**COVID-19 vaccines for patients with lupus: everything you need to know**

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**Abstract**

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the virus causing Coronavirus disease 2019 (COVID-19), has had a huge impact on health services, with a high mortality associated with complications including pneumonia and acute respiratory distress syndrome. Patients with systemic lupus erythematosus (SLE) are at increased risk of viral infections, and recent data suggests they may be at an increased risk of poor outcomes with COVID-19. This may be particularly true for those on rituximab.

A huge international effort from the scientific community has so far resulted in the approval of three vaccines which offer protection against SARS-CoV-2, with over 30 other vaccines being evaluated in ongoing trials. Although there has historically been concern that vaccines may trigger disease flares of SLE, there is little convincing evidence to show this. In general lupus patients appear to gain good protection from vaccination, although there may be reduced efficacy in those with high disease activity or those on immunosuppressive therapies, such as rituximab or high dose steroids.

With the possibility of annual COVID vaccination programmes in the future, prospective data collection and registries looking at the effect of vaccination on SLE disease control, the incidence of COVID-19 in SLE patients and severity of COVID-19 disease course would all be useful. As mass vaccination programmes begin to roll out across the world, we assess the evidence of the use of vaccines in SLE patients and in particular vaccines targeting SARS-CoV-2.

**Introduction**

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a novel single-stranded RNA virus of theCoronaviridae family, which causes Coronavirus Disease 2019 (COVID-19). COVID-19 can have severe respiratory complications including pneumonia and acute respiratory distress syndrome (ARDS), frequently requiring intensive care unit (ICU) admission associated with high mortality rates (1, 2). These severe presentations can be associated with a hyper-inflammatory reaction, sometimes called a ‘cytokine storm’, leading to multi-organ life-threatening complications (3).

Since the onset of the COVID-19 pandemic there has been huge interest in developing a vaccine to provide protection against the SARS-CoV-2 virus, particularly for those vulnerable groups with a higher susceptibility to severe complications and with higher mortality rates. Many vaccines have been rapidly developed. Three have gained temporary authorisation for use under Regulation 174 in the pandemic in the UK (Pfizer-BioNtech, the AstraZeneca/Oxford and the Moderna vaccines (4-6)) with 2 further vaccines (Novavax and Janssen) under MHRA review. Three have been approved for pandemic use in the USA (Pfizer-BioNtech, Moderna and Janssen) and others approved in different countries globally. Mass vaccination programmes are now under way around the world.

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| **Vaccine** | **Type** | **Number of doses** | **Stage of development (all phase 3 trials continue)** |
| Pfizer/BioNtech | mRNA | Two doses at least 21 days apart | Emergency approval in 16+ years old by MHRA, EMA and FDA December 2020 |
| AstraZeneca/Oxford | Replication-deficient chimpanzee adenovirus vector | Two doses given four to twelve weeks apart | Emergency approval in 18+ years olds by the MHRA December 2020 and the EMA and FDA January 2021 |
| Moderna | mRNA | Two doses given 28 days apart | Emergency approval in 18+ years olds for use by the FDA December 2020 and the MRHA and EMA January 2021 |
| SputnikV | Human adenovirus vector | Two doses given 21 days apart | Undergoing phase 3 trial evaluation. Approved for use by Russian government |
| Novavax | Recombinant nanoparticle vaccine | Two doses given 21 days apart | Undergoing phase 3 trial evaluation |
| Janssen | Human adenovirus vector | Single dose | Single dose use emergency approval in 18+ years olds by the FDA February 2021.  2 dose use undergoing phase 3 trial evaluation |
| CoronaVac | Inactivated virus | Two doses given two to four weeks apart | Undergoing phase 3 trial evaluation |
| BBIBP- CoV | Inactivated virus | Two doses three to four weeks apart | Undergoing phase 3 trial evaluation |
| Wuhan | Inactivated virus | Two doses 21 days apart | Undergoing phase 3 trial evaluation |

Table 1. Vaccines targeting SARS-CoV-2 licensed or in Phase 3 development at the time of publication

We explore the existing evidence, looking at the use of other vaccines in SLE, examining their efficacy, safety, and any impact of vaccination on SLE disease course. We also review the literature to assess the therapies frequently used for SLE and their impact on vaccine efficacy and safety.

