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Should Patient with Autoimmune Inflammatory Rheumatic Diseases (AIIRD) be vaccinated with COVID-19 Vaccines?

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ABSTRACT

Vaccination is a very important measure for the prevention of various infections worldwide including the recent COVID-19 disease. However, until now the COVID-19 vaccine with various platforms has not been clinically tested on autoimmune inflammatory rheumatic disease (AIIRD) patients, due to caution against possible side effects and unknown efficacy. Several recent studies proved that there is increased risk of SARS-CoV-2 infection in AIIRD patients and moreover, those patients also have worse COVID-19 outcomes. Thus, patients with AIIRD should be prioritized for vaccination because they have an increased burden of infections, including COVID-19. Many studies showed that inactivated/non-live vaccine is safe for AIIRD patients and do not cause disease exacerbations. We conclude that benefits of vaccination greatly outweigh the risks of infection and therefore, COVID-19 vaccines can also be administered safely in stable AIIRD patients.

1. Introduction

COVID-19 pandemic has hit the world in 2020 with high morbidity and mortality rates in many countries. Various methods of preventing this disease have been carried out, ranging from health protocols to lockdowns in a number of countries.[1] One of the most important measures to end the pandemic is through accelerating vaccination research and development. Vaccinations against COVID-19 have been developed through collaborative efforts by many

countries. Indonesia has several phases of vaccination, and has started vaccinating the priority groups that include medical workers and the elderly earlier this year.[2]

Vaccination is one of the most successful infection prevention measures besides hygiene and sanitation.[3] This has led to the practice of vaccination for the prevention of various infections worldwide and in various human populations, including in patients with different types of autoimmune rheumatic diseases.[4] Until now the COVID-19 vaccine with various platforms has not been clinically tested on autoimmune rheumatic disease patients. This is due to caution against possible side effects and unknown efficacy. Concern about the efficacy and safety of vaccination in autoimmune diseases has long been a matter of debate. Some issues are whether vaccination could trigger autoimmunity, aggravate the degree of disease, and if the efficacy of vaccination in autoimmune diseases is optimal.[5] This narrative review discusses the efficacy and safety of several types of vaccines that have long been used in autoimmune rheumatic disease patients in various parts of the world, and then we extrapolate them with the COVID-19 vaccine that is already approved for use in Indonesia and other parts of the world.

Infection risk and the outcomes of COVID-19 in patients with autoimmune inflammatory rheumatic diseases

During COVID-19 pandemic, infection risk and the outcomes of COVID-19 in patients with autoimmune diseases has been a subject of interest. In Denmark, patients with inflammatory rheumatic diseases (n=58,052) had an increased partially adjusted incidence of hospitalization with COVID-19 compared with the 4.5 million people in the general population (HR 1.46, 95%CI 1.15 to 1.86) with strongest associations for patients with RA (n=29,440, HR 1.72, 95%CI 1.29 to 2.30) and vasculitis (n=4072, HR 1.82, 95%CI 0.91 to 3.64).6 A multicenter study in Italy showed significantly higher prevalence of patients with definite diagnosis/highly suspected of Covid-19 disease, in the whole autoimmune systemic disease series of 1641 patients, compared to "Italian general population" (1.5% vs 0.3%; p = .030, p = .001, p = .000).7 A multicenter study in Hubei province, China, found 42 families in which COVID-19 was diagnosed between Dec 20, 2019, and March 20, 2020, and in every family has family with rheumatic diseases. Within these families, COVID-19 was diagnosed in 27 (63%) of 43 patients with a rheumatic disease and in 28 (34%) of 83 of their family members with no rheumatic disease (adjusted odds ratio [OR] 2·68 [95% CI 1·14-6·27]; p=0·023).8 Thus, we can conclude that there is increased risk of SARS-CoV-2 infection in autoimmune rheumatic diseases patients.

