COVID-19 vaccination in patients with cancer: Position paper from the Indonesian Society of Hematology and Medical Oncology (ISHMO) of Semarang

Eko Adhi Pangarsa1*, Budi Setiawan1*, Santosa1, Ridho Monotoc Naibaho1, Daniel Rizky1, Suyono1, Mika Lumban Tobing1, Muchlis Achsan Udji Sofro2, Catharina Suharti1

ABSTRACT

Patients with active cancer (cancer on treatment, those planning to start treatment, and those immediately post-treatment) should be vaccinated as early as possible. There are various other risk factors for cancer patients which must be considered related to complications of COVID-19, such as age, other comorbid diseases, demographic and social factors. All of these factors should be judged as a comprehensive evaluation of an individual patient. The use of masks, physical distancing, hygienic activities such as washing hands with soap and hand sanitizers are still needed during this pandemic. Caregivers and households should certainly be included in the vaccination strategies.

Keywords: COVID-19, vaccine, cancer, recommendation.

INTRODUCTION

The world is currently impacted by the coronavirus disease 2019 (COVID-19) pandemic. It started in Wuhan, Hubei Province, China, and has brought many challenges to public health in various countries, including Indonesia. The disease is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a highly contagious virus associated with a considerable mortality rate. Indonesia has now reached over a million COVID-19 cases, with daily incidence hitting records from week to week in January 2021. As we all know, the COVID-19 pandemic has major catastrophic consequences on all aspects of life worldwide on the health and wellbeing. There are three ways out the pandemic 1) to continue stringent precautions forever, but people will get eventually infected, and it will spread for a long period with economic, psychological, political impacts that will be long lasting, 2) to obtain herd immunity, basically let the masses get infected but cost high toll of human lives or 3) to get enough people vaccinated to break this vicious cycle of infection and control the pandemic. Currently, we already have the SARS-CoV-2 vaccine that is used for the community. However, especially for cancer patients, there is still a lack of data on efficacy, safety, and immunogenicity.

The Indonesian Food and Drug Advisory Agency (Badan Pengawas Obat dan Makanan: BPOM) has granted the use of vaccine in Indonesia as an Emergency Use Authorization (EUA) to prevent COVID-19 disease supported by scientific studies. This position paper was formed to make practical considerations according to the latest information that may continue to evolve based on the latest
studies. Clinicians could use this position paper to consider COVID-19 vaccination for the cancer population under EUA until specific data are available.

**SCOPE OF THE PROBLEM**

We know from other countries that patients with cancer may have more severe COVID-19 infection than those without cancer;15,16 we are not particularly sure if they are at higher risk of getting it. It truly depends on what environment that they are living in. However, it is very important to think about cancer patients regarding any immunocompromised and defects in their immune system.

Cancer patients infected with COVID-19 had a significant risk of admission to ICU (OR 2.84; 95% CI 1.59-5.08, p <0.01) and death (OR 2.34; 95% CI 1, 15-4.77, p = 0.03). The Case Fatality Rate (CFR) for hematologic cancer and lung cancer was found to have high percentages, namely 33.3% and 18.8%, respectively.5,6 So, the population of cancer patients must be a priority for receiving the COVID-19 vaccine. A recent publication by Desai et al. of more than 5300 papers reports the outcome of this combination altogether: cancer and COVID-19. If we go through, from a meta-analysis, there is a very high risk of mortality ranging from 15 to 30% in hospitalized patients.7 If we compared to the number in normal population only 2-3%, we can understand how much is the problem for this group of patients.1,2,8

The other important information is derived from the UKCC project, where the author reported all the comorbidities. For cancer, there is a higher risk of mortality. The highest risk is for cancer patients before five years of diagnosis, particularly in less than one year, mainly patients in active treatment.9 A single hospital case series from New York, USA,6,10 showed CFR in hematologic malignancies and solid cancer were 37% and 25%, respectively. COVID-19 outcomes in cancer patients are influenced by various factors such as old age, comorbid diseases, advanced disease, and quality of care.11

**IMMUNIZATION IN CANCER PATIENTS AT A GLIMPSE**

Various studies with vaccines such as influenza, pneumococcus, and herpes zoster suggest vaccines’ protective effect in cancer patients.12 The influenza vaccination protected chemotherapy cycle disruption and the risk of death. However, cancer patients tend to have a poor antibody response compared to immunocompetent people13,14, but cancer patients’ morbidity and mortality can be reduced with the vaccine administration.15