**SLE and COVID-19**

Lupus patients have a higher incidence of several viral infections, likely due to a combination of immune dysfunction, immunosuppressive therapy, and co-morbidities. Data from the COVID-19 Global Rheumatology Alliance (C19-GRA) has suggested that SLE patients may be at higher risk of hospitalisation from COVID-19 compared to those with other rheumatic diseases (7). Data from the OpenSAFELY electronic platform, an English database holding the primary care health records of approximately 17 million adults, found a slight increase in death for those with rheumatic disease (SLE, rheumatoid arthritis or psoriatic arthritis), when adjusted for age, sex, ethnicity, social deprivation and the presence of other chronic health conditions (adjusted HR 1.19; 95% CI 1.11–1.27) (8). Results should be interpreted with caution as three heterogenous rheumatic diseases were assessed in combination and other factors such as the roles of steroid use, disease modifying antirheumatic drugs (DMARDs) use, and disease activity were not considered. The Registration of Complex Rare Diseases Exemplars in Rheumatology (RECORDER) project looked at the risk of death from COVID-19 among those with rare autoimmune diseases and found a higher mortality rate compared with the general population (1.1% vs 0.6%) with women having similar risk of death compared to men in this cohort (9).

Diabetes mellitus, hypertension and obesity are significant risk factors for hospitalisation and mortality in COVID-19 (10). Lupus patients have higher rates of hypertension, diabetes mellitus, obesity and sedentary lifestyle (11), putting them at higher risk from COVID-19 due to excess co-morbidity. Many SLE patients will also have organ damage from previous disease flares, such as chronic renal impairment or interstitial lung disease, again increasing the risk of severe disease course.

Although short-term use of dexamethasone in hospitalised patients requiring respiratory support improves outcomes in COVID-19 (12), data from the C19-GRA registry has suggested that long-term use is associated with poorer outcomes, with glucocorticoid use equivalent to ≥10 mg prednisolone/day being associated with an increased risk of hospitalisation (16% vs 7% for doses ≥10 mg/day, p=0.01) and death (OR 1.69, 1.18 to 2.41) compared to no glucocorticoid intake (7, 13). Glucocorticoids are frequently used for treatment of SLE patients, potentially making these patients vulnerable to a more severe COVID-19 disease course. Current evidence is reassuring that DMARDs commonly used to treat SLE, including hydroxychloroquine, azathioprine, methotrexate and mycophenolate have not been shown to increase risk of contracting or suffering a severe disease course in COVID-19 (7, 13). However, the C19-GRA registry data shows rituximab use to be associated with a higher risk of death as compared with methotrexate monotherapy in connective tissue disease (CTD) and vasculitis patients (OR 3.72; 95% CI 1.21-11.48). A similar association was not seen with belimumab, although the number of patients on this therapy were small (13).

Ethnic minority groups appear to have poorer outcomes with COVID-19 (14, 15). The C19-GRA also demonstrated that Black, South Asian and Latino patients with rheumatic disease have a higher risk of hospitalisation (16). SLE is well recognised as being more common and more severe in Black and Asian populations (17) and this group may be at increased risk of a severe disease course with COVID-19.

**SLE and other vaccines**

Due to the nature of the disease, immunosuppressive medications, and excess co-morbidities, SLE patients are more susceptible to infection than the general public. Therefore, the evidence based 2019 update of European league against rheumatism (EULAR) recommendation highlighted the importance of annual vaccination status assessment in adult SLE patients (18).

*Vaccination and SLE onset or flare*

The aetiology of SLE includes autoantibodies formation; with T-cell receptors binding to major histocompatibility complex (MHC), cytokine production and B-cell activation. While various types of vaccine produce immunity in different ways, the majority work by producing an antigen-specific antibody response (19). It has therefore become an area of interest to look at whether vaccine-induced immune system upregulation could be a trigger for the onset of SLE. In addition, the components or adjuvants used in vaccines could be considered as potential risk factors for SLE or SLE flare.

To date, no recommended licensed vaccines have been confirmed to have a role in triggering SLE (20). However, a small retrospective analysis reported the temporal relationship between the hepatitis B vaccine and the occurrence of immunological or biopsy confirmed SLE in 10 patients; mean latency interval being 56.3 days from first dose of vaccination to the onset of autoimmune features; possibly due to molecular mimicry and cross-reactive antinuclear antibodies (21). One study looking at seasonal and pandemic influenza vaccination showed that although some patients had elevated anti-dsDNA antibodies titres after influenza vaccination, the antibodies titres were back to baseline in 12 weeks and no disease flare was reported (22). Female SLE patients are at higher risk of contracting genital human papilloma virus (HPV) and cervical dysplasia (23). Initially concerns were raised that HPV vaccination may trigger the onset of SLE (24, 25), however, larger studies have since been reassuring that this does not appear to be the case (26-28).

