COVID-19 vaccination and antirheumatic therapy

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COVID-19 Vaccine Clinical Guidance Summary for Patients with Rheumatic Diseases

- **growing number of SARS-CoV-2 vaccines are in use worldwide, including mRNA, adenoviral vector, protein subunit and inactivated virus vaccines.**
- **We will focus our discussion on two mRNA vaccines and two adenoviral vector vaccines, which have been most widely studied in patients with rheumatic diseases**

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- **BNT162b2 (Pfizer/BioNTech) mRNAvaccine was 95% effective**
- **the mRNA01273 (Moderna) vaccine was 94.1% effective in preventing symptomatic COVID-19 infection following the second dose.**
- **Phase III trials found the Ad26. COV2.S (Janssen/Johnson & Johnson) single-dose vaccine to be 66.9% effective**
- **Oxford/AstraZeneca/Serum Institute of India) vaccine to be 70.4% effective following the second dose**

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- **SARS-CoV-2 vaccineimmunogenicity can be measured by humoral IgG to spike protein (not nucleocapsid protein) or cellular T-cell reactivity via interferon (IFN)-γ response to SARS-CoV-2 peptide.**

- **Antibody responses are reported as ‘seroconversion’ (newly positive antispike protein IgG), or by post vaccination antibody titres.**

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- **The role of T-cell responses to SARS-CoV-2 vaccines are not fully understood, however emerging evidence suggests that T-cell responses may confer protection even in the absence of humoral response.**

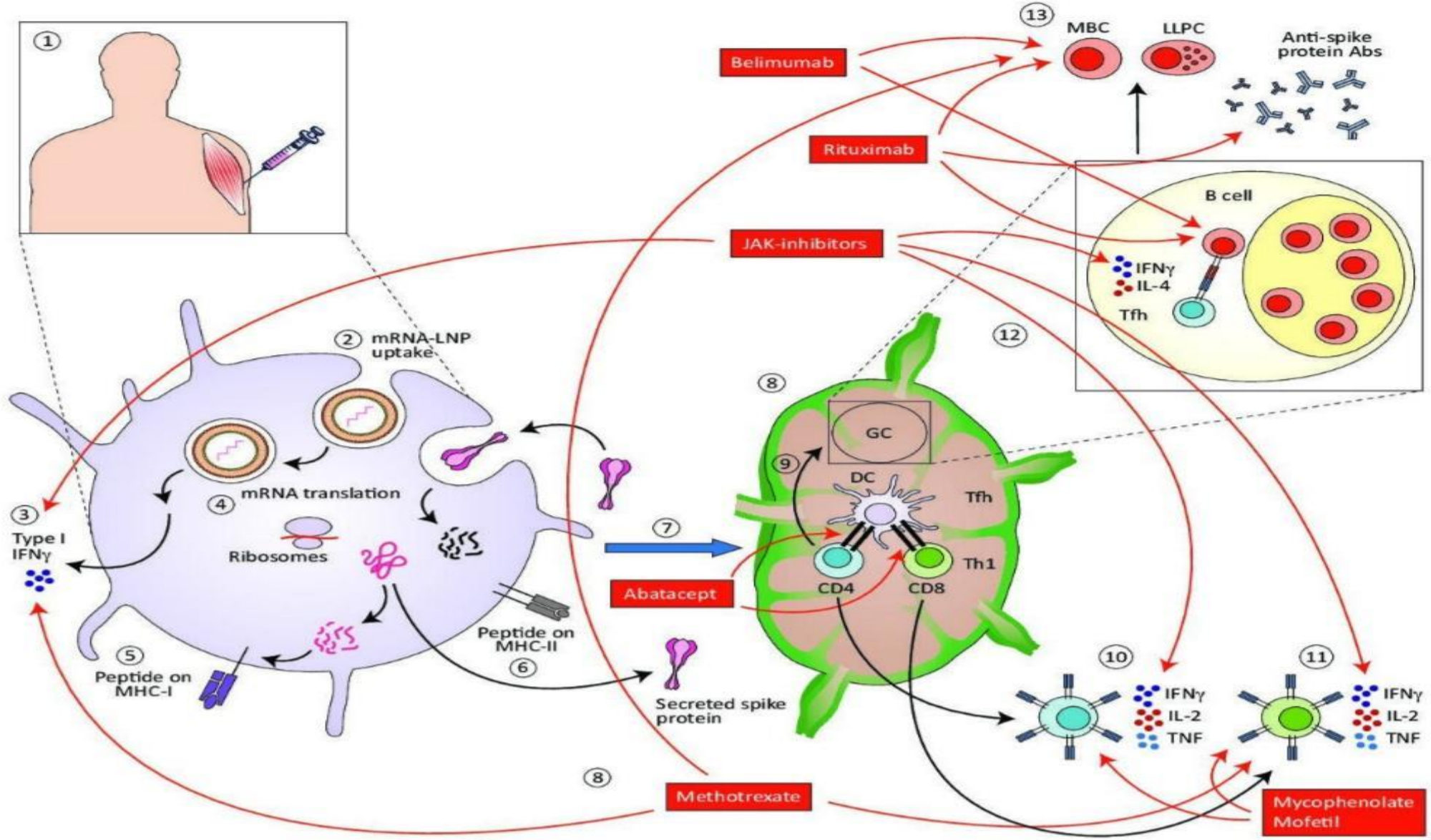
- **However, we do not yet know how immunogenicity cut-offs correlate with efficacy, whether reduced absolute titres may still be adequate titres, or whether immune responses wane over time, making SARS-CoV-2 immunogenicity studies difficult to fully interpret.**