We are aware that there is insufficient data; patients with cancer requiring therapy and immunocompromised were usually excluded from pivotal trials.12,16 For those on active treatment, immunosuppressive therapy, chemotherapy, or those with immunotherapy, we do not have a specific study about the response in the SARS-CoV-2 vaccine. However, we can extrapolate data from other vaccine studies especially inactivated vaccines. From that data, cancer survivors, patients with stable disease, cure, or incomplete remission could mount an adequate immune response.31 In general, vaccination in active cancer patients is not contraindicated.17–19 However, specific requirements in terms of disease state, type of vaccine can be given safely according to immunity status, and the most important, vaccination timing.

Although specific data for SARS-CoV-2 vaccination in the cancer population is lacking, around 4% of patients included in the BNT162b2 mRNA vaccine trial had a prior history of malignancy (733 any malignancy, 22 lymphoma, 12 leukemia, and 4 solid metastatic tumors).20 Although these peoples may not respond well to the vaccine, no particular safety concerns are anticipated. The benefit-to-risk ratio for patients with cancer is considered more beneficial than the possible risk for getting vaccinated because they may be at higher risk from COVID-19.20

A total of 56 vaccines for SARS-CoV-2 are in clinical development, of which 11 are in phase 3 trials and another 166 in preclinical development (information

Table 1. Dose and type administration from available various SARS-CoV-2 vaccine in Indonesia

<table>
<thead>
<tr>
<th>Platform</th>
<th>Developer</th>
<th>Total dose</th>
<th>Schedule</th>
<th>Phase 1 / 2 trials</th>
<th>Phase 3 trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated virus</td>
<td>Sinovac21 Research and Development Co., Ltd.</td>
<td>2 (0.5 mL per dose)</td>
<td>Day 0, 14</td>
<td>NCT04551547</td>
<td>NCT04617483</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NCT04383574</td>
<td>NCT04582344</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NCT04532608</td>
<td>NCT04050875</td>
</tr>
<tr>
<td>Inactivated virus</td>
<td>Sinopharm24 + Beijing Institute of Biological Products</td>
<td>2 (0.5 mL per dose)</td>
<td>Day 0, 21</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ChiCTR2000031809</td>
<td>N/A</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>ChiCTR2000032459</td>
<td>N/A</td>
</tr>
<tr>
<td>Inactivated virus</td>
<td>PT Bio Farma</td>
<td>2 (0.5 mL per dose)</td>
<td>Day 0, 14</td>
<td>N/A</td>
<td>NCT04050875</td>
</tr>
<tr>
<td>Viral vector (non-</td>
<td>AstraZeneca25–27 + University of Oxford</td>
<td>1 – 2 (0.5 mL per dose)</td>
<td>If 2 doses,</td>
<td>NCT04324606</td>
<td>NCT04400838</td>
</tr>
<tr>
<td>replicating)</td>
<td>Novavax28</td>
<td>2 (0.5 mL per dose)</td>
<td>Day 0, 28</td>
<td>NCT04400838</td>
<td>NCT044611802</td>
</tr>
<tr>
<td>Protein subunit</td>
<td></td>
<td></td>
<td></td>
<td>NCT04368988</td>
<td>NCT04583995</td>
</tr>
<tr>
<td>RNA-based vaccine</td>
<td>Moderna29–31 + National Institute of Allergy</td>
<td>2 (0.5 mL per dose)</td>
<td>Day 0, 28</td>
<td>NCT04283461</td>
<td>NCT04470427</td>
</tr>
<tr>
<td></td>
<td>and Infectious Disease (NIAID)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RNA-based vaccine</td>
<td>Pfizer Inc.32 + BioNTech</td>
<td>2 (0.3 mL per dose)</td>
<td>Day 0, 28</td>
<td>NCT04380701</td>
<td>NCT04368728</td>
</tr>
</tbody>
</table>

as per January 26, 2021). Indonesian Ministry of Health in the Decree of the Minister of Health document number HK.01.07/Menkes/12758/2020 has determined the SARS-CoV-2 vaccine available in Indonesia. The lists are PT. Bio Farma, Oxford-AstraZeneca, Sinopharm, Moderna, Novavax, Pfizer-BioNTech, and Sinovac (Table 1). There is no basis for the preferential recommendation for one that could be better than the other vaccine under any circumstances. The choice is based on vaccine availability at one moment. Sinovac vaccines have been used since Wednesday, January 13, 2021. Little is known, and much is unknown about the COVID-19 vaccine; thus, until more information, it is wise to receive one type and not a different SARS-CoV-2 vaccine to be given to the same patient.

