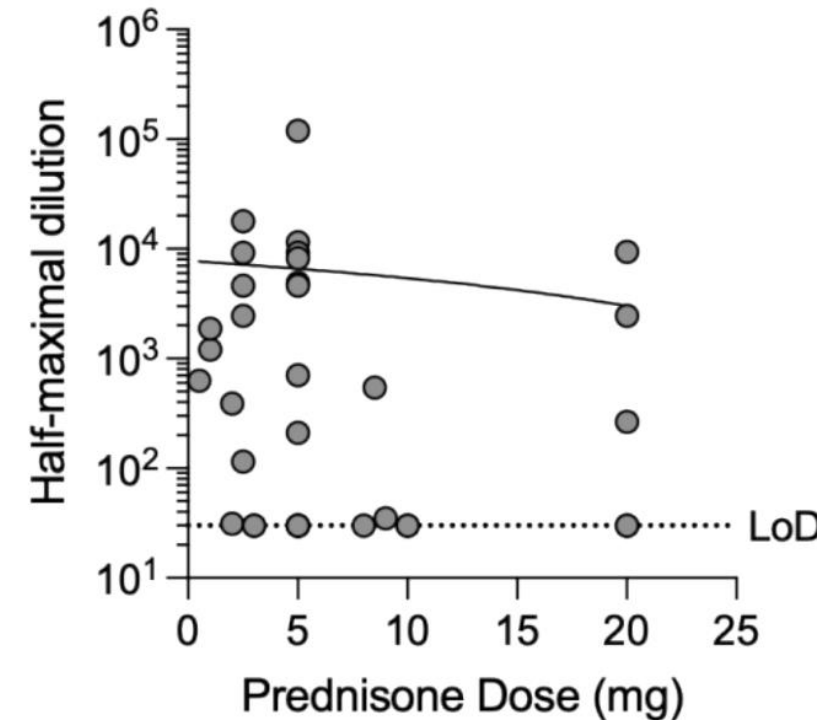
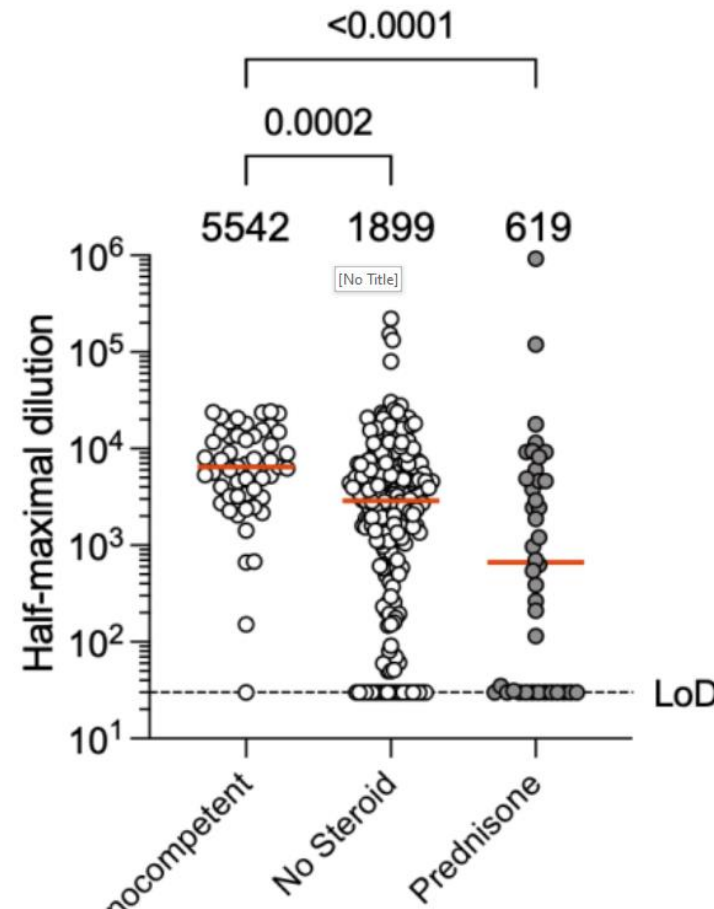
BCDT immunogenicity

~6 month period between last BCDT dose and vaccination associates with serologic response



Glucocorticoid immunogenicity

- 9-fold reduction (n=40) compared to immunocompetent
- Even some on low-dose (≤ 5 mg/day PDN equivalent) mounted very poor responses
 - May be confounded by concomitant medication use
 - Boekel et al, Lancet Rheumatol, 2021
 - Ruddy et al, Ann Rheum Dis, 2021



