PSMID Statement on COVID-19 Vaccines and the Immunocompromised Host (ICH)

February 12, 2021

This document was prepared by the
Adult Immunization Committee of the Philippine Society for Microbiology and Infectious Diseases (PSMID)

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General Statement on COVID-19 Vaccines and the Immunocompromised Host (ICH)

The current data on COVID19 vaccine efficacy and safety in the ICH is sparse. However, the ICH is at risk for severe COVID19 infection, and therefore, vaccination is encouraged. They should undergo individual assessment by their attending physician, where a shared-decision making should occur between the patient and his/her physician, and this should be properly documented.

Vaccine efficacy may be affected by the degree of immunosuppression, and the individual should be counseled on this possibility. As such, the ICH should be advised to continue adherence to the minimum health protocols.

If the ICH's status, or level of disease activity is unknown, vaccination may be delayed, and re-scheduled at a time where disease activity has been assessed as stable.

The type of vaccine should be considered when deciding to give it to ICHs. Generally, live or live attenuated vaccines are not recommended.

The vaccinated ICH and their close contacts should continue to wear masks, maintain physical distancing guidelines, practice hand hygiene and follow other recommendations for COVID-19 prevention (NCCN, 2021).

Caregivers and household/close contacts of the immunocompromised individual should be immunized when they are part of the priority group for vaccination.

This guidance may change as more information becomes available.

Can people with HIV infection receive the vaccine?

Yes, people with HIV (PWH) may receive a COVID-19 vaccine if they do not have a severe or immediate allergic reaction to any of the ingredients in the vaccine. (CDC, 2020)

PWH who are part of the priority group for vaccination may be vaccinated.

Ideally, a CD4 count result within the past 6 months is available. If the patient's status, or level of disease activity is unknown, vaccination should be deferred. (Good practice statement).

Any concurrent opportunistic infection on active treatment should likewise be taken into consideration during the process of evaluation.

PHW are encouraged to adhere to antiretroviral treatment for immune reconstitution and to prevent the occurrence of opportunistic infections. They should visit their attending physician or treatment hub regularly for assessment.

Summary of Evidence

People with HIV may be at increased risk for serious COVID-19 illness. Currently, there is no data on the level and duration of protection afforded by the vaccine to people with HIV. Vaccine safety data for people with HIV is also not currently available. General principles for vaccination for people with HIV include the use of vaccines that do not contain infectious or live virus, and none of the vaccines currently being used and in clinical trials use live vaccines. For some vaccines, people with stable HIV condition have been included in the clinical trials and information on safety and effectiveness should be available soon. (HIVMA, 2021)

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Can patients with autoimmune diseases receive the vaccine?

Yes, patients with autoimmune diseases may receive COVID19 vaccines if they do not have a severe or immediate allergic reaction to any of the ingredients in the vaccine.

It is advised that the vaccine be given when the disease is not in flare (EULAR, 2020; ACR, 2021). It is also recommended that the vaccine doses are completed before starting immunosuppressive medications (EULAR, 2020; ARMA, 2021).

For patients already receiving immunosuppressive agents, they are advised not to stop their medications (ARMA, 2021). Although there is the risk that the vaccine efficacy is reduced, the benefits of getting the vaccinations should be weighed against the risk (ACR, 2021).

Summary of Evidence

Currently, there are no specific trials addressing the safety and efficacy of COVID19 vaccines among participants with autoimmune diseases (ACR, 2021). However, the COVID19 vaccines that are currently available are non-live vaccines, and thus are not an absolute contraindication in this population group (EULAR, 2020). The studies evaluating mRNA vaccines included patients with autoimmune diseases in some vaccine trials, and there was

no difference in adverse events between the vaccine arm and the placebo arm in this subgroup of patients (CDC, 2021).

Thus, persons with autoimmune diseases may receive COVID19 vaccines. The same precautions are observed as that for the general population (ARMA, 2021). It is advised that the vaccine be given when the disease is not in flare (EULAR, 2020; ACR, 2021). It is also recommended that the vaccine doses are completed before starting immunosuppressive medications (EULAR, 2020; ARMA, 2021).