Several studies about outcomes of COVID-19 in AIIRD showed that those patients have worse outcomes compared with COVID-19 patients without AIIRD. There was a multicenter cohort study in Spain, that included 456 rheumatic and non-rheumatic patients, in equal number, mean age 63 (IQR 53–78) years, male sex 41%, rheumatic diseases were inflammatory arthritis (60%) and connective tissue disease (40%). Most patients (74%) had been hospitalized. The study concluded that the risk of severe COVID-19 was 31.6% in the rheumatic and 28.1% in the non-rheumatic patients.[9] Another multinational network cohort study that include 133,589 patients with 48,418 hospitalised with COVID-19 and comorbid of autoimmune diseases compared with 70,660 hospitalised patients with comorbid of influenza. The most prevalent autoimmune diseases were psoriasis (3.5 to 32.5%), rheumatoid arthritis (3.9 to 18.9%), and vasculitis (3.3 to 17.6%). The study concluded that those autoimmune disease patients admitted with COVID-19 had more respiratory complications including pneumonia and acute respiratory distress syndrome, and higher 30-day mortality (2.2% to 4.3% versus 6.3% to 24.6%), compared with hospitalised with influenza.[10]

Immune response after vaccination

The antigen (generally a protein) from the vaccine that is injected into the muscle, will be picked up by dendritic cells, which are activated by adjuvant danger signals via pattern-recognition receptors (PRRs), such as Toll-like receptors. These active/mature dendritic cells will go to the nearest lymph nodes and then present the peptide from the vaccine protein antigen by the MHC molecule so that it activates the T cells through the T cell receptor (TCR). In combination with signaling (by soluble antigen) through the B cell receptor (BCR), the T cells drive B cell development in the lymph node. These activated B cells will produce antibodies that depend on T cells. Development results in maturation of an antibody response to increase antibody affinity and induce antibody of different isotypes. Production of short-lived plasma cells, which actively secrete specific antibodies to vaccine proteins, results in a rapid increase in serum antibody levels over the next 2 weeks. Memory B cells are also produced, which mediate immune memory. Long-lived plasma cells that can continue to produce antibodies for decades run to live in the bone marrow recesses. CD8 + memory T cells can reproduce rapidly when they encounter pathogens, and effector TCD8 + cells are important for eliminating infected cells.[11]

Efficacy and safety profile of COVID-19 vaccine

There are six vaccines currently approved for distribution and permission to enter Indonesia based on the Regulation of the Minister of Health of the Republic of Indonesia No.9860/2020 about vaccination against COVID-19. Indonesian government allows vaccines produced by AstraZeneca, vaccines of China National Pharmaceutical Group Corporation (Sinopharm), Moderna, Pfizer Inc. and BioNTech and Sinovac Biotech. The safety of vaccines is a critical factor in vaccination programs. Safe and effective vaccines to prevent COVID 19 are urgently needed. The followings are profile of the efficacy and safety of the COVID 19 vaccines that is and will be available in Indonesia:

1. Coronavac (Sinovac)

CoronaVac is a vaccine derived from an inactivated virus with alum adjuvant. SARS-CoV-2 virus strain CN2 was extracted from bronchoalveolar lavage (BAL) patients treated in Wuhan China, then cultured in vero cells, cultured and activated using β-propiolactone, then purified and absorbed into aluminum hydroxide.12 The phase 1 clinical trial of this vaccine included 144 healthy subjects aged 18-59 years and achieved antibody seroconversion of more than 75% in all subjects. In phase 2 clinical trials with better purification, seroconversion achieved> 95% in 600 subjects.[13]

Phase III clinical trials in Turkey, Brazil, Chile, and Indonesia, involving around 30,000 participants. The Turkish study showed 91.25% efficacy, the Brazilian study showed 78% efficacy but the latest January data showed a decrease in efficacy to 50.4%.[14] The phase III clinical trial of this vaccine in Indonesia which was conducted in Bandung, Jawa Barat in collaboration with Padjajaran University and Biofarma showed an efficacy of 65.3%. Meanwhile, the side effects reported were mild to moderate in the form of local side effects (pain, redness, swelling) and systemic side effects such as myalgia, fatigue and fever. The immunogenicity data showed good results 14 days after injection with a sero-positive result was 99.74 % and at three months after injection the sero-positive result was 99. 23 %. Based on this data, the Indonesian Food and Drug Monitoring Agency (BPOM) has issued an Emergency Use Authorization (EUA) letter for the use of the Sinovac vaccine.15 Since January 11, 2021, the Sinovac vaccine has started to be used in Indonesia.

