COVID-19 VACCINATION FOR PATIENTS WITH HAEMATOLOGICAL DISORDERS

CONSENSUS STATEMENT

Malaysian Society of Haematology

March 2021

Background

This consensus statement is based on reviews of international guidelines on COVID-19 vaccination. This document does not cover paediatric patients as currently available COVID-19 vaccines are approved for people above 16 - 18 years old. None of the authorized COVID-19 vaccines are live virus vaccines, hence they are considered safe for patients with underlying haematological cancers or those on immunosuppressive drugs. Of note, immunocompromised patients may have a reduced response to the vaccine. However, the vaccine will still offer these patients some protection. Caregivers including healthcare workers, household members and / or close contacts of these patients (adults regardless of age) should be vaccinated as early as possible based on the local guidelines for public vaccinations. It is crucial that people who have received the vaccine should continue to practise the recommended preventive measures even after vaccination.

Disclaimer

This statement is current as of 31st March 2021, and recommendations may change as more data become available. The society and authors do not accept any legal responsibility. Please consult the primary haematologist before vaccination. For further updates and information, please refer to the Ministry of Health guidelines at covid-19.moh.gov.my.

PATIENTS WITH HAEMATOLOGICAL CANCERS

1. Patients who are undergoing active therapy such as chemotherapy are advised to discuss the risks and benefits of the vaccines prior to considering vaccination.

2. Patients who are on long term or maintenance therapy (other than B-cell depleting agents) or have completed treatment can have their COVID-19 vaccination. These include patients with chronic myeloid leukemia, multiple myeloma, lymphomas, chronic lymphocytic leukemia, myelodysplastic syndrome and myeloproliferative neoplasms.

3. In patients who are receiving B-cell depleting agents such as anti-CD20 monoclonal antibodies e.g. Rituximab, the vaccine should be administered preferably 6 months after the last dose; if this is not possible, we recommend completing the full course of vaccination at least 4 weeks prior to the next dose of Rituximab.

4. Patients who are currently receiving other types of cancer treatment are advised to wait for normalization of blood counts before vaccination.

PATIENTS WHO HAVE RECEIVED HAEMATOPOEITIC STEM CELL TRANSPLANTATION (HSCT) AND/ OR CELLULAR THERAPIES

1. Patients can have their vaccination as early as 3 months after autologous HSCT.

2. Patients can have their vaccination starting from 3 - 6 months after allogeneic HSCT if the risk of community transmission is high. Otherwise, we would recommend deferral beyond 6 months after HSCT.

3. Patients who have severe, uncontrolled grades III - IV acute graft versus host disease are recommended to defer vaccination until it is controlled.

4. Consider vaccination in patients with mild chronic graft versus host disease and receiving ≤ 0.5 mg/kg prednisolone (or equivalent).

5. Consider vaccination in patients who have received Chimeric Antigen Receptor - T cells (CAR-T) 3 - 6 months after completion of treatment.

PATIENTS WITH BLEEDING DISORDERS

1. People with bleeding disorders are not at greater risk of contracting COVID-19 or developing a severe form of the disease.

2. The vaccine itself does not present any additional safety concerns for these patients but the intramuscular route of administration may increase the risk of bleeding at the injection site.

3. Patients with a history of allergic reactions to extended half-life clotting factor concentrates containing polyethylene glycol (PEG) should discuss vaccine choice with their physician because some COVID-19 vaccines (e.g. Pfizer-BioNTech vaccine) contain PEG as an excipient.

4. For patients with severe or moderate haemophilia A or B, the vaccine injection should be given after a prophylactic dose of Factor VIII (FVIII) or Factor IX (FIX). For patients with a basal FVIII or FIX level above 10%, no haemostatic therapies are required.

5. For patients with inhibitors, the vaccine injection should be given after a prophylactic dose of bypassing agent.

6. Patients on Emicizumab (with or without an inhibitor) can be vaccinated by intramuscular injection at any time without haemostatic precautions and without receiving a dose of FVIII or bypassing agent.

7. Patients with Type 1 or 2 Willebrand disease (VWD), depending on their baseline von Willebrand factor (VWF) activity levels, should use haemostatic therapies [i.e. tranexamic acid, desmopressin (DDAVP) or VWF concentrate] in consultation with their haematologists. Patients with Type 3 VWD should be given a prophylactic dose of VWF concentrate prior to the intramuscular COVID-19 vaccination.

8. Patients with platelet counts of 50 x 10^9/L and above can proceed with vaccination without additional haemostatic support. Patients with platelet counts below 50 x 10^9/L should defer the vaccination till their platelet counts recover, if possible. For those patients with chronically low platelet counts, vaccination should be performed in consultation with their primary haematologist.

9. Patients with other rare bleeding disorders including platelet function disorders should be vaccinated in consultation with their primary haematologists.