Most COVID-19 vaccine currently under development does not employ a live virus. Exceptions are only made for non-replicating and replicating viral vector-based vaccines. Other vaccines (inactivated, nucleic acid, protein subunit, virus-like protein) are relatively safe for the immunosuppressed, hence, cancer patients. These vaccines generally exert reduced protection. It is suggested that it be beneficial to administer a second vaccine dose or prime booster to increase the seroconversion rate.

**LEGALITY ASPECTS OF SARS-CoV-2 VACCINE IN INDONESIA**

Recommendations for EUA use of COVID-19 vaccine for cancer patients in Indonesia are issued by the Indonesian Ministry of Health and the Indonesian Society of Internal Medicine (PAPDI). This recommendation is prepared based on phase 1/2 publication data on the Sinovac vaccine and the results from phase 3 preliminary data from our population in Bandung (organized by Universitas Padjajaran and PT Bio Farma). The Indonesian Ministry of Health’s main message that a recommendation for the COVID-19 vaccine is made for cancer survivors. However, PAPDI adds an important statement concerning both hematologic malignancies and solid cancer should also get vaccinated. Accordingly, patients with cancer should have a consultation with their physicians before receiving the SARS-CoV-2 vaccine. They should be advised to avail themselves of the SARS-CoV-2 vaccine as soon as it is offered to them.

In the case of limited vaccine supply and high transmission rate of COVID-19 as today, the following criteria can be a priority consideration:

- Patients with active cancer (e.g., cancer on treatment or newly start treatment) and who have just completed treatment (<6 months) consider for vaccination. Those who receive hormonal therapy can be managed as per a healthy population.
- Other risk factors such as old age, comorbid diseases, metastases, hematology, and lung-related cancers, as well as social and demographic factors, need to be considered because they are associated with complications of COVID-19.

**INTERACTIONS BETWEEN VACCINES AND IMMUNE SYSTEM IN CANCER**

This section described several important related considerations of vaccination for adult cancer patients. At least eight types of vaccines have been developed against the coronavirus: inactivated, live-attenuated, replicating vector, non-replicating vector, DNA, RNA, protein subunit, and virus-like particles. Parts or all protein-based or polysaccharide-based viral components products are the main components of inactivated vaccines. Conjugation with protein is added to the polysaccharide vaccine to increase the immune response due to the low immunogenicity. Meanwhile, the induction of the immune response in active vaccines is carried out directly using attenuated pathogens. The recombinant vaccines containing inactive components of antigen with genetic engineering sometimes need to be weakened. Adjuvants can be found in both inactive and recombinant vaccines, aiming to increase the immune response and generate antibody production for specific diseases. All live-attenuated, including replication-competent vector vaccines, are considered contraindicated for patients with active cancer. Fortunately, there is no live vaccine underdeveloped for SARS-CoV-2.

There are some patients with hematological malignancies have a higher risk of severe COVID-19 because their immune system has been weakened, patients who have been through hematopoietic stem cell transplant (HSCT), CAR-T therapy, or other treatments that are designed to knock down the immune systems do have an increased risk of complications related to the disease. As we learn from vaccination recommendations in cancer patients, the non-live vaccines are not contraindicated during chemotherapy. Studies have shown that inactivated vaccines are safe for cancer patients where they reduce the disease-related incidence, although they have limited effectiveness. However, it is not advisable to receive replicative competent vector vaccines or directly attenuated vaccines in patients undergoing aggressive chemotherapy or immunosuppressive agents.