Conclusions

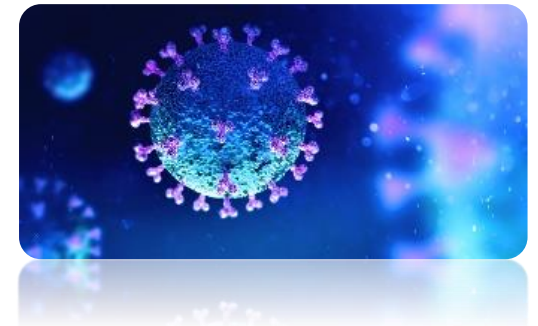
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- Most immunosuppressed patients with CID will mount acute humoral responses
 - Greatest risk of poor responses:
 - BCDT >> MMF >> GCC > MTX/AZA/JAKi/TNFi > immunocompetent



COVID 19 Vaccine in SLE Patients:

- Bottom Line: The TWH lupus clinic is recommending four vaccines for all lupus patients.
- The vaccine is generally very well tolerated (we will get into more detail about this later on!)



Characteristics Associated with Poor COVID-19 Outcomes in People with Systemic Lupus Erythematosus (SLE): Data from the COVID-19 Global Rheumatology Alliance (GRA)

Manuel Ugarte-Gil, Graciela Alarcón, Andrea Seet, Zara Izadi, Ali Duarte-Garcia, Cristina Reategui-Sokolova, Ann Clarke, Leanna Wise, Guillermo Pons-Estel, Maria José Santos, Sasha Bernatsky, Sandra Lúcia Ribeiro, Samar Al Emadi, Jeffrey Sparks, Tiffany Hsu, Kristin D'Silva, Naomi Patel, Emily Gilbert, Maria Valenzuela-Almada, Andreas Jonsen, Gianpiero Landolfi, Micaela Fredi, Tiphaine Goulenok, Mathilde Devaux, Xavier Mariette, Viviane Queyrel, Vasco C Romão, Graça Sequeira, Rebecca Hasseli, Bimba Franziska Hoyer, Reinhard Voll, Christof Specker, Roberto Baez, Vanessa Castro Coello, Edgard Neto, Gilda Ferreira, Odirlei Andre Monticelo, Emily Siroich, Jean Liew, Jonathan Hausmann, Paul Sufka, Rebecca Grainger, Suleman Bhana, Wendy Costello, Zachary Wallace, Lindsay Jacobsohn, Anja Strangfeld, Elsa Frazão Mateus, Kimme Hyrich, Laure Gossec, Loreto Carmona, Saskia Lawson-Tovey, Lianne Kearsley-Fleet, Martin Schaefer, Pedro Machado, Philip Robinson, Milena Gianfrancesco and Jinoos Yazdany

AIM

To assess characteristics associated with poor outcomes in a global population of individuals with SLE and COVID-19

RESULTS

- 1922 individuals with SLE were included.
- Female gender: 1734 (90.4%)
- Mean age: 44.4 (14.1 years)
- Out of 1606 with outcomes:
 - Not hospitalized: 1118 (69.6%)
 - Hospitalized with no oxygenation: 169 (10.5%)
 - Hospitalized with any oxygenation: 214 (13.3%)
 - Death: 105 (6.5%)

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More severe COVID-19 outcomes were seen in:

- older patients (odds ratio, OR=1.03 per year)
- males (OR =1.74)
- patients outside Europe and North/South America (OR=3.77)
- patients on prednisone (0-5 mg/d OR=1.87, 5-10 mg/d OR=2.46, and >10 mg/d OR=2.32)
- patients on no SLE therapy (OR =2.05)
- chronic renal disease (OR =3.21)
- cardiovascular disease (OR =1.64)
- the number of other comorbidities (OR=1.51)
- moderate and high disease activity (OR =1.78 and OR=4.18, respectively)

CONCLUSIONS

- More severe COVID-19 outcomes in individuals with SLE are largely driven by demographic factors, comorbidities, and untreated or active SLE
- Patients using glucocorticoids and rituximab also experienced more severe outcomes

Summary of COVID-19

- Most immunocompromised (including SLE) patients will have poor response to COVID-19 vaccine particularly among those on rituximab and prednisone
- Poor COVID-19 outcomes in SLE patients were driven by factors related to SLE and other comorbidities
- Patients with rituximab and pred experienced most severe outcomes



Paxlovid (Nirmatrelvir/Ritonavir)

Who meets the criteria for Paxlovid use?

- COVID 19 positive (on PCR or Rapid Antigen Test)
- At increased risk of progression to severe COVID-19 disease (those who are immune compromised)

How does Paxlovid help?