10. The currently available COVID-19 vaccines should be administered intramuscularly. There are no data for the subcutaneous route and this should not be done. The smallest gauge needle available (25 to 27 gauge) should be used. Pressure should be applied to

the site for 5 to 10 minutes post-injection to reduce bleeding and swelling. Additionally, self-inspection and palpation of the injection area several minutes and 4 to 6 hours later is recommended to ensure that there is no delayed haematoma. Discomfort in the arm felt for 1 to 2 days after injection should not be alarming unless it progressively worsens and is accompanied by swelling. Any adverse events (e.g. haematoma, allergic reaction) should be reported to the haematology clinic or emergency department.

PATIENTS ON ANTI-COAGULATION AND ANTI-PLATELET AGENTS

Warfarin

1. Patients on warfarin can receive intramuscular vaccination if their most recent international normalized ratio (INR) is below 4, without stopping the drug.

2. On the day of vaccination, warfarin should be taken after the vaccine injection. The risk of haematoma formation is reduced by applying firm pressure at the injection site for at least 5 minutes.

3. Patients on concomitant warfarin and anti-platelet therapy should be managed on an individual basis in consultation with their primary physician.

Direct Oral Anticoagulants (DOAC) and Low Molecular Weight Heparins (LMWH)

1. Patients on maintenance therapy with DOAC, LMWH or fondaparinux can delay the dose on the day of vaccination until after the intramuscular injection but do not need to miss any doses.

Anti-platelet agents

1. Patients on single agent anti-platelet therapy (e.g. aspirin or clopidogrel) can continue on these medications without any adjustment.

2. Patients on dual antiplatelet agents should be managed on an individual basis and in consultation with their primary physician.

PATIENTS WITH HAEMOGLOBINOPATHIES, ENZYMOPATHIES AND RARE INHERITED ANAEMIAS

1. This includes all adults with transfusion-dependent thalassaemia, G6PD (Glucose-6-phosphate dehydrogenase) deficiency and rare inherited anaemias. These patients can receive COVID-19 vaccination.

2. In patients with splenectomy or functional asplenia, all routine vaccines are likely to be effective and therefore these patients should receive COVID-19 vaccination.

PATIENTS WITH AUTOIMMUNE HAEMATOLOGICAL CONDITIONS ON IMMUNOSUPPRESSION

1. There are no clinical trials of COVID-19 vaccine which enrolled immunocompromised patients. Thus, the efficacy and safety of a COVID-19 vaccine have not been established in the different categories of immunocompromised patients.

2. The following categories of immunocompromised patients may have attenuated or absent responses to COVID-19 vaccines:
    a. Primary and secondary immunodeficiencies involving adaptive immunity
    b. B-cell depleting agents [e.g. anti-CD20 monoclonal antibody like Rituximab]
    c. T-cell depleting agents [e.g. calcineurin inhibitors, anti-thymocyte globulin]
    d. Daily corticosteroid therapy with a dose ≥20 mg (or >2 mg/kg/day for patients who weigh <10 kg) of prednisone or equivalent for ≥14 days

3. The risks and benefits of immunocompromised patients receiving the vaccine should be weighed on a case-by-case basis. If plans to proceed with the vaccination are made, we recommend completing the full course of vaccination at least 2 weeks before the initiation of the planned immunosuppressive therapy or splenectomy. If the patient is receiving or has received immunosuppressive therapy, consider vaccination 6 months after the patient has been taken off immunosuppressive therapy to increase the likelihood of mounting an effective immune response.

IF YOU HAVE ANY QUESTIONS OR QUERIES, PLEASE CONTACT YOUR HAEMATOLOGIST

Resources

1. https://b-s-h.org.uk/media/19195/haematology-covid-19-v10-vaccination-statement-231220.pdf
2. https://www.ebmt.org/covid-19-and-bmt. EBMT COVID-19 recommendations update; February 17, 2021
3. https://ehaweb.org/covid-19/eha-statement-on-covid-19-vaccines/recommendations-for-covid-19-vaccination-in-patients-with-hematologic-cancer/
4. https://www.hematology.org/covid-19/ash-astct-covid-19-and-vaccines
5. https://www.mskcc.org/coronavirus/covid-19-vaccine
6. http://www.stjames.ie/services/hope/nationalcoagulationcentre
7. https://www.wfh.org/en/covid-19-communications. COVID-19 World Federation of Hemophilia (WFH) Announcements and Statements 2021
8. Consensus statement by Singapore Society of Haematology 2021

Acknowledgement

Co-authors

Gan Gin Gin
Professor in Internal Medicine and Clinical Haematology
Department of Medicine
University Malaya Medical Centre

Jameela Sathar
Consultant Haematologist
President of Malaysian Society of Haematology

S Fadilah Abdul Wahid
Professor of Clinical Haematology and Transplant Physician
Head of Pusat Terapi Sel
UKM Medical Centre

Reviewers

Goh Ai Sim
Consultant Haematologist and National Head of Haematology Service
Hospital Pulau Pinang

Ng Soo Chin
Consultant Haematologist
Subang Jaya Medical Centre

Vijaya Sangkar Jaganathan
Consultant Haematologist
Pantai Hospital Kuala Lumpur