2. Sinopharm (BBIBP-CorV)

Sinopharm's BBIBP-CorV vaccine is almost similar to the previous vaccine, the virus is cultured on Vero cells, cultured and it was inactivated with β-propiolactone, then purified and absorbed into

aluminum hydroxide. The virus strain used was HB02 which was isolated from bronchoalveolar lavage (BAL) patients treated in Wuhan China.[16,17] The phase 1 clinical trial was involved 192 subjects without any underlying disease. They were separated into two age groups (18–59 years and ≥60 years). Subject were randomly assigned to receive BBIBP-CorV or placebo in a two-dose schedule of 2 μg, 4 μg, or 8 μg on days 0 and 28. In phase 2, 448 participants were randomly assigned to receive the vaccine 8 μg on day 0 or 4 μg on days 0 and 14, days 0 and 21, or days 0 and 28 or placebo.

The most common adverse local reaction was site injection pain. Another local reaction were itch, swelling and induration. Systemic adverse reaction were fever (the most common), fatigue, inappetence, nausea, constipation, mucocutaneous abnormalities, headache, vomiting and itch (non-injection site). They reported that all adverse reactions were in mild or moderate severity. There were no serious adverse event was reported within 28 days post vaccination. The 100% seroconversion rate was reached in all vaccine recipients on day 42.[16,18]

The United Arab Emirates (UAE) Ministry of Health and Prevention have reviewed Sinopharm CNBG's interim analysis of the phase III trials included 31,000 participant across 125 nationalities in the UAE. This trial showed to have 86% efficacy against COVID-19 infection. The vaccine also showed to have 99% seroconversion rate of neutralizing antibody and 100% effectiveness in preventing moderate and severe cases of the disease. No serious safety concerns has been showed in this study.[19,20]

3. Moderna (mRNA-1273)

The Moderna COVID-19 Vaccine (also referred to as mRNA-1273) is mRNA vaccine that encoding a spike protein of SARS-CoV-2, which is encapsulated in lipid nanoparticles. A phase I trial of mRNA-1273 including 45 participant, 18-55 years age, received two doses, 28 days apart (between March 16 and April 14, 2020). The study showed mild or moderate local adverse event. The most common was site injection pain. Systemic adverse events were fever (most common), fatigue, chills, headache and myalgia. Adverse events were common after second injection. Seroconversion was in all participants by day 15.[21,22]

MODERNA phase 3 study enrolled 30,420 participants to receive two doses of mRNA-1273 or placebo 28 days apart in 99 centers among United States, between July and October 2020. The study showed 94.1% efficacy (95% CI, 89.3 to 96.8%; P<0.001). Site injection pain were the most local reaction among vaccine group (84.2 %) after the first dose and 88.6 % after second dose. Another local reaction were characterized by erythema induration, and tenderness. They resolved over 4 to 5 days. Systemic adverse event was higer in vaccine group than placebo were fever, headache, fatigue, myalgia, arthralgia, nausea vomiting and chills. Two death in vaccine group because of cardiac arrest and suicide. Three deaths in the placebo group because of intraabdominal perforation, cardiac arrest, and severe systemic inflammatory syndrome. Hypersensitivity reactions occurred 1.5% in the vaccine group. Bell's palsy occurred less than 0,1 % in the vaccine group (3 participants) and the placebo group (1 participant (0.1%)) during more than 28 days after injection. The limitation of this study was the short duration of safety and efficacy follow-up.[21,23]