For patients already receiving immunosuppressive agents, they are advised not to stop their medications (ARMA, 2021). Although there is the risk that the vaccine efficacy is reduced, the benefits of getting the vaccinations should be weighed against the risk (ACR, 2021). It is thus important to have a shared decision making with your healthcare provider in this setting (ARMA, 2021).

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Can transplant recipients be vaccinated with COVID19 vaccine?

Yes, transplant recipients may receive the COVID19 vaccine if they do not have a severe or immediate allergic reaction to any of the ingredients in the vaccine.

They should undergo individual assessment by their attending physician.

Although timing for COVID-19 vaccine is not yet defined for these patients, vaccination guidelines for solid organ transplant recipients recommend that transplant candidates should be vaccinated prior to transplantation. Ideally, vaccination series should be completed at least 2 weeks prior to transplantation. In general, inactivated vaccines are recommended at least 2 weeks prior to transplantation, or starting at 3 to 6 months after transplantation (Danziger-Isakov & Kumar, 2019).

If only 1 dose of the vaccine is received before transplantation, the optimal timing of the second dose is not established. Expert opinion suggests administering the second dose at least 4 weeks after transplantation in order to allow time to decrease immunosuppression (AST, 2021).

The safety of COVID-19 vaccine among these patients is still being studied. It is thought that the mRNA vaccines in particular are unlikely to trigger rejection episodes (CST, 2020).

If the transplant recipient has any acute illness, or receiving active treatment for acute graft rejection, vaccination should be delayed.

Summary of Evidence

In a recent cohort study comparing the outcome of COVID-19 in solid organ transplant recipients versus non transplant population, it showed that transplant recipients with COVID-19 had a 30% increased risk of death or mechanical ventilation compared with matched controls (OR = 1.63, 95% CI 1.04–2.56; p = .03) (Nair, et al., 2020). Hence, transplant recipients can be categorized under "population with significantly elevated risk of severe disease or death due to underlying medical condition" and may be designated as priority group for earlier vaccination (WHO, 2020).

Currently, there are no published studies focusing on the efficacy of COVID-19 vaccine among transplant recipients. Further studies are needed since transplant recipients have an altered immune system compared with non-transplant patients because they may have lower antibody responses and their antibody titers may wane as documented with other vaccines (AST, 2021).

Based on expert opinion, the potential benefits of vaccination outweigh potential risks among transplant patients, hence they recommend vaccinating transplant recipients with COVID-19 vaccine (AST, 2021; CST, 2020). Though safety of COVID-19 vaccine among these patients is still being studied, it is thought that the mRNA vaccines in particular are unlikely to trigger rejection episodes (CST, 2020).

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Can patients on chronic systemic steroids receive COVID19 vaccine?

Yes, patients on chronic systemic steroids may receive COVID19 vaccine, except the live virus type, as long as they do not have contraindications to the vaccine.

They should be counseled that their response to the vaccine may be variable and must adhere to minimum public health protocols.

Summary of Evidence

Systemic corticosteroids are generally used as an immunosuppressant, with degree of immunosuppression dependent on the dose and duration of intake. The Centers for Disease Control and Prevention (CDC) has identified steroid treatment of either ≥2 mg/kg of body weight or ≥20 mg/day of prednisone or equivalent for persons who weigh >10 kg

administered for ≥14 consecutive days, termed "high dose steroid", to produce immunosuppression that would make it unsafe to be vaccinated with live virus vaccine. (Ezeanolue, et al 2020).

At present, published SARS-CoV-2 vaccine trials excluded individuals receiving systemic corticosteroids for more than 14 days. However, patients who took steroids via inhalation/nebulization, intra-articular, intra-bursal or topical routes received the COVID19 vaccines and were considered in the reported efficacy.

