Stem Cell Collection and Haematopoietic Stem Cell Transplantation (HSCT) in Malaysia during COVID-19 Pandemic V2.0

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Overview

Since WHO had announced the Coronavirus Disease 2019 (COVID-19) outbreak as a pandemic on 12 March 2020, the number of cases has continued to rise rapidly all over the world. While the Covid-19 vaccines bring a silver lining to this pandemic, the emergence of several mutated SARS-CoV-2 strains in several countries are worrisome.

In Malaysia, we are currently facing the third wave of infections which began on September 2020, with higher numbers of infected individuals than during the first and second waves. Although the fight against COVID-19 is still far from over, it is recognized that delaying certain medical procedures due to COVID-19 pandemic, for instance, haematopoietic stem cell transplantation (HSCT), might result in devastating harm to certain patients, owing to the fact that HSCT can be a life-saving treatment for those patients.

Therefore, resuming and maintaining the transplant service is deemed necessary in order to continue providing optimal care to patients with haematological diseases requiring HSCT as life-saving treatment.

This guideline is written with the purpose of maximizing the safety of patients, donors, and care-takers, while protecting healthcare staff from infection of the COVID-19. It has been reviewed by haematologists in the Ministry of Health and Ministry of Education, which will adopt this guideline in their respective institutions. This guideline provides basic management of transplant service in the era of COVID-19 pandemic. It may be amended in accordance to the needs of each institution.

General

1. All patients who were/are diagnosed to have COVID-19 are not eligible for any transplant procedures (PBSC Collection, Autologous HSCT, Allogeneic HSCT, and DLI), regardless of the risk profile of the underlying disease and should be deferred as per guideline. (*Please refer to Table 1*)

2. All donors who were/are diagnosed to have COVID-19 are excluded from stem cell harvest, regardless of the risk profile of the respective recipient's underlying disease. (*Please refer to Table 1*)

3. For recipients and donors who have symptoms of upper respiratory tract infection (URTI)/ other symptoms suggestive of COVID-19/ Influenza-like illness (ILI), or history of close contact with COVID-19 case, please refer to *Table 1* for further recommendation and action.

4. Priority of transplant will be based on treatment intent and risk: benefit ratio of treatment. (*Please refer to Table 2*)

5. In terms of stem cell source, fully Matched Sibling Donor (MSD) will be our priority due to its lower complications and mortality as compared to Matched Unrelated Donor (MUD) and Haploidentical Transplant.

6. PBSC will be used as allograft, unless there is a strong indication for bone marrow graft.

7. Owing to the possibility that donors of Allogeneic HSCT recipients becoming infected by COVID-19, or unable to be admitted on time for PBSC collection due to logistic reasons / travel restriction across borders, donors are required to be admitted earlier for PBSC collection and cryopreservation of the stem cells, prior to starting conditioning chemotherapy for recipients.

8. RT-PCR screening test for COVID-19 are mandatory for patients who are planned for PBSC collection, Autologous HSCT patients, Allogeneic HSCT patients, donors and carers, prior to admission for transplant. Validity of the test is not more than 7 days from the admission date. Samples from both nasopharyngeal and oropharyngeal swabs are required (*follow Guidelines COVID-19 Management in Malaysia ANNEX 5a - Guidelines on Laboratory Testing for Novel Coronavirus For Patients Under Investigation*). The test will be carried out in respective referring hospitals. Please liaise with your hospital management team about the arrangement of the screening test, as near as possible to the scheduled admission dates. Results from recognized private hospitals/labs are acceptable. After the screening test is performed, patients, donors and carers MUST be advised to self-quarantine at home until admission for transplant.

9. All patients and donors travelling to transplant centre for transplant procedures, should be advised to travel by private car instead of public transportations (e.g. bus, train, plane).