4. Biontech/Pfizer (BNT162B2)

BNT162B2 is a nucleoside-modified mRNA (modRNA) vaccine that encodes part of the spike protein of the SARS-CoV-2, stabilized in the prefusion conformation. The phase 1 trial of BNT162B2 that conducted in the United States between May 4 and June 22, 2020, enrolled 195 participants which devided into two group, age of 18 to 55 years and age of 65 to 85 years. They reported mild to moderate local reaction (pain on site injection, redness and swelling). It was more frequent after 7 days of second dose. There were severe systemic events (fatigue, head-ache, chills, muscle pain, and

joint pain) reported in small numbers of younger recipients of BNT162b2.

The immunogenicity of BNT162b2 decreased with age. Humoral responses in adults 65 to 85 years of age was lower than in those 18 to 55 years of age. The highest neutralization titers were measured on day 28 or on day 35. Antibody responses in both younger and older adults showed a clear benefit of a second dose.24 BioNTech/Pfizer has published their randomized double blind study (phase III) of mRNA vaccine with 43,548 participant, 16 years of age or older at 152 sites worldwide between July 27 and November 14, 2020. They were received two doses, 21 days apart, of either placebo or the BNT162b2 vaccine candidate (30 µg per dose). The efficacy between the first and second doses was 52% , and seven or more days after the second dose, vaccine efficacy then rose to 95%. The most local reaction reported in the vaccine recipient group after the 7th day of injection were mild to moderate pain and less than 1% experienced severe pain. It was less frequently among older participant (> 55 years) than younger. Another local reactions were redness and swelling. All local reaction were resolved in 1-2 days. These did not increase after the second injection. Systemic event reported were fatigue (59%), headache (52%) and fever (16 %) among younger vaccine recipient. Vaccine recipient group reported more adverse event (27%) than placebo (12 %). Serius adverse event were shoulder injury related to vaccine administration, right axillary lymphadenopathy, paroxysmal ventricular arrhythmia, and right leg paresthesia. Two vaccine recipient were died due to arteriosclerosis and cardiac arrest, and four placebo were died due to stroke and myocardial infarction. No death were related to vaccine and placebo.[25]

5. Oxford/Astrazeneca (ChAdOxl nCOV19)

This is the first an adenoviral vector-based vaccine developed University of Oxford in the United Kingdom, in collaboration with the AstraZeneca. Phase 1/2 trial of ChAdOx1 on June 2020 with 52 participants aged between 18 and 55 years. They received two standard dose of ChAdOx1 nCoV-19 at a 56 day interval. The reactogenicity profile after the second dose was lower than after the first. The most frequently local and systematic reactions were tenderness and fatigue. The study reported that a booster dose of ChAdOx1 nCoV-19 is safe and better tolerated and also induced stronger antibody responses than a dose-sparing half-dose boost.[26]

Phase III clinical trials of this vaccine were carried out in United Kingdom, Brazil and South Africa between April 23 and Nov 4, 2020 and 23,848 participants were enrolled aged 18–55 years. An interim primary efficacy analysis of 11,636 participants (7548 in the UK, 4088 in Brazil) showed vaccine efficacy was 70.4% (95·8% CI 54·8–80·6; 30 [0·5%]) after two standard doses. There were ten cases hospitalized for COVID-19 in the control group after 21 days of first dose; two were severe COVID-19 and one death. The study reported 175 serious adverse events (84 events in the vaccine group and 91 in the control group). There were 3 cases of transverse myelitis side effects; one was report 14 days after ChAdOx1 nCoV-19 booster vaccination, one case accured 10 days after first ChAdOx1 nCoV-19 vaccination and one case accured after 68 days of MenACWY vaccination. All were recovered. Another tolerable side effect is local reaction at injection area. The study also reported four non-COVID-19 deaths (one in the ChAdOx1 nCoV-19 arm and three in the control arm) that were all considered unrelated to the vaccine. The cause of death were road traffic accident, blunt force trauma, homicide, and fungal pneumonia.[27,28]