Vaccinations

- **Vaccinations exert their protective effect by stimulating both humoral and cellular immune responses. The relative importance of humoral and cellular immunity in conferring protection from infection varies with each infective organism**

- **Immunosuppressive therapy such as the DMARDs,used to treat most of our patients, may impair vaccine responses**

Effect of DMARD therapy of vaccine efficacy



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Friedman MA, et al. Ann Rheum Dis 2021

Table 1 Impact of disease-modifying antirheumatic drugs on vaccine immunogenicity

	Influenza	Pneumococcal	Herpes zoster	Hepatitis B	Human papilloma virus	Tetanus	SARS-CoV-2 (mRNA)
Methotrexate	↓[14 22 24]	↓[50 51]	OK (ZVL)[52]		OK[117 132 133]	↓[121]	↓[82 84 85]
TNF inhibitors	OK[14 16 20 27 28]	OK[14 56]	OK (ZVL)[64]	↓[103–105]	OK[117 132]	OK[121 124]*	OK[84 85 88]
Rituximab	↓↓[14–17 19–21 24 134]	↓↓[14 18 45–47]				↓[18 121]	↓↓[81–84]
Abatacept	↓[24 26]	↓[45 46]				OK (SQ)[122] ↓(IV)[123]	↓[84]
JAK inhibitor	OK[30]	↓[30]				OK (tofacitinib)[120] ↓(baricitinib)[53]	↓[82 84]
IL-6R inhibitor	OK[31]	OK[31]				OK[125]	OK[84]
IL-12/IL-23 inhibitor	OK[32]	OK[54]		↓[105]		OK[54]	OK[82]
IL-17 inhibitor	OK[33–35]	OK[55]				OK[55]	OK[84]

Corticosteroids

- **Corticosteroids affect vaccine efficacy in a dose-dependent manner. Several studies have assessed the impact of corticosteroid therapy on humoral response to the pneumococcal and influenza vaccines .**
- **Doses >10mg prednisolone daily were associated with a degree of impaired humoral immunity in a longitudinal study; however, lower doses had little impact .**
- **Steroid doses >10mg daily prednisolone were associated with poorer outcomes in hospitalized patients with COVID-19.**

csDMARDs

- **Other than MTX, there is limited evidence for significant impairment of humoral vaccine responses to other conventional synthetic DMARDs (csDMARDs).**

- **Sulfasalazine, hydroxychloroquine, azathioprine and leflunomide may reduce vaccine antibody titres but have not been shown to inhibit a seroprotective response to the vaccines**