10. Although it is a usual practice for all transplant patients, it must be emphasized that they must strictly adhere to preventive practices such as hand hygiene and physical distancing to minimize their risk of contracting COVID-19. (*Please refer to website http://covid-19.moh.gov.my/infografik*)

11. HCWs who are taking care of transplant patients, either inpatient or outpatient, are required to follow MOH guideline in the management of workplace, preventive measures, and management of suspected cases (if there is any). (*follow Guidelines COVID-19 Management in Malaysia ANNEX 21 – Management of Healthcare Worker (HCW) During COVID-19 Pandemic*)

PBSC Collection for Autologous SCT Patients ***(Refer to Flow Chart A)***

1. All patients must have COVID-19 PCR test negative, not more than 7 days from the admission date. Result must be informed to Transplant Team prior to admission. After the screening test is performed, patients MUST be advised to self-quarantine at home until admission for PBSC collection.

2. G-SCF stem cell mobilization is preferred. However, if there is a need for chemo-mobilization, to discuss with collection centre.

3. Patients may receive subcutaneous G-CSF injection for stem cell mobilization at respective referring hospital.

4. All patients planned for mobilization should be admitted to ONE designated ward and cubicle. After admission, specialists in-charge of the ward must take the responsibility to screen through the cases again. If the patients show new onset of URTI symptoms / other symptoms suggestive of COVID-19 and fulfil criteria for suspected case, necessary measures must be taken (*follow Guidelines COVID-19 Management in Malaysia Annex 2 - Suspected, Probable and Confirmed COVID-19*), and inform Apheresis/Transplant Team.
5. "Home Leave" is not advisable, to minimize patients' mobilization and risk of contact with others, which subject the patients to risk of contracting COVID-19 prior to PBSC collection.

6. Proceed with PBSC collection if patients are asymptomatic and does not fulfil definition of suspected case.

Autologous HSCT Candidates *(Refer to Flow Chart B)*

1. Advice must be given to patients: for at least 2 weeks prior to admission for transplant, they should follow strictly MOH Guideline on hand hygiene, physical distancing, home isolation, and protective measures. (*Please refer to website http://covid-19.moh.gov.my/infografik*)

2. All patients must have COVID-19 PCR test negative, not more than 7 days from the admission date. Result must be informed to Transplant Team prior to admission. After the screening test is performed, patients MUST be advised to self-quarantine at home until admission for transplant.

Allogeneic HSCT Candidates *(Refer to Flow Chart C)*

1. All patients are still required to attend counselling session in transplant centre prior to Allogeneic HSCT. HLA confirmatory test and necessary transplant work up investigations will be sent on the day of counselling.

2. Only patient, 1 main carer, and 1 identified donor are allowed to attend the counselling session.

3. Advice must be given to patients: for at least 2 weeks prior to admission for transplant, they should follow strictly MOH Guideline on hand hygiene, physical distancing, home isolation, and protective measures. (*Please refer to website http://covid-19.moh.gov.my/infografik*)

4. All patients must have COVID-19 PCR test negative, not more than 7 days from the admission date. Result must be informed to Transplant Team prior to admission. After the screening test is performed, patients MUST be advised to self-quarantine at home until admission for transplant.

HSCT Donors *(Refer to Flow Chart C)*

1. Advice must be given to donors: for at least 28 days prior to admission for transplant, they should follow strictly MOH Guideline on hand hygiene, physical distancing, and protective measures. (*Please refer to website http://covid-19.moh.gov.my/infografik*)

2. Since cryopreservation of PBSC is strongly recommended, donors will be given earlier admission date for stem cell harvest, prior to starting conditioning chemotherapy for recipients.

3. All donors planned for mobilization should be admitted to ONE designated ward and cubicle. After admission, specialists in-charge of the ward must take the responsibility to screen through the cases again. If the patients show new onset of URTI symptoms / other symptoms suggestive of COVID-19 and fulfil criteria for suspected case, necessary measures must be taken (*follow Guidelines COVID-19 Management in Malaysia Annex 2 - Suspected, Probable and Confirmed COVID-19*), and inform Apheresis/Transplant Team.

4. "Home Leave" is not advisable, to minimize donors' mobilization and risk of contact with others, which subject the donors to risk of contracting COVID-19 prior to PBSC collection.

5. All donors must have COVID-19 PCR test negative, not more than 7 days before their admission date. Result must be informed to Transplant Team prior to admission. After the screening test is performed, donors MUST be advised to self-quarantine at home until admission for transplant.