6. Merah Putih Vaccine

The Indonesian Institute of Sciences (LIPI), the University of Indonesia (UI), the Eijkman Institute for Molecular Biology and Airlangga University The Bandung Institute of Technology (ITB) and Gadjah Mada University (UGM) have joined the national team for the development of an future Indonesia's COVID-19 vaccine that called The Merah Putih Vaccine. The

candidate vaccine is about 55 percent through the laboratory stage. The candidate vaccine is now set to undergo trials in February and March 2021.[2]

All of the vaccines above (except merah putih vaccine) already underwent clinical trial showed that they have good immunogenicity and efficacy and good safety profile, however, all of them never been tried in AIIRD patients.

Could vaccination induce autoimmunity?

Autoinflammatory/autoimmunesyndrome induced by adjuvant (ASIA) is an autoinflammatory/ autoimmune response after exposure to adjuvant that results in aberrancy of immune response leads to autoimmune features. The onset of this phenomenon ranging from days to years later after adjuvant exposure. Watad, et al, in 2016 figure that mean of onset was 16.8 years after exposure with UCTD as the most frequent manifestations and proposed that there is relation between adjuvant type and clinical manifestations. Some previously known disease, such as Gulf War Syndrome, siliconosis, macrophagic myofasciitis syndrome, and post vaccination syndrome has been identified for having ASIA features.[29]

Some publications identified several adjuvants that claimed to be related with ASIA, there are cosmetic fillers (containing mineral oil, hyaluronic acids, polyalkylimide, polyacrylamide, and collagen), metal implants, and silicone breast implants. While vaccines that reported to induce ASIA were hepatitis B, HPV, influenzae, hepatitis A, DTaP, MMR, and swine flu vaccines.[30,31]

Since ASIA been proposed, controversies remain unsolved. The definite pathogenesis, multifactorial involvement, unidentified genetic backgrounds, and many other "mysteries" of autoimmunity remains unclear and ASIA still remains a controversy. Critics and opinion are gaining, regarding the broadness of "external stimuli" in the major criteria without a definite timeframe, "typical" clinical presentation that can be found in several diseases and conditions, resulting in high sensitivity and less specificity of this criteria. In other words, the criteria encompassess almost all autoimmune disease manifestations, where musculoskeletal, neurologic, and mucous membrane are commonly involved. In clinical settings, measurement of autoantibodies against suspected adjuvant is not a routine examination and probably not widely available.[32]

Systematic review by Hawkes, et al, in 2015 including 10 case with various stimuli including metal, silicone implant, HPV vaccination, and influenzae vaccination showed that some issues need to be questioned. Some of them are: (1) time to event; (2) dose response relationship; (3) cofounding factors that hard to be eliminated, i.e giant cell arteritis (GCA) following influenzae vaccination, which more than 60% of people receiving influenzae vaccination were more than 65 years old, and older age are the risk factors for GCA.32 Vadala et al. 2017 in their narrative review showed that even if there were reports of suspected post vaccination autoimmune diseases, the epidemiologic studies proved that there was no causal relationship.[33]

Currently ASIA should be seen as possible mechanism explaining several events after adjuvant exposure, unfortunately the time range identified are widely ranging from days to 10 years after exposure. The incidence could not be determined currently regarding lack of data that represent worldwide incidence.34 Regarding vaccination, some of adverse events following vaccination (kejadian ikutan pasca imunisasi, KIPI), should be considered, reported and closely monitored when it presents, BUT should not considered as reason to delay vaccination, considering safety, efficacy and benefit of vaccination as part of disease prevention strategies.