An international case-control study looked retrospectively at SLE diagnosis and any vaccination 12 and 24 months prior to the first presentation. 105 SLE cases and 701 controls were compared, 16.2% of cases (n=17) and 20.8% of controls (n = 148) (adjusted OR 0.9;95% CI 0.5–1.6) and 21.0% of cases (n = 22) and 25.4% of controls (n = 181) (adjusted OR 0.9;95% CI 0.5–1.5), received any vaccine at 12 months and 24 months respectively. No significant relationship was observed between onset of SLE and vaccination (OR 0.9;95% CI 0.5–1.5) (29).

*Efficacy and safety of vaccines in SLE*

Vaccination programmes play a major role in reducing the health burden from infections in a population. The targeted vaccination rate has not been met in SLE patients, due to concerns regarding efficacy and safety of vaccines, according to the long-term cross-sectional German LuLa cohort analysis (30). The safety and efficacy of vaccinations in patients on immunosuppressive therapy have been evaluated in a number of different studies (31). Immunogenicity to a vaccine relies on both humoral (B-cell mediated) and cellular (T-cell mediated) response (31, 32). To assess vaccine efficacy, many trials rely on antibody titres as markers of immunogenicity, with a few also evaluating the cellular response (31).

Live-attenuated vaccines

In SLE patients taking significant immunosuppressive medications, live vaccines are usually avoided due to the risk of excessive viral replication, leading to severe and life-threatening infections. Significant immunotherapy includes short term high-dose corticosteroids, >40mg prednisolone per day for more than 1 week; long-term lower dose corticosteroids, >20mg prednisolone per day for more than 14 days; DMARDs e.g. methotrexate >25mg per week or azathioprine >3.0mg/kg/day and those who have received rituximab in the last 12 months (33). Live vaccines can be considered with caution if entirely necessary, the optimal time point being at least 4 weeks prior to starting immunosuppression (18).

Herpes zoster/ varicella-zoster (VZV) vaccine

Patients with rheumatic disease are at high risk of herpes zoster. The new adjuvant subunit VZV vaccine (Shingrix) is preferred in the immunosuppressed population but is not available in all countries. The live-attenuated VZV vaccine can cause vaccine-related VZV infection. A prospective, case-control 12-week study of a small cohort of 10 SLE patients showed no significant difference between both groups in either safety or immunogenicity arm (51.3% infection reduction rate) of live-attenuated VZV vaccine. The cell-mediated immunogenicity by ELISpot showed 44% response in both groups after 12 weeks post vaccine (p=0.006). No significant change in SLEDAI was recorded throughout the study (34). A later randomised placebo-control trial with 90 patients supported these findings of safety and immunogenicity (35). These studies have suggested the VZV vaccine is safe and effective for SLE patients, however guidelines continue to recommend avoiding live vaccines for SLE patients on significant immunosuppressive therapy as outlined above (33).

Polio vaccine

Most countries now use the inactivated polio vaccine (IPV) as opposed to the live-attenuated oral polio vaccine (OPV), in line with WHO recommendations (36). However, a retrospective study did seek to compare flare rates in SLE patients post OPV and IPV. The study looked at 73 SLE patients and demonstrated the same flare rate of 5% in patients receiving the OPV or IPV (37).

Non-live vaccines

Non-live vaccines are considered both safe and effective in patients with autoimmune disease receiving immunosuppressive medications, the recommended time window being at least two weeks prior to immunosuppressive therapy if possible (18).

Influenza vaccines

According to the World Health Organisation (WHO), 5-10% of the population has influenza every year, and the incidence rate is higher in elderly patients with inflammatory rheumatic diseases (38). Annual seasonal influenza vaccination is strongly recommended in SLE patients by EULAR (18, 39). A systematic review and metanalysis showed good safety data for inactivated influenza vaccines; H1N1, H3N2 and B strain in SLE patients. Sero-protection rates were reduced in SLE patients compared to healthy controls for H1N1 (RR 0.79; 95% CI 0.73–0.87) and B strain (RR 0.75; 95% CI 0.65–0.87), but not for H3N2 (RR 0.84; 95% CI 0.68–1.03). Subgroup analyses demonstrated that SLE patients on azathioprine and prednisone had significantly lower sero-protection rates, compared with healthy controls (40). A similar study looking at sero-protection rates in juvenile SLE patients found reduced rates after H1N1 vaccination compared to healthy controls (73.7% versus 95.1%; P < 0.001). Amongst the SLE patients, those with active disease, as defined by a SLEDAI-2K ≥ 8, had a lower chance of seroconversion (odds ratio 0.42; 95% CI 0.18-0.98; P = 0.045) (41).

