

CORONAVIRUS DISEASE COVID-19: Updated EBMT RECOMMENDATIONS **(8th March 2020)**

A novel coronavirus: named currently SARS-CoV-2 of a zoonotic origin has emerged and the infection called Coronavirus Diseases 2019 (COVID-19) started spreading worldwide. As on 8th March the virus is present in 93 countries, with fatality rate of approximately 2-3%.

Incubation period: Time from exposure to symptom development is between 2-14 days.

Prophylaxis and treatment: Avoiding exposure by adhering to recommended hygiene procedures, isolation of SARS-CoV-2-infected persons and social distancing are the only prevention strategies (see: Box 1. The WHO recommendations).

Currently there is no approved treatment options in Europe and there is no available vaccine. At this point no recommendations can be made on specific therapies due to limited data and unknown risk vs benefit; additional recommendations will be forthcoming. Even less data is available for pediatric patients. Treatment for viral, bacterial, and fungal co-pathogens should be optimized. Several drugs have been studied in prior coronavirus outbreaks (SARS-CoV and MERS-CoV) and though some benefit has been demonstrated, the data are inconclusive. There are ongoing clinical trials (mostly in China). Tocilizumab has also been used in China for therapy of severe cases suspected having cytokine associated pathology).

EBMT guidelines: Due to fast spreading of SARS-CoV-2 a panel of experts of EBMT recommends the following guidelines for recipients and donors of hematopoietic cells before the beginning of any of the transplant procedures (mobilization, apheresis, marrow harvest, conditioning). These guidelines will be updated when new information is obtained about COVID-19 epidemiology and clinical outcome.

Prevention policies and procedures: This document will not cover specific infection prevention policies and procedures; local and institutional guidelines should be followed. In the setting of known high community prevalence of SARS-CoV-2, clinic visits that are not critical should be either deferred or substituted with telemedicine visits if deemed appropriate and feasible.

Diagnostic procedures: Should be according to national guidelines. Patients, who have been to areas with high risk of transmission of SARS-CoV-2 or who have been in close contact to a person to such areas should be tested for the virus.

All patients positive for SARS-CoV-2 in an upper respiratory tract sample should undergo chest imaging.

Routine bronchoalveolar lavage (BAL) is not recommended if patient tested positive with SARS-CoV-2 given risk of transmission amongst health care workers, unless a co-infection is suspected. If chest imaging abnormal and in patients for whom it is clinically indicated (e.g., those receiving invasive mechanical ventilation), a lower respiratory tract aspirate or BAL sample should be collected and tested for SARS-CoV-2. Co-pathogens should be evaluated and treated.

Patients with no known exposure residing in areas perceived to be low-risk for SARS-CoV-2 developing symptoms of an acute respiratory tract infection (fever, cough or other symptoms attributed to viral respiratory infections), shall be tested for respiratory viral infections preferably by multiplex PCR and depending on which virus is detected, deferral of HCT should be considered.

Recommendation recipients:

1. In case of diagnosis of COVID-19: In patients with no or only upper respiratory symptoms, no therapy is recommended. In patients with lower respiratory tract symptoms, the possibilities of installing therapy should be investigated with participation in a clinical trial recommended if possible.
2. The EBMT Infectious Diseases Working Party (IDWP) invites you to participate in a prospective survey about the impact of covid-19 on patients having undergone stem cell transplantation. The survey is in two steps:

1. Please, fill in the [registration form](#) for each patient diagnosed with covid-19 at your center and submit the completed form to the EBMT IDWP Data office. **The form is protected with a password: covid_idwp**
2. We will then send you a more detailed form asking for more details of the clinical course and outcome of covid-19

For any question about this survey, please email idwp.ebmt@lumc.nl

3. According to ECDC recommendations, patients ought to be deferred for at least three months. However, this is not always possible due to the risk from the underlying disease. Therefore, in patients with high risk disease, HCT should be deferred until the patient is asymptomatic and has three repeated virus PCR negativity at least one week apart (deferral of 14 days minimum). In patients with low risk disease a three-month HCT deferral is recommended.
4. In case of close contact with a person diagnosed for COVID-19 any transplant procedures (PBSC mobilization, BM harvest, conditioning) shall not be performed within at least 14 preferably 21, days from the last contact. Patient should be closely monitored for the presence of COVID-19, with confirmed PCR negativity.
5. Stem cell transplant patients should refrain from non-necessary travel to areas designated as high-risk areas by the WHO.
6. In case of travel to a high-risk area or a close contact with person travelling from a high-risk area for COVID-19 (as defined by health authorities*), any transplant procedures (PBSC mobilization, BM harvest, conditioning) should not be performed within at least 14 preferably 21 days from the last contact.

Recommendations donors:

SARS-CoV and MERS-CoV have been detected in blood, although there have not been any reports of transmission from donor to recipient either in transfusion of blood products or cellular therapies. WMDA has produced recommendations and the EBMT endorses these guidelines.

1. In case of diagnosis of COVID-19, donor must be excluded from donation. At this time, it is not possible to give recommendations when such an individual can be cleared for donation but at least three months deferral can be considered unless the need for donation is urgent when individual consideration should be made.
2. In case of close contact with a person diagnosed with SARS-CoV-2, the donor shall be excluded from donation for at least 28 days. Donor should be closely monitored for the presence of COVID-19.
3. If the patient's need for transplant is urgent, the donor is completely well and there are no suitable alternative donors, earlier collection may be considered subject to careful risk assessment if local quarantine requirements permit
4. In case of travel to high risk areas for COVID-19 (as defined by health authorities*) or being a close contact with person travelling from such an area, donor shall be excluded from donation for at least 28 days.
5. Consider cryopreservation of the graft if there is concern that the donor is at risk of community-acquired infection after the patient starts conditioning. Cryopreservation in this scenario could allow patient conditioning to be withheld until a successful collection is confirmed
6. If possible, ensure that an alternative stem cell source will be available.
7. Donors within 28 days before donation should practice good hygiene (see: Box 1. The WHO recommendations) and avoid crowded places and large group gatherings.

| Box 1. The WHO recommendations on how to protect yourself and the others from COVID-19 |
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| <ol style="list-style-type: none"> 1. Wash your hands frequently with an alcohol-based hand rub or with soap and water. 2. Maintain social distancing of at least 1 meter between yourself and anyone who is coughing or sneezing. 3. Avoid touching eyes, nose and mouth. 4. Practice respiratory hygiene (covering your mouth and nose with your bent elbow or tissue when you cough or sneeze and then dispose of the used tissue immediately). 5. If you have fever, cough and difficulty breathing, seek medical care early, but call in advance and follow the directions of your local health authority. 6. Stay informed and follow advice given by your healthcare provider, your national and local public health authority since they can provide you with reliable information on whether COVID-19 is spreading in your area. 7. Additionally, in case of persons who are in or have recently visited (past 14 days) areas where COVID-19 is spreading, stay at home if you begin to feel unwell, even with mild symptoms, until you recover, but if you develop fever, cough and difficulty breathing, seek medical advice promptly by calling your health provider to so you can be quickly directed to the right health facility. |

(*) On day 6.03.2020: China, Republic of Korea, Italy, Iran. For updated information see:
https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200306-sitrep-46-covid-19.pdf?sfvrsn=96b04adf_2

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