Care-taker (for both Autologous and Allogeneic HSCT Candidates)

1. One main and permanent care-taker for patient must be identified prior to transplant.

2. The main care-taker is responsible to take care of the patient during procedure of Autologous or Allogeneic HSCT in transplant ward, and during post-transplant period if the patient is staying at Midway House *(applicable to Ampang Hospital patients).*

3. Care-taker must have COVID-19 PCR test negative, not more than 7 days before their admission date. Result must be informed to Transplant Team prior to admission. After the screening test is performed, patients MUST be advised to self-quarantine at home until admission for transplant.

4. No visitors are allowed to the Midway House *(applicable to Ampang Hospital patients).*

5. Care-taker must be counselled and informed that he/she will be monitored for signs and symptoms of respiratory tract infection and other symptoms suggestive of COVID-19, including temperature monitoring on daily basis, by staff nurse, throughout the patient's stay in the ward for transplant procedure.

6. Care-taker MUST comply to proper usage of personal protective equipment (PPE).

References

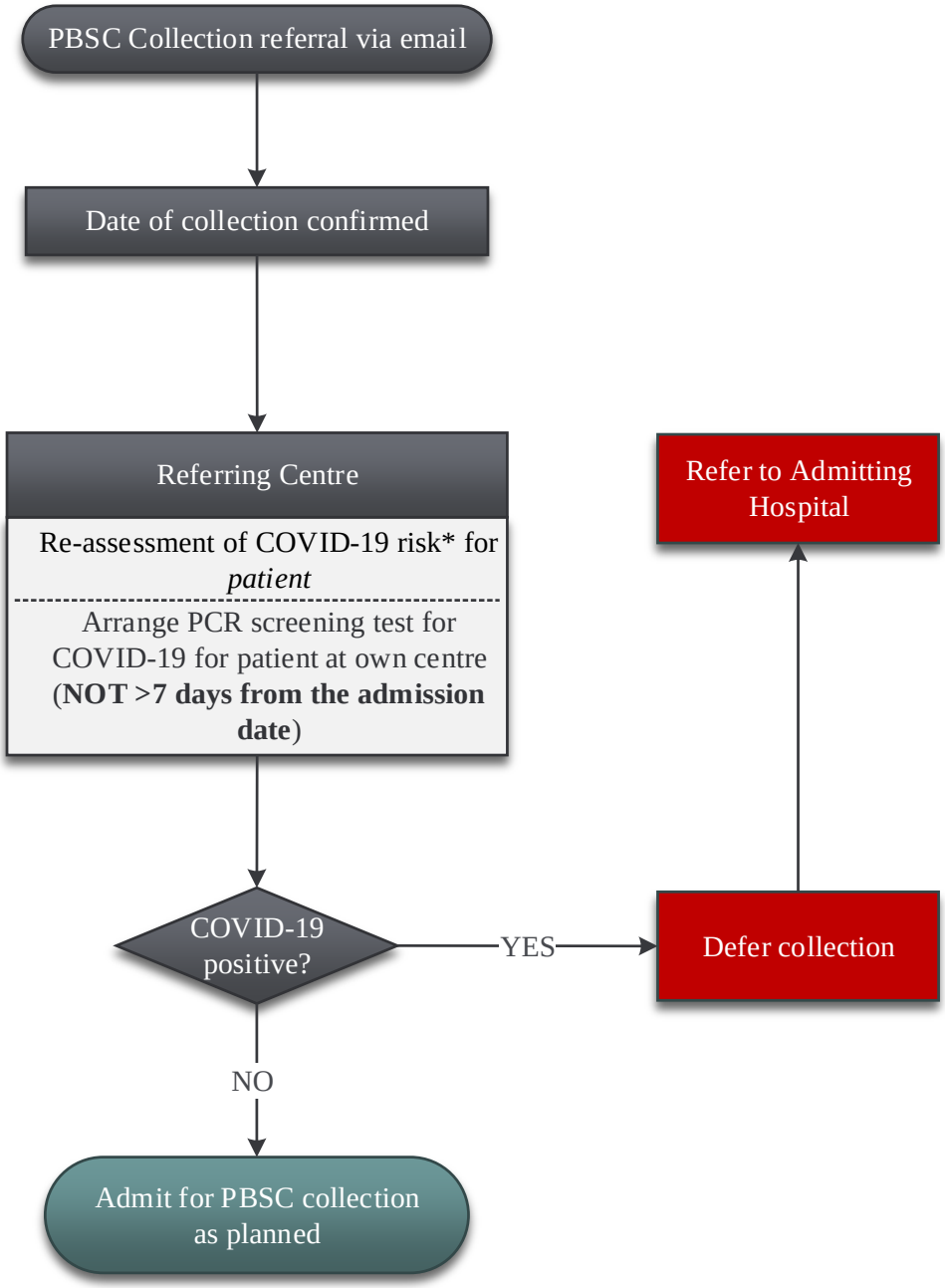
1. Coronavirus Disease COVID-19: EBMT Recommendations Version 13 – December 22, 2020.