Pneumococcal vaccines

SLE patients have a 13 times higher risk of getting pneumococcal infection than the general population (42). PPSV23 (polysaccharide) or PVC13 (conjugate) pneumococcal vaccines are recommended in the over 65 age group and in younger, high-risk populations (43). A randomised controlled trial (RCT) was conducted to assess the safety and efficacy of the PPSV23 vaccine; pneumococcal vaccination was immunogenic in the majority of SLE patients, however 5 (20.8%) of 24 patients with SLE responded either to none, or to only 1 of the 7 polysaccharides, suggesting that a subset of patients remained unprotected; however, the vaccine is considered safe with no reports of SLE flare (44).

Diphtheria, pertussis and tetanus (DPT) vaccine

The diphtheria toxoid is as effective in SLE patients as with the general population. The pertussis vaccine requires booster doses as it cannot produce a life-long immunity. Protective levels of tetanus anti-toxoid IgG were reported in 90% of SLE patients after vaccination, which is the same figure as the general population (45).

Hepatitis A and B vaccine (HAV and HBV)

In patients with autoimmune conditions, the two-dose regime for HAV at a six month interval is recommended in immunocompromised states. Vaccine efficacy data is limited, however one study showed effectiveness in 93% of SLE patients, which is equivalent to the non-SLE population (46).

Haemophilus influenzae type B (Hib) vaccine

Hib vaccine is recommended by the CDC as part of the childhood immunisation programme, and for adults with asplenia and after stem cell transplant (47). It is considered safe and 88% protective in SLE patients, although the immune response can be lower during high disease activity (48).

Human papilloma virus (HPV) vaccine

The HPV vaccine is recommended in SLE patients due to an increased susceptibility to HPV infection and cervical dysplasia compared with the general population (23). 80-90% of SLE patients achieved sero-protection from HPV vaccination, equivalent to the general population (49).

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|  | Positive effect of vaccination in SLE | Negative effect of vaccination in SLE |
| Disease | Provides protection against many infective agents which SLE patients are suspectable to, including influenza and pneumococcus | Possible disease flare with live vaccines |
|  | Female SLE patients are at higher risk of HPV. HPV vaccination helps protect against cervical dysplasia |  |
| Safety | Multiple studies supporting the safety of non-live vaccines in SLE, live vaccines appear safe in patients with mild disease not receiving significant immunosuppression. | Live vaccinations can lead to severe infections in patients on significant immunosuppressives (i.e. High dose steroids, high dose methotrexate or azathioprine or recent biologics) |
| Efficacy | Several studies show that SLE patients achieve sero-protection levels equivalent to the general population, or at a level required to provide protection from disease | Possible lower sero-convertion rates in some SLE patients with high disease activity or those receiving significant immunosuppressive therapies |

Table 2. Potential positive and negative effects of immunisation in SLE

**SLE treatment and vaccination**

There is concern that immunosuppressive therapies may impede the immune response to vaccines required to provide protection from infectious agents. Here we highlight current data on the safety and immunogenicity of vaccinations with some of the more commonly used agents in the treatment of SLE.

*Prednisolone*

Current guidance advises against live vaccinations in patients who have been given high doses of prednisolone, defined as doses of greater than 40mg per day for more than 1 week, and lower doses of prednisolone, defined as 20mg per day, or 1mg/kg per day, for more than 14 days, 3 months prior to vaccination (50).

Immunogenicity post vaccination with inactivated vaccines appears to depend on the dose and duration of prednisolone therapy (51). A study of the influenza vaccine in patients with SLE showed a trend of reduced immunogenicity in patients taking prednisolone > 10mg daily (mean number of immune responses 1.14 vs 1.65), although this was not a significant difference(52). Dosage related reduction in antibody response has also been observed with the pneumococcal vaccine (53). A study of the response to the influenza vaccine in asthmatic patients given short course of high dose prednisolone did not show any difference in sero-protection compared to the control group (54).Therefore, duration as well as dosage of prednisolone may be factors in developing an appropriate immune response to vaccination.

