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General information about vaccines

The capacity of vaccine to induce humoral and cellular immunity is defined as ***Immunogenicity***.

-*Efficacy* :is the vaccine capacity to prevent infection.

-for some disease ,immunogenicity correlates with efficacy but not for other.

Introduction

- Considering both the underlying pathogenic mechanisms of **autoimmune/ autoinflammatory rheumatological diseases (AIIRDs)** and the immunosuppressive drugs used in treatment, vaccination for COVID-19 deserves special attention in such patients.

Definition: Autoimmune inflammatory rheumatic diseases

- ▶ Rheumatoid arthritis, juvenile idiopathic arthritis
- ▶ Adult Still's disease
- ▶ Systemic lupus erythematosus, Sjogren's syndrome, antiphospholipid syndrome
- ▶ Systemic sclerosis, mixed connective tissue disease
- ▶ Polymyositis, dermatomyositis, antisynthetase syndrome, clinically amyopathic dermatomyositis, inclusion body myositis, eosinophilic myositis, eosinophilic fasciitis
- ▶ Psoriatic arthritis, spondyloarthropathy
- ▶ Polymyalgia rheumatica
- ▶ (ANCA)-associated vasculitis: granulomatosis with polyangiitis, microscopic polyangiitis, eosinophilic granulomatosis with polyangiitis (Churg-Strauss syndrome)
- ▶ Giant cell arteritis, Takayasu arteritis
- ▶ Polyarteritis nodosa
- ▶ Cryoglobulinemic syndrome
- ▶ Anti-glomerular basement membrane (GBM) antibody disease (Goodpasture disease)
- ▶ Behcet disease
- ▶ Relapsing polychondritis
- ▶ Periodic fever syndromes
- ▶ Familial Mediterranean fever

Immunosuppressive agents



Glucocorticoids

Synthetic DAMARDS:

methotrexate/leflunomide/sulfasalasin/hydroxychloroquine/azathioprine

Mycophenolate

Calcineurin inhibitors:cyclosporine/tacrolimus

Cyclophosphamide

Biologic

DAMARDS:infliximab/etanercept/adalimumab//golimumab/abatacept/tocilizumab/r
rituximab/anakinra

Targeted synthetic DAMARDS: tofacitinib/baricitinib



Based on the data for the mRNA COVID-19 vaccines available in the U.S., there is **no preference** for one COVID-19 vaccine over another. Therefore, AIIRD patients should receive either **vaccine available** to them.

RMD = rheumatic and musculoskeletal disease; AIIRD=autoimmune and inflammatory rheumatic disease; EUA = emergency use authorization; FDA = Food and Drug Administration; mRNA = messenger RNA; CDC = Centers for Disease Control; ICU = Intensive Care Unit



Healthcare providers **should not routinely** order any lab testing (e.g., **antibody tests** for IgM and/or IgG to spike or nucleocapsid proteins) to assess immunity to COVID-19 post-vaccination.

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EUA = emergency use authorization; FDA = Food and Drug Administration; mRNA = messenger RNA; CDC
= Centers for Disease Control; ICU = Intensive Care Unit



Following COVID-19 vaccination, RMD patients
should continue to follow all public health
guidelines regarding physical distancing and
other preventive measures.

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Household members and other frequent, close
contacts of AIIRD patients should undergo
COVID-19 vaccination when available to them to
facilitate a 'cocooning effect' that may help
protect the AIIRD patient

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While vaccination would ideally occur in the setting of well-controlled AIIRD, except for those patients with life-threatening illness (e.g., in the ICU for any reason), COVID vaccination should occur as soon as possible for those for whom it is being recommended, irrespective of disease activity and severity.

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For a multi-dose vaccine, AIIRD patients should receive the second dose of the same vaccine, even if there are non-serious adverse events associated with receipt of the first dose, consistent with timing described in CDC guidelines.

Antirheumatic drugs and vaccines

- **Low degree of immunosuppression** usually occurs with doses of **prednisone or equivalents < 20 mg/day**, **MTX doses ≤ 0.4 mg/kg/week**, and **azathioprine doses ≤ 3.0 mg/kg/day**.
- The CDC advises that the **vaccines can be used safely in such patients**. Hagiwara et al. reported that **azathioprine combination with infliximab (IFX)** may **reduce trivalent influenza vaccine antibody titers**. Therefore, one should be more careful with such combinations.