Below are considered an immunodeficiency state and immunocompromised conditions associated with an attenuated or blunted immune response to SARS-CoV-2 vaccine:

a. Primary and secondary immunodeficiencies involving adaptive immunity
b. Post-splenectomy or functional asplenia
c. The use of B lymphocyte-directed therapies (e.g., monoclonal antibodies against CD20 or CD22, bispecific agents like blinatumomab, CD19- or CD22-directed CAT-T cell therapies, BTK inhibitors)
d. The use of T lymphocyte-directed therapies (e.g., calcineurin inhibitors, anti-thymocyte globulin (ATG), alemtuzumab)
e. Cytotoxic chemotherapy, especially those receiving intensive regimen as in acute leukemia
f. High-dose corticosteroids (>2 mg/kg daily of prednisone or equivalent)
g. Hematopoietic stem cell transplantation (HSCT), especially within the first 3-6 months after autologous HSCT and longer after allogeneic HSCT.
h. Graft versus host disease (GvHD)
Table 2.  Suggested timing for COVID-19 vaccination for patients in systemic cancer therapy

<table>
<thead>
<tr>
<th>Systemic anticancer therapy</th>
<th>Suggested timing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytotoxic chemotherapy</td>
<td>When blood counts have maximally recovered (towards the end of a cycle) – avoid on the same day of chemotherapy</td>
</tr>
<tr>
<td>Monoclonal antibodies (single agents) should not be a contraindication</td>
<td>No specific timing issues (providing that complete blood count is normal or within an acceptable range)</td>
</tr>
<tr>
<td>Monoclonal antibodies (with cytotoxic chemotherapy)</td>
<td>When blood counts have maximally recovered (towards the end of a cycle) – avoid on the same day of chemotherapy</td>
</tr>
<tr>
<td>CD20 – monoclonal antibodies, e.g., Rituximab</td>
<td>No specific timing issues – when blood counts are optimal. Where clinically possible vaccine should be given 4 weeks or more before rituximab. There may be suboptimal responses to the vaccine especially in patients within 6 months of their last dose or those on maintenance treatment.</td>
</tr>
<tr>
<td>Immunotherapy single agent</td>
<td>No specific timing issues (providing that complete blood count in normal or within an acceptable range)</td>
</tr>
<tr>
<td>Immunotherapy (with cytotoxic chemotherapy)</td>
<td>When blood counts have maximally recovered (towards the end of a cycle) – avoid on the same day of chemotherapy</td>
</tr>
<tr>
<td>Small molecule TKI</td>
<td>No specific timing issues (providing that complete blood count in normal or within an acceptable range)</td>
</tr>
<tr>
<td>Immunomodulator drugs (IMIDs)</td>
<td>When blood counts have maximally recovered (towards the end of a cycle) – avoid on the same day of chemotherapy</td>
</tr>
<tr>
<td>Protein kinase inhibitors e.g., Bortezomib, Ixazomib</td>
<td>When blood counts have maximally recovered (towards the end of a cycle) – avoid on the same day of chemotherapy</td>
</tr>
<tr>
<td>PARP inhibitors e.g. Olaparib</td>
<td>No specific timing issues (providing that complete blood count in normal or within an acceptable range)</td>
</tr>
<tr>
<td>CDK 4/6 inhibitors e.g. Abemaciclib, Ribociclib, Palbociclib</td>
<td>When blood counts have maximally recovered (towards the end of a cycle) – avoid on the same day of chemotherapy</td>
</tr>
<tr>
<td>Hormone treatments and other supportive treatments</td>
<td>No specific timing issues, vaccination at any time when available</td>
</tr>
<tr>
<td>High dose steroids (Prednisone or Prednisolone ≥ 2 mg/kg/day or equivalent)</td>
<td>No specific timing issues</td>
</tr>
<tr>
<td></td>
<td>If feasible, patients treated with steroids are vaccinated prior to therapy</td>
</tr>
</tbody>
</table>


Table 3.  COVID-19 vaccination suggestion for hematological malignancies patients

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Vaccine Timing</th>
<th>Type of vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receiving induction chemotherapy (e.g., Cytarabine / Anthracycline-based therapy for acute myeloid leukemia or multiagent chemotherapy in acute lymphoblastic leukemia) Marrow failure from disease and/or therapy expected to have limited or lack of predicted recovery Long-term maintenance therapy (e.g., targeted agents for chronic lymphocytic leukemia or myeloproliferative neoplasm)</td>
<td>Delay until absolute neutrophil count recovery</td>
<td>Non-lived vaccine: [RNA-based*, inactivated**, protein subunit**, and viral vector (non-replicating) vaccines**]</td>
</tr>
<tr>
<td>Marrow failure from disease and/or therapy expected to have limited or lack of predicted recovery</td>
<td>Vaccinated at any time</td>
<td></td>
</tr>
</tbody>
</table>