Efficacy, immunogenicity and safety of vaccines in autoimmune rheumatic disease patients

Vaccination is a method to prevent certain infectious diseases, but there are some concerns regarding the efficacy and safety of vaccinations in patients with autoimmune rheumatic diseases.[4,35]

The concerns are generally due to the immunosuppressed state of patients with autoimmune rheumatic diseases that are on DMARDs treatment and the potential of flare ups of autoimmune rheumatic disease activity after vaccination.[36]

Generally, vaccines that had been investigated in clinical trials involving autoimmune rheumatic diseases showed good efficacy, good immunogenicity and mild adverse events that were comparable with healthy controls.[36,37] The table below summarize efficacy, immunogenicity and safety of several vaccines that are commonly used in autoimmune rheumatic diseases patients:

Table Efficacy, immunogenicity and safety of vaccines in autoimmune rheumatic disease patients[36]

Vaccine	Efficacy	Immunogenicity	Safety
Influenza	Reduced all-cause mortality rate, risk of hospitalisation for influenza-related complications, and self reported rate of influenza infection	similar immunogenicity (development of anti-bodies (titre value ≥40, as measured by the haemagglu-tination inhibition assay) between autoimmune rheumatic disease patients and healthy controls, except for patients treated with rituximabthat showed decreased immunological response to the vaccine	Influenza vaccination did not cause flare ups of autoimmune rheumatic disease activity. Adverse events were similar with healthy controls
Pneumococcal	Good efficacy	Good immunogenicity	The safety of the vaccine is good, except for patients with CAPS (cryopyrin associated periodic syndrome) that showed the vaccine might induce severe local systemic reactions (fever, headache, meningismus, nausea).
Hepatitis A	No studies on the efficacy of HAV vaccination in patients with AIIRD	The vaccine is less immunogenic in autoimmune rheumatic disease patients compared to healthy persons. Single dose of HAV vaccine is not sufficient so the patient should get a second dose of HAV vaccine after 6 months and measure the antibody titres after the vaccination.	No data on the influence of vaccination to disease activity. Adverse events were generally mild, reported in up to 17% patient. There is a case report of meningoencphalitis in RA patients tha happened 2.5 weeks after the second dose of HAV vaccine.
Hepatitis B	No studies of efficacy in autoimmune rheumatic disease patients	Good immunogenicity, except for patients treated with TNF-blocking agents.	Hep B vaccination did not increase risk of flare ups of disease
Tetanus toxoid	No studies of efficacy in autoimmune rheumatic disease patients	Adequate response rate	No serious adverse events
Herpes zoster	Reduced incidence of herpes zoster in patients with autoimmune rheumatc disease over the age of 60.	Lower cell-mediated immunity compared to healthy controls.	The vaccine didn't increase risk of flare ups of disease. However, this is a live-attenuated vaccine and must be considered carefully . It is important to determine Varicella zooster status of the patient. If the patient is seronegative for herpes zooster, a less potent VZV vaccine approved for primary varicella in chldren might be used.
HPV	No studies of efficacy in autoimmune rheumatic disease patients	Immunogenicity os high and similar to healthy controls	Adverse events similar to HC Disease activity after vaccination was stable

From the table above we can conclude that there are good immunogenicity, mild adverse events and no

increased in disease activity of autoimmune inflammatory rheumatic disease patients post vaccination.

Vaccination guidelines for autoimmune rheumatic diseases in several countries

There were sixteen key recommendations that have been formulated regarding vaccination recommendations for autoimmune inflammatory rheumatic disease patients in Switzerland, 2015.[38] Several important recommendations are:

a. Vaccination does not trigger autoimmune inflammatory rheumatic diseases, nor their exacerbations (Quality of evidence [QoE]: low, strength of recommendation [SoR]: strong);
b. Benefits of vaccination greatly outweigh the risks of infection;
c. In already treated AIIRD patients, vaccines should ideally be administered when immunosuppressive therapy is lowest (QoE: low, SoR: strong);
d. It is generally safe to administer inactivated vaccines to patients with AIIRD under immunosuppressive treatment; the immunogenicity may be reduced (QoE: moderate, SoR: strong);
e. Vaccination should preferentially be administered during stable disease (QoE: low, SoR: weak).