Indirect evidence from existing vaccine technology among patients on chronic steroids were examined. Chronic steroid use even on low dose showed immunosuppressive effects on the humoral immunity with noted variability on the response of an individual to different vaccines. (Fedor & Rubinstein, 2006). Patients given sub-unit pneumococcal vaccine showed acceptable humoral and functional response, but those given subunit vaccine hepatitis B vaccine showed low probability of response with antibody titers decreasing over time (6 months and beyond). (Winthrop, et al., 2018; Chaparro, et al. 2020). Inactivated influenza vaccine showed significant seroconversion as compared to placebo. In a post-hoc sub-analysis, there were significantly lower seroconversion rates among those who received high dose systemic corticosteroids as compared to no vaccine. (Hanania, Sockrider, Castro, Holbrook, Tonascia, Wise, et al., & American Lung Association Asthma Clinical Research Centers, 2004). Patients 60 years old and above and on chronic/maintenance steroids (daily dose of 5-20 mg of prednisone or equivalent) given live attenuated zoster-varicella vaccine showed higher antibody titers with no significant adverse events. (Russell, et al., 2015).

CDC recommended that mRNA COVID-19 vaccines may be given to immunocompromised individuals as long as they do not have any contraindications to vaccination. (CDC, 2021) The Infectious Disease Society of America has stated that immunocompromised individuals be studied in post-authorization observational studies. (IDSA, N.d.)

There is no current evidence to support efficacy and safety of COVID19 vaccine among patients on chronic systemic steroids, and response of this subgroup of population to any type of vaccines is variable.

Until more data becomes available, inactivated and fractionated vaccines may be recommended to patients who receive systemic corticosteroids. Issues such as poor immunologic response should be discussed with patient. Live attenuated vaccines, meanwhile, are contraindicated in patients receiving high dose corticosteroids.

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Can individuals with cancer OR those undergoing chemotherapy receive COVID 19 vaccines?

Yes, patients who are diagnosed with cancer and who are, or will be, undergoing active chemotherapy may be vaccinated with COVID-19 vaccine at any time before and/or during chemotherapy sessions, if they have no contraindications to the vaccine.

Although there is limited safety and efficacy data in these patients, as an at-risk population, there is a clear need for vaccinating these patients to avoid excess morbidity and mortality

during the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) pandemic (NCCN, 2021).

Vaccinated patients and close contacts should continue to wear masks, maintain physical distancing guidelines, and follow other recommendations for COVID-19 prevention (NCCN, 2021), and wear face shield (DOH, N.d.).

Summary of Evidence

The characterization of COVID-19 in patients with cancer remains limited in published studies and nationwide surveillance analyses. In the state of New York in the US, patients with cancer comprised 8.4% of deceased individuals (New York State Department of Health, 2020). Population based studies from China and Italy suggested a higher COVID-19 death rate in patients with cancer (WHO, 2020; Onder, Rezza, & Brusaferro, 2020). In the study conducted by Robilotti, et al. (2020) from March 10 to April 7, 2020, there were 423 cases of symptomatic COVID-19 illness diagnosed in Memorial Sloan Kettering Cancer Center (from a total of 2,035 cancer patients tested). Of these, 40% were hospitalized for COVID-19 illness, Twenty percent developed severe respiratory illness, (including 9% who required mechanical ventilation, 11% requiring high-flow oxygen), and 12% died within 30 days. Age >65 years and treatment with immune checkpoint inhibitors (ICI) were predictors of hospitalization and severe disease, while receipt of chemotherapy and major surgery were not. In the multivariate analysis (Robilotti, et al., 2020), the following risk factors were independently associated with hospitalization: non-white race, hematologic malignancy, a composite measure of chronic lymphopenia and/or corticosteroid use, and treatment with ICI therapy. Age >65 years, former or current smoker, hypertension and/or chronic kidney disease, and history of cardiac disorder were significant predictors in univariate analysis (Robiliotti, et al., 2020). Other large cohort studies have demonstrated that cancer patients are high risk for COVID-19 associated complications.

As an at-risk population, there is a clear need for vaccinating these patients to avoid excess morbidity and mortality during the severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) pandemic. Individuals with active cancer or with active, recent (less than 6 months), or planned cancer treatment should be considered highest priority to receive the currently available vaccine approved by the Food and Drug Administration (FDA) for emergency use authorization (EUA) [NCCN, 2021).