*Based on a specific recommendation for SARS-CoV-2 vaccination

**Based on previous vaccination of other diseases in cancer patients

i. Low white blood cell count (absolute neutrophil count <500/uL and/or absolute lymphocyte count <200/uL)

Healthy subjects and cancer patients showed similar antibody responses to SARS-CoV-2. Although previous reports stated that the induction of antibody production was insufficient with the administration of inactivated and unconjugated vaccines, it is still a matter of debate whether vaccine effectiveness can be achieved in this subset of the population. At present, there is still little data on cancer patients who have been involved in the phase 2/3 vaccine trial. Cancer patients may be included in the trial based on inclusion criteria and exclusion criteria which are summarized in three categories: 1) previous cancer history; 2) current immunosuppressive therapy (chemotherapy, radiotherapy,
immunomodulating agents, systemic immunosuppressants); 3) immune deficiency and instability at the discretion of the investigators.11,16

WHEN SHOULD CANCER PATIENTS RECEIVE THE COVID-19 VACCINE?

In essence, cancer patients are the priority for receiving the vaccine right after the healthcare workers.2,11,17 They should be advised to avail of the SARS-CoV-2 vaccine as soon as it is offered to them. Vaccination timing for cancer and immunosuppressed patients must be adjusted as described below.

Patients receiving cancer therapy (on treatment)
The concern about giving the vaccine to cancer patients is not a safety issue. We do not believe that cancer patients are at higher complication risk when getting vaccinated than the risk of severe and death due to COVID-19. The main issue is whether they will have enough immune response to the vaccine to protect them from the virus in the future because they may have immunosuppressed status because of cancer itself or associated with the treatment. Thus, receiving a COVID-19 vaccine before treatment starts may improve its effectiveness. Nevertheless, on several occasions, patients may need to start treatment before having the vaccine.10 Below are several different scenarios that may encounter concerning cancer patients (Table 2).

Individuals with cancer who should recommend avoiding vaccination would be very limited. Those who have had a severe allergic reaction to the first vaccination or individuals who had a recent stem cell transplantation would be individuals who have had a severe allergic reaction. Individuals with a recent stem cell transplantation may still be immunosuppressant medication, compromising their immune system and ability to tolerate the vaccination. It seems to be significantly better to give vaccine shots between cycles than at the same time as the cytotoxic chemotherapy using the influenza vaccine as a prototype.18 The timing of vaccination is ideal before they start systemic therapy. However, it is still reasonable to vaccinate cancer patients if the patient has already started systemic therapy. Vaccines can be given during systemic therapy with several precautions as described below.11

Patients with rituximab have the highest risks for COVID-19-associated morbidity and mortality if infected by SARS-CoV-2. Also, a low immune response is seen in patients taking rituximab. It is recommended that patients should be vaccinated before initiation of therapy, when feasible. A similar treatment was applied for other anti-CD20, anti-thymocyte globulin (ATG), and alemtuzumab. Consideration of delaying the vaccine can be made considering completion of 6 months of therapy or lymphocytes has shown recovery evidence.40

Cancer phase-specific suggestion for COVID-19 vaccine
Cancer patients do not represent a homogenous population. In this section, we are deemed to separate this population into three different pathways and scenarios: 1) patients with active disease, newly diagnosed patients or already on treatment, 2) those with the chronic disease after specific treatment, and 3) patients in the survivorship phase. Among these criteria, along with other vulnerable populations, the priority of COVID-19 vaccination in patients with active cancer needs to be considered.8 Surprisingly, not only those with active cancer but also patients with cancer history or within the survivorship phase also carry a higher risk of COVID-19-related complications than the noncancer population in terms of risk of hospitalization, ICU admission, and 30-day mortality.41 A large percentage of our cancer populations may be cancer survivors. Like the general population, cancer survivors are at risk of getting COVID-19. We encourage all of these individuals to get vaccinated.

DISEASE-SPECIFIC SUGGESTION FOR COVID-19 VACCINE

Patients with hematological malignancies (non-HSCT setting)
Patients with hematological malignancies are at the highest risk among other cancer who will develop more severe complications associated with SARS-CoV-2 infection. Concerning the high community transmission in Indonesia currently, vaccination is continued to patients when a vaccine is available and offered to them. Patients with hematological malignancies, particularly patients on or planned to have a B lymphocyte depleting therapies, should consult the optimal vaccination timing to their hematologist – medical oncologist.