From five vaccination general recommendation for AIIRD patient in South Korea, 2020, there are several important key recommendations, i.e.:[39]

a. vaccination is unlikely to cause or aggravate AIIRD and generally recommended in AIIRD patients (level of evidence [LOE]: Low, strength of recommendation [SOR]: Strong);
b. vaccines need to be administered to patients when their AIIRD is in a stable state (LOE: Very low, SOR: Strong);
c. AIIRD patients on immunosuppressive agents should not take live attenuated vaccines (LOE: Very low, SOR: Weak against).

EULAR recommendation for vaccination in AIIRD patients, 2019, has six important general principles. Some of them are:

a. vaccination in patients with AIIRD should preferably be administered during quiescent disease (level of agreement: 94%);
b. vaccines should preferably be administered prior to planned immunosuppression, in particular B cell depleting therapy (level of agreement: 100%);
c. Non-live vaccines can be administered to patients with AIIRD also while treated with systemic glucocorticoids and DMARDs (level of agreement: 100%);
d. live-attenuated vaccines may be considered with caution in patients with AIIRD (level of agreement:53%);
e. for DMARDs-naïve patients, vaccine is preferably administered before planned immunosupression, particularly if using B cell depleting therapy.

From the three different recommendations above, we see several important recommendations in common, i.e:

a. vaccination should administered during stable (quiescent) disease activity;
b. vaccination is unlikely to cause and/or aggravated AIIRD,
c. it is generally safe to administer non live vaccines to AIIRD patients under treatment with systemic glucocorticoids and DMARDs, however, the immunogenicity may be reduced;
d. it is not recommended to administer live - vaccine in AIIRD patients taking immunosuppressive agents;
e. for DMARDs-naïve patients, vaccine is preferably administered before planned immunosupression, particularly if using B cell depleting therapy.

COVID-19 Vaccination guidelines/position statements for autoimmune inflammatory rheumatic diseases

Some rheumatology organization around the world has begun publishing their consensus on vaccination for autoimmune inflammatory rheumatic disease (AIIRD) patients. One of the most prominent recommendations is from the American College of Rheumatology COVID-19 Vaccine Clinical Guidance Task Force that was published in February, 8th, 2021.[40] This recommendation stated that AIIRD patients should be prioritized for vaccination before the nonprioritized general population of similar age and sex. ACR also stated that there are no known additional contraindications to COVID-19 vaccination for AIIRD patients beside known allergies to vaccine components. 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.

Similarly, The European Alliance of Associations for Rheumatology (EULAR) also stated that in regard of COVID-19 vaccinations, non live vaccines can be used safely in patients with rheumatic musculoskeletal disease as well as in patients receiving drugs that influence the immune system. EULAR recommends that COVID-19 vaccinations should preferably be given when the disease is in a quiet phase.[41]

In South East Asia, Singapore Chapter of Rheumatologist is one of the first rheumatology organizations in the region that published their recommendation for COVID-19 vaccination in people with rheumatic disease. Their rationale is that because people with rheumatic diseases (PRD) are vulnerable patients, there is an urgent need for a consensus for vaccination against SARS-CoV-2 in rheumatic disease patients. They strongly recommend that eligible rheumatic disease patients and household contacts be vaccinated against SARS-CoV-2. Immunomodulatory drugs, other than rituximab, can be continued alongside vaccination. Since Singapore use many different platforms of COVID-19 vaccines, any of the approved COVID-19 vaccines may be used in rheumatic disease patients, with no particular preference.[42]

2. Conclusion

Patients with AIIRD should be prioritized for vaccination because they have an increased burden of infections including COVID-19. Inactivated/non-live vaccine is safe for AIIRD patients, vaccinations do not cause autoimmune inflammatory rheumatic diseases, nor their exacerbations. Vaccination in AIIRD patients is preferably administered in quiescent state of the disease. Benefits of vaccination greatly outweigh the risks of infection and. Therefore, COVID-19 vaccines can be administered safely in AIIRD stable patients.

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