Guidance Related to the Use and Timing of Vaccination and Immunomodulatory Therapies in Relation to COVID-19 Vaccination Administration in RMD Patients*



Hydroxychloroquine;

apremilast;

IVIG;

Glucocorticoids

, prednisone-equivalent dose <20mg/day

No modifications to either immunomodulatory therapy or vaccination
timing

Strong-Moderate

Sulfasalazine;
Leflunomide;
Mycophenolate;
Azathioprine;
Cyclophosphamide (oral);
TNFi;

(TNFi = tumor necrosis factor inhibitor)

IL-6R;
(IL-6R = sarilumab; tocilizumab)

IL = interleukin

IL-1 (IL-1R = anakinra, canakinumab;); IL-17 (IL-17 = ixekizumab, secukinumab); IL-12/23 (IL-12/23 = ustekinumab); IL-23; (IL-23 = guselkumab, risankizumab;)

Belimumab;
oral calcineurin inhibitors;

Glucocorticoids, prednisone-equivalent dose $\geq 20\text{mg/day}^{**}$

No modifications to either immunomodulatory therapy or vaccination timing

Moderate

Implications for COVID-19 vaccines and CS DMARDs

- Data on the effects of **hydroxychloroquine, sulfasalazine, and leflunomide** on vaccine responses are scarce
- hydroxychloroquine was found not to be beneficial in either the treatment or prevention of COVID-19 infection in SLE patients
- it should not be prescribed to prevent or treat COVID-19 infection.



Methotrexate

Hold MTX 1 week after each vaccine dose, for those
with well-controlled disease;
no modifications to vaccination timing

Moderate



Rituximab

at list 6 months after the administration and 4 weeks before the next course of rituximab therapy ,based on the state of clinical practice.



Cyclophosphamide IV

Time CYC administration so that it will occur approximately 1 week after each vaccine dose, when feasible

Moderate

Guidance Related to the Use and Timing of Vaccination and Immunomodulatory Therapies in Relation to COVID-19 Vaccination Administration in RMD Patients*

JAKi = janus kinase inhibitor

(JAKi = baricitinib, tofacitinib, upadacitinib)

Hold JAKi for 1 week after each vaccine dose; no
modification to vaccination timing

Moderate

Implications for COVID-19 vaccines and biological agents

- JAK inhibitors may be withheld for 1 week after each vaccine dose
- Because of interferon inhibition, in addition to other mechanisms, tofacitinib reduces antibody responses after vaccination, especially in combination with tofacitinib/methotrexate.
- If the patient is in remission, it may be appropriate to discontinue the drug before vaccination and to start again after 14 days.

Implications for COVID-19 vaccines and biological agents

- Blockade of TNF- α or IL-6 did not influence humoral immunity to influenza or pneumococcal vaccines
- their effects on cellular immunity have been less studied
- Since overproduction of TNF- α and IL-6 can drive a detrimental hyper-inflammatory response (cytokine storm) in severe COVID-19 cases, those medications should be continued
- Baricitinib prevented the progression to severe COVID-19 pneumonia and increased the production of antibodies against the SARS-CoV-2 spike protein
- AIIRD patients on IL-1, IL-6, or JAK inhibitors showed a low incidence of COVID-19, suggesting that b/tsDMARDs may inhibit the development symptomatic/aggressive COVID-19 infection



Implications for COVID-19 vaccines and prednisone- MTX- azathioprine

- The CDC advises that the vaccines can be used safely in such patients:
 - ✓ prednisone or equivalents < 20 mg/day
 - ✓ MTX doses ≤ 0.4 mg/kg/week
 - ✓ azathioprine doses ≤ 3.0 mg/kg/day

; CDC = Centers for Disease Control



Implications for COVID-19 vaccines and CS treatment

- According to (CDC) recommendations, a prednisolone equivalent of **≥ 20 mg/day for ≥ 2 weeks** contraindicates the use of live-attenuated vaccines because of the risk of viral reactivation
- When corticosteroids (prednisolone **equivalent** of > 10 mg/day):
 - ✓ increased risk of COVID-19 complications
 - ✓ higher disease activity among AIIRD patients
 - ✓ altered antibody response
- COVID-19 vaccine should be given during the inactive period of the disease while the patient is on lower doses of CS(**below 10 mg/day** prednisolone or its equivalent)