*Hydroxychloroquine*

Hydroxychloroquine is not thought to be associated with an increased risk of systemic infection post vaccination with live vaccines, and these vaccines are therefore not contraindicated in patients taking hydroxychloroquine(55). Studies suggest hydroxychloroquine does not have a significant negative impact on the antibody response post influenza vaccines (56). Similar results are seen with other vaccines, such as the pneumococcal vaccine (44).

*Azathioprine*

Live vaccines are contraindicated in patients who have had azathioprine at a dosage of >3mg per kg per day in the preceding 3 months (57). For inactivated vaccines, most studies show no significant impact on post vaccination antibody levels (58, 59). However, studies by Huang et al (40)and Holvast et al (60)suggest lower post influenza vaccine antibody levels in patients with SLE taking azathioprine. Hepatitis B surface antigen levels also appear to be lower in patients with inflammatory bowel disease on azathioprine treatment (61). However, the prevailing opinion is that patients on azathioprine still develop immunogenicity to these vaccines, albeit reduced, and should be considered for vaccination with inactivated vaccines (40).

*Methotrexate*

Expert opinion recommends the avoidance of live vaccines in association with methotrexate, when used at dose of greater than 25mg per week in the 3 months preceding vaccination (18). A trial by Winthrop et al looking at rheumatoid arthritis patients suggests that doses below this threshold do not result in an increased risk of live herpes virus vaccine related infection (62).

Studies evaluating humoral responses to vaccination with inactivated vaccines and concurrent methotrexate therapy have revealed mixed results. Although some studies show no significant difference from controls (59), other studies suggest methotrexate may reduce humoral response to inactivated vaccines such as the hepatitis A vaccine, pneumococcal vaccine and the influenza vaccine (63, 64). This effect on the influenza virus was replicated in a prospective randomised parallel group trial by Park et al (65). This study compared humoral responses to influenza vaccination in patients with rheumatoid arthritis in whom methotrexate was suspended for a specified length of time versus patients who continued methotrexate therapy. Although antibody response was improved by suspending methotrexate, all groups were found to have significant overall response to the vaccination. Thus, despite suggestions of improved response to vaccination with a suspension of methotrexate, this needs to be weighed up on the risk of disease flare, and a significant response to vaccination may still be achieved with continued methotrexate therapy.

*Mycophenolate*

There is limited data on the safety of live vaccines with mycophenolate. The American Advisory committee on immunization practices (ACIP) has issued guidance on the safety of certain DMARDs such as methotrexate, azathioprine and 6-mercaptopurine based on perceived immunosuppressive effects, but does not provide any information on mycophenolate (57). Therefore, use of live vaccinations whilst on mycophenolate is dependent on the clinician’s judgement. This in turn would depend on factors such as the risk of the infection to the individual patient, potential benefit of prevention and risk of flaring on discontinuing or delaying therapy.

In patients post solid organ transplants, mycophenolate has been shown to result in reduced humoral responses to the influenza vaccine, pneumococcal vaccine and tetanus toxoid vaccines (66, 67)**.** Mok et al (68) demonstrated that SLE patients on combination mycophenolate and low doses prednisolone therapy have a reduced immunogenicity to the human papilloma virus (HPV) vaccine. Therefore, when considering inactivated vaccines, this potential for reduced immunogenicity needs to be weighed up against the risks of suspending treatment by the treating physician.

*Rituximab*

Rituximab, an anti-CD20 monoclonal antibody, causes B-cell depletion, thereby impairing the antibody responses to vaccination (69, 70). Live vaccines are not recommended in patients who have received rituximab in the 12 months prior (18, 71). A number of studies have shown a reduced humeral response post influenza and pneumococcal vaccination in patients with rheumatoid arthritis on rituximab therapy (72-74). Westra et al (70) demonstrated that IgG antibody levels recover after six-ten months, but IgM antibody levels remain impaired. However, a study by Arad et al (75) showed that cellular responses were preserved in patients on rituximab for rheumatoid arthritis. Due to these observations, EULAR guidelines recommend ideally giving these inactivated vaccines four week before and six months after rituximab therapy (18). The British society of rheumatology (BSR) have now recommended that If a patient is offered a date for vaccination, vaccinate and delay rituximab for four weeks where clinically appropriate. [ref]

*Belimumab*

Belimumab is a monoclonal antibody which inhibits the soluble B-lymphocyte stimulating (BLyS) protein, licensed for adult patients with active, antibody positive SLE, receiving standard SLE therapy (77). Live vaccines are contraindicated with concurrent belimumab therapy and, as with other biologic therapies, it is recommended to delay live attenuated vaccines for 12 months after the last dose (71).