2. COVID-19 rapid guideline: haematopoietic stem cell transplantation. NICE Guideline Updated: 29 July 2020.

3. Bhagirathbhai Dholaria and Bipin N. Savani. How do we plan hematopoietic cell transplant and cellular therapy with the looming COVID-19 threat? British Journal of Haematology, 2020, 189, 239–240

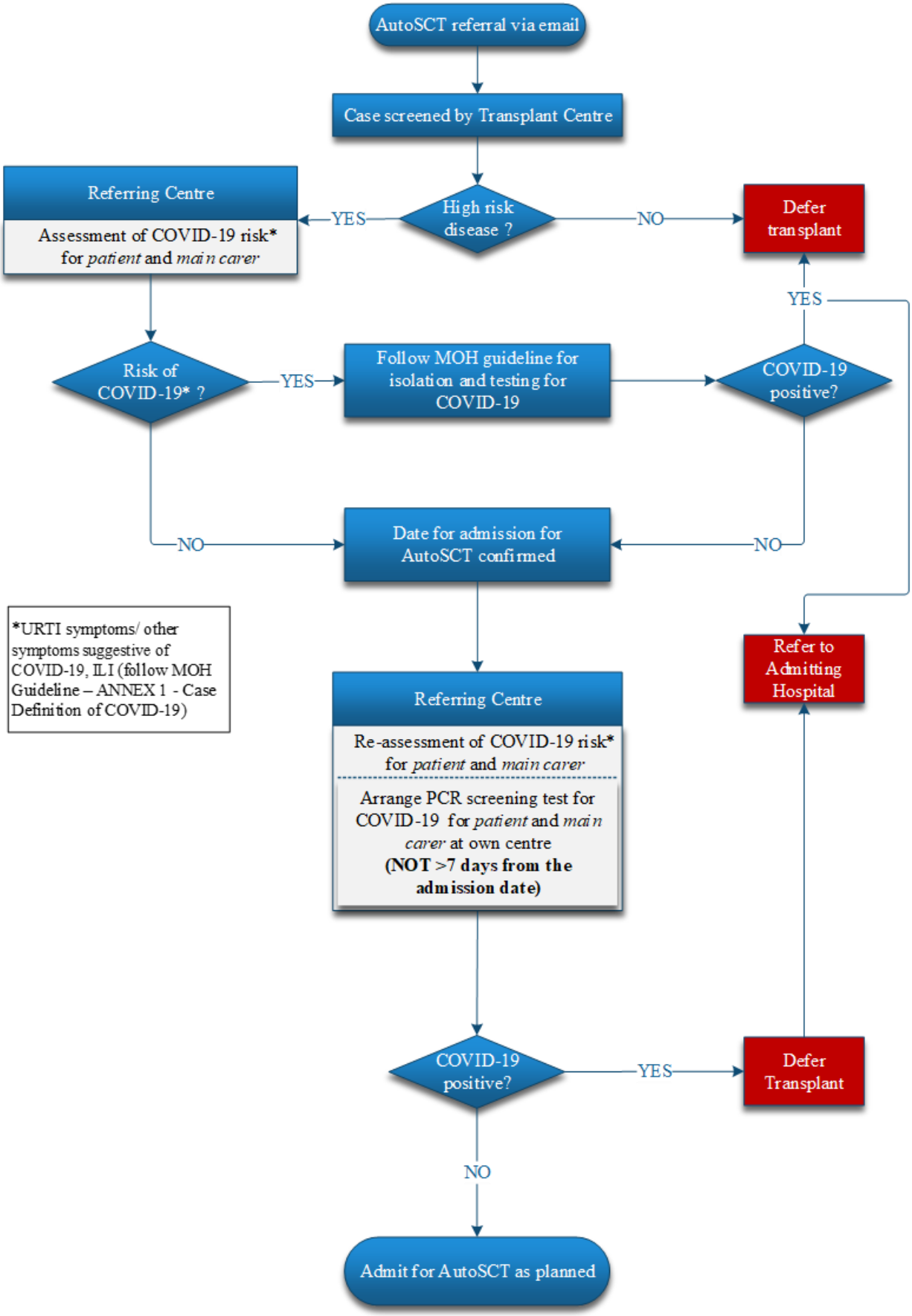
4. http://covid-19.moh.gov.my/

Flow Chart A: PBSC Collection for Patients



*URTI symptoms/other symptoms suggestive of COVID-19, ILI (follow MOH Guideline – ANNEX 1 - Case Definition of COVID-19)