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Mycophenolate mofetil

- **Much of the trial data on mycophenolate is from organ transplant patients.**

- **Mycophenolate was shown to reduce antibody titres but not below the threshold for seroprotection.**

- **Mycophenolate mofetil : hold for 1 week after each vaccine dose.**

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MTX

- **MTX: hold for 1 week after each mRNA dose; hold for 2 weeks after single-dose vaccine.**

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Another Drugs

- **TNF, IL-6R, IL-1, IL-17, IL-12/23, IL-23, oral calcineurin inhibitors, belimumab††, azathioprine, sulfasalazine, leflunomide, hydroxychloroquine, apremilast, intravenous immune globulin (IVIG) and glucocorticoids <20 mg/ day††: no modification.**

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Abatacept

- **Abatacept subcutaneous: hold 1 week before and 1 week after the first vaccine dose, no interruption for the second vaccine dose.**

- **Abatacept intravenous: time the first vaccine dose 4 weeks after abatacept and postpone next infusion by 1 week; no adjustment for the second vaccine dose**

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Janus kinase inhibitors

- **JAK inhibitors: hold for 1 week after each vaccine dose.**

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Anti-CD20

- **Improved vaccine response if vaccinated >6months after RTX therapy**

- **Rituximab: as long as possible after the last dose, 2–4 weeks before the next dose.**

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Anti-CD20

- **Risk factors for a poor humoral response on rituximab include a shorter duration between rituximab dose and vaccine, and lack of B-cell reconstitution.**

- **Despite a reduced humoral response, early data suggest that rituximab-treated patients may still mount a normal cellular vaccine response, such that the net impact on clinical protection is not clear.**

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Risk stratifying and timing vaccinations

Where appropriate:

- Avoid vaccination during disease flare.
- Taper steroid therapy to <10 mg prednisolone daily.
- Consider withholding MTX for 2 weeks post-vaccination both when used as monotherapy and in combination with other DMARDs. (As two doses of current vaccines are required, this may would need to be done twice).
- Avoid vaccinating ideally for 6 months post-rituximab; if vaccination is imminent consider delaying rituximab infusion if no risk of organ failure/disease flare. If a patient is unlikely to receive vaccination for 6 months there is an argument for expediting RTX treatment.
- If there is insufficient time to alter or amend DMARD/biologic treatment, then we would recommend vaccination and reassessment of vaccine response at a later date.

Medication	(applies to both primary vaccination and supplemental [booster] dosing)	Consensus
Abatacept IV	**Time vaccination so that it occurs one week prior to the next dose of IV abatacept**	**Moderate**
Abatacept SQ	**Hold for one to two weeks (as disease activity allows) after each COVID vaccine dose**	**Moderate**
Acetaminophen, NSAIDs	Assuming that disease is stable, hold for 24 hours prior to vaccination. No restrictions on use post vaccination to treat symptoms.	Moderate
Belimumab SQ	**Hold for one to two weeks (as disease activity allows) after each COVID vaccine dose**	**Moderate**
TNFi, IL-6R, IL-1R, IL-17, IL12/23, IL-23, and other cytokine inhibitors†	**The Task Force failed to reach consensus on whether or not to temporarily interrupt these following each COVID vaccine dose, including both primary vaccination and supplemental (booster) dosing**	**Moderate**
Cyclophosphamide IV	**Time CYC administration so that it will occur approximately 1 week after each vaccine dose, when feasible**	**Moderate**
Hydroxychloroquine	**No modifications to either immunomodulatory therapy or vaccination timing**	**Strong**
Rituximab or other anti-CD20 B-cell depleting agents	**Discuss the optimal timing of dosing and vaccination with the rheumatology provider before proceeding‡**	**Moderate**
All other conventional and targeted immunomodulatory or immunosuppressive medications except those listed above§	**Hold for one to two weeks (as disease activity allows) after each COVID vaccine dose**	**Moderate**

Take Home Message

- **Rituximab significantly reduced vaccine immunogenicity**
- **JAK inhibitors and MTX moderately reduced antibody titres**
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- **Other therapies (TNF, IL-12/IL-23 and integrin inhibitors) had a modest impact on antibody**

THANKS