COVID-19 Vaccination in Patients with Autoimmune Inflammatory Rheumatic Diseases (AIIRD)

A Position Statement from the Philippine Rheumatology Association
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KEY POINTS:

1. The Philippine National Deployment and Vaccination Plan for COVID-19 espouses a whole-of-society approach for the successful vaccination for all Filipinos.
2. Patients with Autoimmune Inflammatory Rheumatic Diseases (AIIRD) may benefit from COVID-19 vaccination.
3. Patients with AIIRD must be informed of the possibility of a reduced response to vaccination and the importance of adhering to protocols to avoid infection.
4. Post-vaccination monitoring is important.
5. Patients with AIIRD who have questions regarding COVID-19 vaccination should consult their rheumatologist to arrive at a shared decision.

Background

The Philippine National Deployment and Vaccination Plan for COVID-19 prepared and approved by the National Task Force Against COVID-19 is now in the initial steps of implementation. It requires a whole-of-society approach to ensure the delivery of safe, effective, and accessible vaccines for all Filipinos. One specific sector of society that may need guidance is patients with autoimmune diseases.

On 14 January 2021, the Philippine Food and Drug Administration (FDA) granted its first Emergency Use Authorization (EUA) to Pfizer-BioNTech COVID19 Vaccine (BNT162b2) Suspension for IM Injection.[1] On 28 January 2021, FDA also announced that AstraZeneca has obtained its EUA.[2] In issuing the EUA for both vaccines, FDA assured the public that based on currently available data, the benefits outweigh the known and potential risks of the product and that the safety and efficacy were reviewed by a panel of clinical experts and the quality of data was reviewed by technical experts from FDA Center for Drugs Regulation and Research (CDRR).

Vaccines developed by Moderna, Covovax, Gamaleya, Sinovac Biotech, and Sinopharm are yet to be given an EUA at the time this statement was made.

This document from the Philippine Rheumatology Association aims to guide physicians taking care of patients with AIIRD and patients taking immunosuppressive medication about the efficacy and safety of COVID-19 vaccines with existing EUA in the Philippines. It is not a substitute for careful clinical judgment in individualizing patient care. Neither is this a statement on standard of care. This will be updated as verified scientific information becomes available.

Patients with AIIRD are at higher risk for severe COVID-19 illness and related mortality.

People with autoimmune rheumatic diseases are at increased risk of infections due to the underlying immunologic dysfunction, the immunosuppressive effects of drugs used to control them, and their comorbidities.[3] An example is systemic lupus erythematosus (SLE) where infections account for 20% to 55% of all deaths in patients with SLE.[4]

Williamson et al. reviewed the primary care health records of 10,926 COVID-19-related deaths in a population of about 17 million adults in England. She observed that SLE, rheumatoid arthritis (RA), or psoriasis, combined to make up 5.1% of the study population, had a higher risk of death (adjusted HR 1.19; 95% CI 1.11–1.27) about COVID-19 compared to people without one of these diagnoses. This finding persisted after

consideration of other factors like age, sex, ethnicity, social deprivation, and the presence of other chronic health conditions.[5] The ACR COVID-19 Vaccine Clinical Guidance Task Force likewise acknowledges this increased risk for morbidity and mortality among COVID-19 patients with AIIRD.[6]

A review of factors associated with hospitalization among 600 cases of COVID-19 in patients with rheumatic diseases from the COVID-19 Global Rheumatology Alliance (C19-GRA) database showed that older age and the presence of additional underlying health conditions were factors associated with hospitalization. The use of high-dose glucocorticoids (≥10 mg per day of prednisolone-equivalent) was also associated with an increased risk of hospitalization (adjusted OR 2.05; 95% CI 1.06–3.96).[7]

Types of vaccines

The vaccines recently granted EUA by the Philippine FDA are not live, attenuated vaccines and do not belong to the category of vaccines that have a risk of reversion to virulence.[8]

Pfizer-BioNTech COVID19 Vaccine (BNT162b2) is a lipid nanoparticle-formulated, nucleoside-modified mRNA vaccine encoding the prefusion spike glycoprotein of SARS-CoV-2, the virus that causes coronavirus disease 2019 (COVID-19).[9] Vaccination with the Pfizer-BioNTech COVID-19 vaccine consists of 2 doses (30 µg, 0.3 mL each) administered intramuscularly, 3 weeks apart.

COVID-19 messenger RNA vaccines that encode for the viral spike protein are prepared as mRNA wrapped in a lipid nanoparticle that gets incorporated into human cells upon vaccination. The spike protein that the host cell produces upon instruction from the mRNA vaccine stimulates an immune response that will ultimately protect against SARS-CoV-2.

Safety data from 37,586 of 44,000 individuals randomized in an ongoing phase 1/2/3 trial comparing Pfizer-BioNTech COVID-19 Vaccine and saline control showed that in individuals 16 years of age and older there were no specific safety concerns that would preclude the issuance of an EUA.[10]

The vaccine was 95% effective (95% credible interval 90.3, 97.6). This was based on efficacy data from 36,532 participants, {12 years or older, without SARS-CoV-2 infection, seven days before the second vaccine dose}, where only 8 developed COVID-19 as compared to 162 in the placebo group.