Flow Chart B: Autologous HSCT Candidates



Flow Chart C: Allogeneic HSCT Candidates and Donors

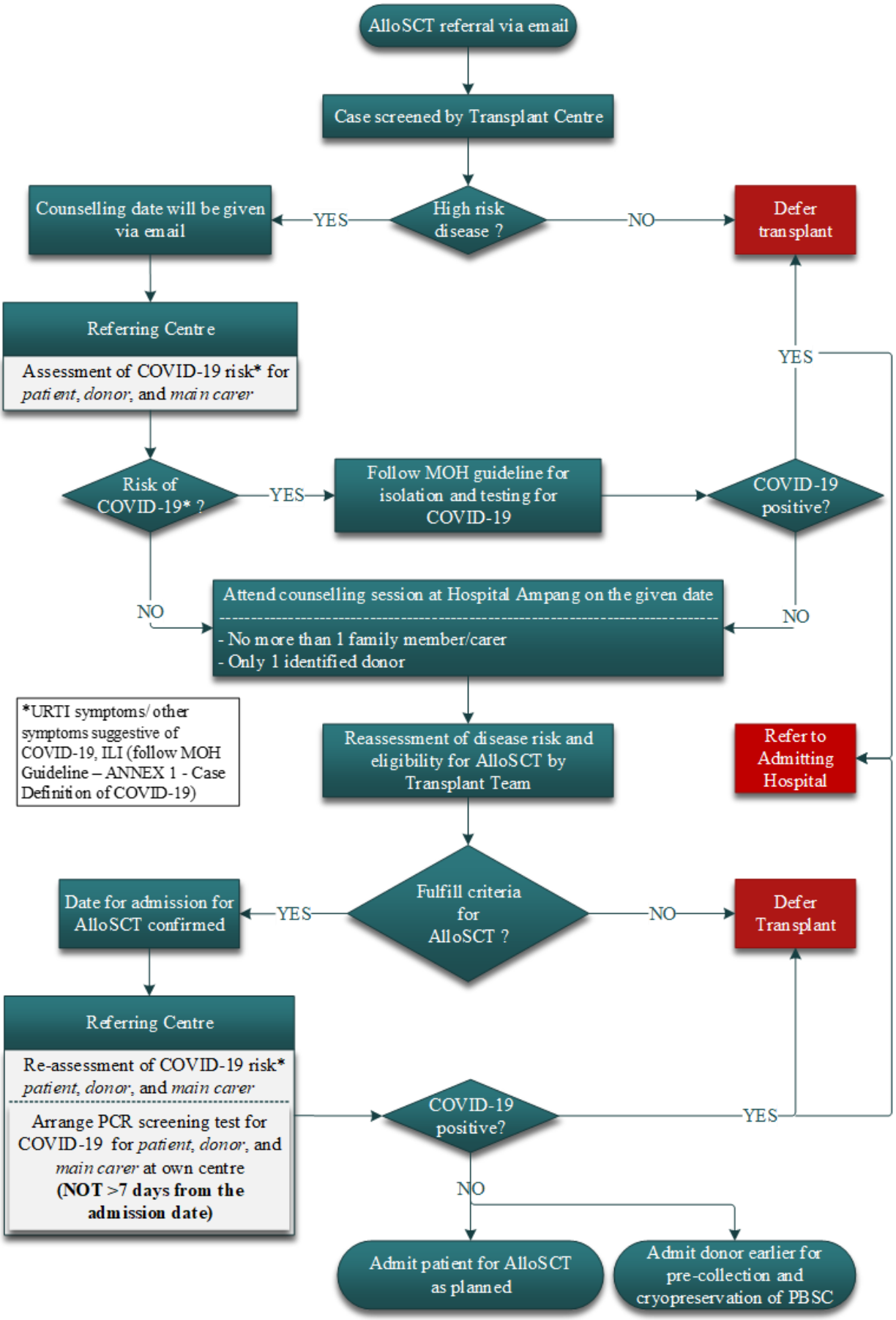


Table 1. Recommendation for COVID-19 and HSCT in Malaysia

Recipients			
Scenario	Low Risk Disease*	High Risk Disease*	Notes
History of / Current Confirmed COVID-19 Infection	Defer transplant	Defer transplant	Once the risk associated with COVID-19 pandemic have passed, and patient is still eligible for transplant (at least 3 months from the diagnosis of COVID-19), discussion can be made with Transplant Team again
Symptoms of URTI / other symptoms suggestive of COVID-19 / ILI	Consider deferral	Consider deferral	COVID-19 testing on case-by-case basis per MOH guidelines
Close contact with COVID-19 case	Defer transplant	PCR test for COVID-19 Deferred for 14 – 21 days	Follow MOH guideline for isolation and testing for COVID-19
Donors			
History of / Current Confirmed COVID-19 Infection	Collection should be deferred for at least 14 days after recovery	Collection should be deferred for at least 14 days after recovery	Risk assessment should be based on: the date of full recovery, the duration and severity of COVID-19, and the results of post-recovery testing
Close contact with COVID-19 case	Excluded from donation for at least 14 days Closely monitor for the presence of COVID-19	Excluded from donation for at least 14 days Closely monitor for the presence of COVID-19	Follow MOH guideline for isolation and testing for COVID-19 If transplant is really urgent, donor is well, negative PCR test for COVID- 19, no suitable alternative donors, earlier collection maybe considered after discuss with Transplant Team