As a relatively new drug, limited information exists regarding the effect of belimumab on vaccination. However, Chatham et al (78) demonstrated a comparable positive antibody response to the pneumococcal vaccine in patients on belimumab to those in the control group. A substudy from the BLISS-76 phase three, double blinded, randomised, placebo-controlled trial showed that antibody responses to pneumococcus, influenza and tetanus were preserved in patient who had past vaccinations. It also suggested a reduced antibody response to a smaller group of patients given the influenza vaccine during belimumab therapy when compared to the control group. However, this response was still deemed to be significant and likely to offer protection (77).

*Cyclophosphamide*

Cyclophosphamide is used in the management of severe lupus and is a potent immunosuppressive agent (79). Live vaccines are contraindicated in patients on cyclophosphamide therapy (80). There is a paucity of data when looking at inactivated vaccines, however, one study showed that patients on cyclophosphamide receiving the influenza vaccine appeared to produce a comparable immune response when compared to controls (81)**.**

*Calcineurin inhibitors*

Calcineurin inhibitors such as ciclosporin and tacrolimus are used in the management of patients with moderate to severe SLE (79). A study of 19 post-transplant patients on calcineurin inhibitors who were unintentionally given the yellow fever vaccine showed no increased risk of infection (82). However, due to its small sample size it is difficult to draw firm conclusions from this data. There are mixed results on the immune responses to inactivated vaccines on calcineurin inhibitors. Dengler et al (83) demonstrated that post-transplant patients on ciclosporin developed appropriate immune responses to 8 out of 9 pneumococcus vaccine serotypes, but also showed reduced responses to the Influenza vaccine.

Key summary points:

* The evidence suggests that the potential harm to SLE patients from vaccines is low
* SLE patients are at increased risk from viral infection and may be at increased risk from COVID-19
* Therapies used to treat SLE, in particular rituximab and high dose steroids, may reduce the efficacy of vaccines
* Decisions regarding delays in patients SLE treatment due to vaccination need to be tailored to the individual patient with reference to appropriate guidelines

**COVID vaccination: looking to the future**

As SARS-CoV-2 continues to mutate and other strains emerge it is likely some new variants will evade current vaccines. There is already concern that a SARS-COV-2 variant, known as 501Y.V2 first identified in South Africa, may evade the AstraZeneca/Oxford vaccine. To deal with this situation vaccines will need to be modified to target new variants. Due to mutations globally and the success of all approved vaccines so far in preventing hospitalisation and death but with a variable and as-yet unknown effect on transmission, COVID-19 is likely to become another endemic respiratory virus that may require annual or intermittent booster immunisation. There are studies currently investigating the effect of vaccine combinations, which may be a prevention strategy in the future (84). Current guidance recommends that SLE patients receive their annual influenza vaccination (18) and it may be that in the future SARS-CoV-2 vaccination is added to these recommendations.

**How should SLE patients be managed with regards to vaccination against COVID-19?**

**To date data looking at outcomes for SLE patients with COVID-19 have shown that there may be an increased risk of hospitalisation and death compared to the general population, possibly with greater risk for those patients on rituximab (7, 13). While this data must be interpreted with caution, immunisation against COVID-19 will be important for people with SLE. As mass vaccination begins, SLE patients are likely to be amongst the first in the population to be vaccinated, due to potentially increased vulnerability to viral infections related to disease factors, excess co-morbidity, and immunosuppressive therapy use. Historically, live**-attenuated **vaccines have been avoided for many SLE patients; as none of the currently emergency approved COVID-19 are l**ive-attenuated vaccines this is not issue for the current situation. Although the AstraZeneca/Oxford and Janssen vaccines are non-replicating viral vector vaccines they are considered safe for people with immunodeficiencies (71). **Studies have shown that non-live vaccines have good safety data in SLE patients and are unlikely to lead to a disease flare. SLE patients, particularly those on significant immunosuppressive medications, have been shown to have a reduced antibody response to vaccination, although response may still be significant enough to achieve sero-protection. The timing of vaccination for patients on immunotherapies, including rituximab which may impend response for over six months, needs to be tailored to the patient situation with thought given to the risk of under-treating SLE, balanced against the individual patient risk of potentially contracting COVID-19.**

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