AstraZeneca and University of Oxford COVID-19 vaccine (AZD1222) is a ChAdOx1-Sn Cov-19 nonreplicating chimpanzee AdV5 expressing spike protein. It is given as two standard doses (SD/SD cohort) of approximately 5×10^{10} viral particles per dose administered 28 days apart.

Interim efficacy results from two of the four ongoing trials with 11636 participants reported that no COVID-19-related hospital admissions occurred in ChAdOx1 nCoV-19 recipients, whereas ten (two of which were severe) occurred in the control groups. Vaccine efficacy for the prespecified primary analysis (combining dose groups) against the primary endpoint of COVID-19 occurring more than 14 days after the second dose was 70·4% (95·8% CI 54·8 to 80·6; 30 [0·5%] of 5807 participants in the ChAdOx1 nCoV-19 group vs 101 of 5829 [1·7%] participants in the control group).[11]

Immunization for Immunosuppressed Individuals

The 2018 Philippine Clinical Practice Guideline (CPG) on Adult Immunization of the Philippine Society of Microbiology and Infectious Diseases (PSMID) states that certain vaccines may be given to immunocompromised individuals but the response is dependent on the degree of immunosuppression.[12] Several organizations and national health authorities also recommend vaccinations for immunocompromised adults. These include the Centers for Disease Control and Prevention (CDC), Infectious Disease Society of America (IDSA), American College of Rheumatology (ACR), European Alliance of Associations for Rheumatology (EULAR), Canada National Advisory Committee on Immunization (NACI), and the Department of Health of Australia.[13-18]

The 2013 IDSA CPG specifically recommends that patients with chronic inflammatory illness treated or about to be treated with immunosuppressive agents be administered inactivated vaccines, including Inactivated Influenza Vaccine (IIV), as immunocompetent persons are vaccinated. The guideline extensively discusses the immune response to vaccination among patients maintained on disease-modifying drugs. Exacerbations of autoimmune disease temporally related to influenza vaccination have been reported, yet prospective controlled trials do not support a cause-and-effect relationship.[13-19]

Patients with autoimmune and/or rheumatic diseases can receive the COVID-19 vaccine.

The Center for Disease Control and Prevention (CDC), on its 21 January 2021 advisory, issued Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines Currently Authorized in the United States. It asserts that persons with immunocompromised conditions, or who take immunosuppressive medications or therapy who might be at increased risk for severe COVID-19 may receive COVID-19 vaccination if they have no contraindications to vaccination. It provides that these individuals should be counseled about the unknown vaccine safety profile and effectiveness in immunocompromised populations, as well as the potential for reduced immune responses, and the need to continue to follow all guidelines to protect themselves against COVID-19.[20] Similar guidelines have been released by the NACI.[21]

Whether vaccination triggers the development or exacerbation of the autoimmune disease is being closely monitored.

The mRNA-based vaccine platform used in the development of the Pfizer-BioNTech COVID19 Vaccine (BNT162b2) has been reported to induce potent type I interferon response which is associated with inflammation and autoimmunity.[22] However, compared to placebo, there have been no reports signaling an increase in symptomatic cases consistent with autoimmune conditions or inflammatory disorders.

In the AstraZeneca and University of Oxford COVID-19 vaccine (AZD1222) trial, three cases of transverse myelitis occurred 14 days after booster vaccination. Following an evaluation by an independent panel of neurological experts, these cases were adjudicated as unlikely to be related to vaccination with AZD1222. All three patients are reported to be clinically stable, improving, or recovered.[11]

Among SLE patients receiving the influenza vaccine, a diminished immune response was associated with the following factors: ancestral background, immunosuppression with prednisone, presence of lupus hematologic criteria, and evidence of increased likelihood of disease flares.[23]

Vaccines may also trigger the short-term generation of autoantibodies. SLE patients who were vaccinated against influenza showed an increase in anticardiolipin antibodies but not in anti-B2 glycoprotein serum levels. Although this may raise concerns about an increase in the risk for thrombosis, the spike in autoantibody levels was transient and did not seem to have long-term clinical effects.[24]

A study on vaccination reported that influenza and pneumonia vaccines were safely tolerated by Filipino SLE patients.[19,25] Cumulative evidence suggests that vaccines are best administered when a systemic autoimmune condition is quiescent.[6,26]

Timing mRNA Vaccination in AIIRD patients receiving Immunomodulatory Therapies

The American College of Rheumatology "COVID-19 Vaccine Clinical Guidance Summary for Patients with Rheumatic and Musculoskeletal Diseases" emphasize that "no modifications to either immunomodulatory therapy or vaccination timing is needed for: Hydroxychloroquine; IVIG; glucocorticoids, prednisone-equivalent dose <20mg/day; Sulfasalazine; Leflunomide; Mycophenolate; Azathioprine; Cyclophosphamide (oral); TNFi; IL-6R; IL-1; IL-17; IL-12/23; IL-23; Belimumab; oral calcineurin inhibitors".[6]

Methotrexate, cyclophosphamide and Janus Kinase Inhibitors (baracitib, tofacitinib) may be resumed (1) week after each vaccine dose.

Post-vaccination monitoring is important.

While Covid-19 vaccine clinical trials did not exclude patients with known autoimmune conditions, data specific to this subset of patients are yet to be analyzed.[27,28] Thus, it will take some time to determine differences in vaccine response between these subjects and the general healthy population. Any information related to this will have to be monitored from reports that will follow the ongoing vaccine rollout.

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