(Modified CORONAVIRUS DISEASE COVID-19: EBMT RECOMMENDATIONS VERSION 13 – December 22, 2020)

Abbreviations: PCR: polymerase chain reaction; MOH: Ministry of Health; HSCT: Haematopoietic Stem Cell Transplantation
URTI: Upper Respiratory Tract Infection; ILI: Influenza-like Illness
*Refer to Table 2. Prioritizing treatment for patients having haematopoietic stem cell transplantation

Table 2. Prioritising treatment for patients having haematopoietic stem cell transplantation

Priority level	Categorization based on treatment intent and risk: benefit ratio of treatment
1	Urgent allogeneic HSCT where delaying the procedure presents a high risk of disease progression, morbidity or mortality.
2	High-grade lymphomas and other urgent cases needing autologous HSCT for curative intent (for example, diffuse large B-cell lymphoma and Hodgkin lymphomas).
3	Chronic conditions including most non-malignant indications and low-risk malignant indications for allogeneic HSCT (most should be deferred until the risks associated with the COVID-19 pandemic have passed).
4	Allogeneic HSCT recipients with a relatively low predicted survival (for example, 20% to 30% at 5 years based on pre-HSCT characteristics; all but exceptional cases should be deferred until the risks associated with the COVID-19 pandemic have passed).
5	Autologous HSCT for myeloma, low-grade lymphoproliferative diseases and non-malignant indications (all but exceptional cases should be deferred until the risks associated with the COVID-19 pandemic have passed).

Adapted from the BSBMTCT recommendations for the management of adult patients and allogeneic donors during the COVID-19 outbreak (March 2020)