The National Comprehensive Cancer Network (NCCN) COVID-19 Vaccination Advisory Committee feels strongly that COVID-19 vaccines should be given to all cancer patients, as well as household contacts and caregivers (NCCN, 2021). Recognizing the limited clinical data available in cancer patients, individuals should be vaccinated with the highest priority group for which they qualify. Finally, data from vaccine trials have demonstrated that vaccines decrease the incidence of COVID-19 disease and complications, but it is unclear if these vaccines prevent infection and subsequent transmission. Therefore, even if vaccinated, patients and close contacts should continue to wear masks, maintain social distancing guidelines, and follow other recommendations for COVID-19 prevention (NCCN, 2021).

Due to limitations in prospective data relating to vaccination use in patients with active malignancy, recommendations are based on expert opinion of the committee (NCCN, 2021):

- Patients with cancer should be prioritized for vaccination and should be immunized when vaccination is available to them.
- Immunization is recommended for all patients receiving active therapy, with the understanding that there are limited safety and efficacy data in these patients.
- Reasons for delay of vaccines are like those for the general population and cancer-specific factors. Vaccination should be delayed for at least 3 months following hematologic cell transplantation (HCT) or engineered cellular therapy (e.g. CAR-T cells) to maximize vaccine efficacy.
- Caregivers and household/close contacts should be immunized when possible.

A. Hematopoietic Cell Transplantation (HCT)/Cellular Therapy

Patients who underwent allogeneic transplantation, autologous transplantation and cellular therapy (e.g., CAR-T cell) may receive the vaccine at least 3 months post HCT/cellular therapy (NCCN, 2021).

Summary of evidence

Immune responses to vaccination are expected to be blunted in graft vs host disease (GvHD) and immunosuppressive regimens to treat GvHD (e.g., systemic corticosteroids and targeted agents). In addition, patients who are on maintenance therapies (e.g., rituximab, Bruton tyrosine kinase inhibitors, janus kinase inhibitors), may also have attenuated response to vaccination. A delay in vaccination can be considered until immunosuppressive therapy is reduced (NCCN, 2021).

B. Hematologic malignancies

Patients who are receiving intensive cytotoxic chemotherapy (e.g., cytarabine/anthracycline-based induction regimens for AML) may delay vaccination until recovery of absolute neutrophil count (ANC) (NCCN, 2021).

Patients who have bone marrow failure from disease and/or therapy, who are expected to have limited or no recovery and patients who are on long-term maintenance therapy (e.g., targeted agents for chronic lymphocytic leukemia or myeloproliferative neoplasms) may be vaccinated as soon as the vaccine is available to them (NCCN, 2021).

Summary of evidence

Immunologic response to vaccination is not affected by low WBC levels. However, it can be used as a surrogate marker for recovery of adequate immunocompetence to respond to vaccines and sufficient platelet recovery to avoid bleeding complications from intramuscular administration in the setting of profound immunosuppression for patients with hematologic malignancies (NCCN, 2021).

C. Solid tumor malignancies

Patients who are receiving cytotoxic chemotherapy, targeted therapies, checkpoint inhibitors or other kinds of immunotherapy and radiation may be vaccinated as soon as the vaccine is available to them (NCCN, 2021).

For patients who will undergo major surgery, it is recommended to complete the vaccination series for at least a few days before surgery (NCCN, 2021).

Summary of Evidence

Solid tumor malignancies induce short periods of neutropenia; hence they can receive the vaccine once it is available to them. The optimal timing of vaccination in relation to cycles of chemotherapy for solid tumor malignancies is unknown because of the variability of specific regimens and intervals between cycles. Therefore, it is difficult to determine whether immunization will be effective if administered before, during or in between cycles of chemotherapy when the WBC might be at its nadir. Due to the absence of data, it is recommended that these patients receive the vaccine as soon as it is available to them (NCCN, 2021).

There is no data on the timing of vaccine administration in patients who are receiving immune checkpoint inhibitors, therefore vaccination may be considered on the same day as immunotherapy for convenience and to reduce clinic visits. However, one must keep in mind that there is a theoretical risk of exacerbated immune related adverse events in these patients (NCCN, 2021).

The vaccination series must be completed in patients with solid tumor malignancies before undergoing surgery in order to avoid confusion if symptoms (e.g., fever) are related to vaccine vs surgery. For more complex surgeries (e.g., splenectomy or which may lead to an immunosuppressive state), it is recommended that vaccines be administered +/- 2 weeks from surgery (NCCN, 2021).

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