Hematologic malignancies patients have to meet these criteria:40 The candidates for vaccination should have an adequate cellular and humoral immune response. Vaccination can be given in these requirements and timing (Table 3):

a. Patients who have not yet started lymphocyte-depleting therapies can receive 2-dose scheduled 14 days before initiating lymphocyte-depleting therapy.

b. Patients that have completed therapy with stable lymphocyte counts (Absolute Lymphocyte Count (ALC) ≥ to 1.0 (normal range: 1.3 - 4.0 x 10^3 cells/µl) or B cell counts ≥ 50 cells per microliter).

c. Patients on therapy with stable lymphocyte counts.

Acute leukemia and aggressive lymphoma
Vaccination should not be delayed in patients with acute leukemia and aggressive lymphoma with induction chemotherapy for a newly diagnosed disease. The consolidation or maintenance phase was the recommended time which the vaccine should be given due to the patient showing hematologic recovery. The vaccination doses should be given before steroid pulse. In lymphoma, the vaccine can be planned after completing therapy. We must assume they did not require further therapy and already in remission. For relapsed or refractory disease, systemic therapy should not be deferred for vaccination. Only the optimal timing should be adjusted to give the optimal immunologic response.18,19,40

Multiple myeloma
Vaccination in myeloma patients does not have contraindications related to specific diseases or treatments. Vaccination can
be given to patients on lymphodepletion therapy (e.g., high-dose melphalan with SCT, cyclophosphamide/fludarabine, or anti-CD52 monoclonal antibody conditioning for cellular therapy) according to cellular therapy guidelines and HSCT with proven lymphocyte recovery. Before vaccination, make sure the patient is not neutropenic (ANC <500/µL).18,40,42

**Indolent lymphoma**

Except for indolent lymphomas, where the asymptomatic disease will be managed conservatively, B-cell depleting therapy should be postponed until 1 month after completing the vaccination series. If they need systemic therapies, the proposed strategy would be different. For asymptomatic patients, B-cell depleting therapy could be postponed until 1 month after completion of vaccination dosages. For patients that need systemic therapies, the proposed strategy would be different. We would recommend treating with the induction regimens followed by complete vaccination dosages, and the maintenance therapy might be temporarily postponed until there is evidence of B lymphocyte recovery. During the high transmission rate, such as the current situation, vaccination is still advocated to generate T-cell memory responses.18,19,40,42

**Myeloid malignancies**

This section covers acute myeloid leukemia (AML), myelodysplasia syndrome, myeloproliferative disorders, and chronic myeloid leukemia (CML). In AML, induction therapy should be given, and vaccination can be given during the consolidation phase. MDS patients treated with hypomethylating agents (HMA) should also be considered for vaccination, as well as polycythemia vera, essential thrombocytosis, or primary myelofibrosis while on active treatment or just observation. CML patients receiving tyrosine kinase inhibitors (TKI) should also be considered for vaccination at any time, with or without remission.18,19,40,42

**SPECIAL CONSIDERATIONS IN HSCT**

Hematopoietic stem cell transplantation is an integral part of treatment in many hematological malignancies. Whether the COVID-19 vaccination will be planned before autologous stem cell transplantation (ASCT), then plan to complete the schedule before stem cell harvest (Table 4).40,43 If considering vaccination post-ASCT, then the administration's timing should be initiated within 3 months, and COVID-19 vaccination should prioritize the regular vaccination schedule.44 For patients receiving tandem ASCT, vaccination should be initiated after the last planned stem cell infusion. Allogeneic HSCT patients still are regarded as immunosuppressed for two years post-transplant. A live-attenuated vaccine should not be given until these two years, as long as no GvHD, no immunosuppressive medication is needed, no relapse, and no recent administration of immunoglobulin.19,40,46 However, vaccination may be initiated as early as 3-4 months post-HSCT with a non-live vaccine (time-frame within 6 months based on local vaccine availability and transmission rate in the community).47 During that time, stay at home, double down on social distancing, wash hands frequently, and avoid contact with other people, especially large groups.