- This drug is made up of two antiviral medications with when given together help stop the coronavirus from multiplying; therefore, helping your body overcome the infection in a safer and faster manner

Where Do I Get Paxlovid?

This medication is available at many pharmacies and COVID-19 treatment centers. You can find these centers using this link:

<https://covid-19.ontario.ca/covid-19-treatments> - this will show you which pharmacies have this medication

<https://covid-19.ontario.ca/assessment-centre-locations> - this will show you which assessment/treatment sites are close to you by entering your postal code

****Remember**** - Paxlovid is not a drug to be used for prophylaxis (preventing COVID-19 infection). You can only get this drug if you are proven COVID-19 positive proven by PCR or rapid antigen test

How to Take This Medication:

- Cannot use this medication for longer than five days
- There are over 20 medications that are contraindicated to take with Paxlovid, make sure you tell your health care provider which medications you are taking before using this medication – some common ones include: rivaroxaban (xarelto), Colchicine, Sildenafil (for pulmonary hypertension)
- Paxlovid comes as a blister pack. You are to take 2 pink tablets (Nirmatrelvir) and 1 white tablet (Ritonavir) twice daily for five days.



Frequently Asked Question's Related to the COVID Vaccine:

Q: If I get COVID 19 symptoms or test positive for COVID, do I need a vaccine?

A: Yes, because the immunity after COVID illness may not protect you for a long period of time.

Q: Is COVID 19 vaccine safe during pregnancy? A: Yes!! (but always check with your OB)

Q: What should I do if I get COVID-19 illness and I have not received the vaccine ?

A: You can be prescribed Paxlovid (for immune compromised patients only) OR Evushel (this can protect you for 6 months) [pre-exposure prophylaxis of COVID-19 in immune-compromised individuals]

Q: Can the vaccine cause a lupus flare?

A: Yes, but this is not very common [lets look at the data together]

Tolerance of COVID-19 Vaccination in Patients with Systemic Lupus Erythematosus: The International VACOLUP Study

Renaud Felten, Lou Kawka, Maxime Dubois, Manuel F Ugarte-Gil, Yurilis Fuentes-Silva, Matteo Piga, Laurent Arnaud

The study included 696 participants (669 [96%] women and 27 [4%] men) from 30 countries, with a median age of 42 years (IQR 34–51)

All patients received at least one dose of vaccine and 343 (49%) patients received a second dose (

The most common vaccines were:

Pfizer-BioNTech (399 [57%] participants)

Sinovac (156 [22%] participants)

AstraZeneca (73 [10%] participants)

Moderna (57 [8%] participants)

3% rate of flare in SLE after vaccination

<https://www.thelancet.com/action/showPdf?pii=S2665-9913%2821%2900221-6>

Side-effects after first vaccine dose	316 (45%)
Timing of onset of side-effects after first dose, days	0 (0–1)
Side-effects after second vaccine dose	181/343 (53%)
Timing of onset of side-effects after second dose, days	0 (0–1)
Consultations or admissions to hospital for side-effects (first and second doses together)	
Medical consultation	81/1039 (8%)
Emergency consultation	14/1039 (1%)
Admission to hospital	5/1039 (<1%)
SLE flare after vaccination	21 (3%)
SLE flare manifestations	
Fever (temperature >38°C or 100.4°F)	10/21 (48%)
Cutaneous (skin) flare (medically confirmed)	12/21 (57%)
Musculoskeletal symptoms (joint, arthritis, arthralgia, or myalgia; medically confirmed)	19/21 (90%)
Pleuritis or pleurisy (medically confirmed)	1/21 (5%)
Pericarditis (medically confirmed)	1/21 (5%)
Renal involvement (medically confirmed)	2/21 (10%)
Neuro-psychiatric manifestations (medically confirmed)	0
Cytopenia (anaemia, thrombocytopenia, or leukocytopenia; medically confirmed)	8/21 (38%)
Low complement (medically confirmed)	5/21 (24%)
Increase in anti-dsDNA antibody titre (medically confirmed)	7/21 (33%)
Fatigue	18/21 (86%)
Consequences of SLE flare	
Change in SLE treatment	15/21 (71%)
Medical consultation	21/21 (100%)
Admission to hospital	4/21 (19%)
COVID-19 after vaccination	0

Tolerance of COVID-19 Vaccination in Patients with Systemic Lupus Erythematosus: The International VACOLUP Study

In conclusion, the VACOLUP study suggests that COVID-19 vaccination appears well tolerated in patients with SLE, with only a minimal risk of flare, if any, including after the mRNA vaccines