**PATIENTS WITH SOLID CANCER**

Patients with solid cancers should be offered for vaccination as long as vaccine components are not contraindicated. The impact of the humoral and cellular responses is variable across solid tumor types and treatment paradigms. Special caution on lung cancer treated with immune checkpoint inhibitors; existing data suggested that they are at a higher risk for severe COVID-19 (Table 5).46

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**Table 4. COVID-19 vaccination suggestion in HSCT patients**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Vaccine Timing</th>
<th>Type of vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autologous transplantation</td>
<td>At least 3 to 6 months post-HSCT or at least a few days</td>
<td>Non-lived vaccine: [RNA-based*, inactivated**, protein subunit**, and viral vector (non-replicating) vaccines**]</td>
</tr>
<tr>
<td>Allogeneic transplantation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellular therapy (e.g., CAR-T cell)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Based on a specific recommendation for SARS-CoV-2 vaccination10,42
**Based on previous vaccination of other diseases in cancer patients10,19

**Table 5. COVID-19 vaccination suggestion in solid cancer**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Vaccine Timing</th>
<th>Type of vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytotoxic chemotherapy</td>
<td>In the middle of the cycle to assure better mounting of the immune response, just before the next cycle of chemotherapy</td>
<td>Non-lived vaccine: [RNA-based*, inactivated**, protein subunit**, and viral vector (non-replicating) vaccines**]</td>
</tr>
<tr>
<td>Targeted therapy, hormone therapy</td>
<td>Vaccinated at anytime</td>
<td></td>
</tr>
<tr>
<td>Checkpoint inhibitor</td>
<td>Vaccinated at anytime</td>
<td></td>
</tr>
<tr>
<td>Major surgery</td>
<td>Separate date of surgery from vaccination by at least a few days</td>
<td></td>
</tr>
</tbody>
</table>

*Based on a specific recommendation for SARS-CoV-2 vaccination10,42
**Based on previous vaccination of other diseases in cancer patients10,19
If vaccine supplies are constrained, those patients should be prioritized along with other high-risk cancer patients: age >74 years old, multiple comorbidities, active treatment, and metastatic disease.40,50

There is generally no contraindication to receipt of the COVID-19 vaccine across the broad range of cancer therapies. In the high COVID-19 transmission rate currently, clinicians should not hold or pause cancer therapy for vaccination. Optimal vaccination timing concerning cytotoxic chemotherapy and other cancer-directed therapies has not been established, giving data paucity. But whichever type of chemotherapy is chosen for particular cancer, vaccination should be planned at the furthest possible time point away from the cytotoxic effect (i.e., nadir point) during a given cycle is recommended.18,40,42

Radiotherapy can also cause indirect immunosuppression. However, the degree of immunosuppression depends on the type, and total-body irradiation (TBI) seems to cause obvious white blood cell reduction. TBI is typically given to hematological malignancies before HSCT as part of the conditioning regimen.40 For cancer patients undergoing surgery, no specific timing is recommended relative to surgery except for elective splenectomy. The first dose of vaccination should occur ≥2 weeks before splenectomy in the postsurgical period after recovery. In patients with asplenia, the COVID-19 vaccine should also be prioritized over other recommended vaccine schedule.51

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POST-VACCINATION FOLLOW-UP

At this time, post-vaccine serologies are not recommended in the general population. Post-vaccine serologies monitoring should be considered in clinical studies only. Further clinical studies to measure humoral and cell-mediated immunity to COVID-19 vaccination is recommended.50

CONCLUSION

Given the global plans made by national health authorities in every country worldwide for the widespread vaccination in individuals against SARS-CoV-2, the ISHMO of Semarang chapter herein presents the latest information concerning to-date authorized vaccinations as well as the peer-group position about the vaccination in cancer patients. In general, a non-live vaccine can be safely given to immunocompromised patients. Live-attenuated and replicating viral vector vaccine should not be administered to patients who are considered to be highly immunocompromised. All the SARS-CoV-2 vaccine types planned to be distributed in Indonesia do not contain live viruses, which theoretically leads us to conclude that SARS-CoV-2 vaccination in cancer patients is considered safe. It is clear that we need more data and specific studies in patients with cancer, but this should not delay access to priority vaccination. As we see, patients interested in vaccination should discuss with their hematologist-medical oncologist to check if they met the vaccination requirements. We also encourage social distancing, mask-wearing, good hand washing, and limiting exposure as much as possible. Caregivers and household or close contact with the patients should also encourage to have vaccinated.

DISCLOSURES

None to disclosed.

CONFLICT OF INTERESTS

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