Updated 27th March 2020

BSBMTCT recommendations for the management of adult patients and allogeneic donors during the COVID-19 (causative agent the SARS-CoV-2 virus) outbreak.

It is now clear that the UK has entered into a period of high SARS-CoV-2 infection rates and COVID-19 prevalence with a probable peak in early April and risks will remain high for several weeks thereafter.

The following recommendations are based on the updated guidance obtained from several sources including the EBMT, ASTCT, WMDA, Anthony Nolan and NHSBT. Individual centres should continue to use these recommendations for general guidance only as circumstances will vary from centre to centre and institutional procedures should be followed. These recommendations have been produced in order to provide support to BMT teams in the UK. Advice may change as the COVID-19 prevalence increases in the UK.

Transplant teams are advised to carefully read the guidance from the EBMT and ASTCT.
EBMT guidance: https://www.ebmt.org/covid-19-and-bmt
ASTCT guidance:
https://higherlogicdownload.s3.amazonaws.com/ASBMT/a1e2ac9a-36d2-4e23-945c-45118b667268/UploadedImages/COVID-19_Interim_Patient_Guidelines_3_18_20.pdf
Anthony Nolan on donor issues: https://www.anthonynolan.org/anthony-nolan-response-covid-19

BSBMTCT Collaborative group advice:

Prophylaxis and treatment:
Transplant units will be familiar with the prevention of spread of respiratory viruses within their programs. It is vital that programs continue to review their existing respiratory pathogen management procedures, policies and, for the current outbreak, align with local hospital and national policies and procedures. Patients at any time during their transplant pathway should be screened for possible upper respiratory tract infections (URTI) by careful history taking, particularly paying attention to respiratory symptoms, fevers, cough. SARS-CoV-2 appears to mainly cause fever, dry cough and sore throat with coryza occurring in only a minority of cases. Any patient pre, peri or post-transplant with respiratory symptoms should be isolated and tested for respiratory viral pathogens including SARS-CoV-2 by nasal and throat swabs for PCR. Local guidelines must be followed for any patients identified as positive for SARS-CoV-2. Note that other respiratory viral pathogens are already known to be a serious risk to transplant recipients and if identified during screening appropriate measures should be taken including deferral of transplantation.

At this time there are no proven effective anti-viral agents recommended specifically for SARS-CoV-2, however anti-microbial therapy should be optimised with treatment directed according to any positive isolates. There is emerging evidence that part of the COVID-19 pathology is due to an inflammatory response to the virus that occurs 5-7 days following the appearance of symptoms. Several potential anti-inflammatory agents are under investigation and may be recommended in the future.

Pre-SCT:
- As a preventative measure patients should be advised to avoid crowded places, public transport, use good hand hygiene measures and remain in self-isolation for 14 days prior to the start of conditioning.

- Careful history taking to determine whether the patient has had a recent contact with an individual proven to have COVID-19 or symptoms suggestive of COVID-19 (see PHE website). Travel to high risk countries has become a redundant screening tool.

- Any planned transplant should be reviewed and deferred if possible. It is anticipated that the peak risk from infection in the community will be in early April and may last up to 9 weeks and possibly longer. Whenever possible SCT should be deferred. This is in order to reduce the pool of high risk patients and in anticipation of a shortage of intensive care beds and possibly trained BMT unit staff.

Ideally all patients should be tested for SARS-CoV-2 by nasal and throat swabs by PCR before starting conditioning, as there is an asymptomatic period testing should be repeated at least twice, 1 week apart, but practice and availability of testing may vary between institutions. However it would be important to test transplant patients prior to the start of conditioning if they have a history of recent contact with symptomatic individuals.

The following table may help in determining transplant prioritisation:

Priority level	**Categorisation based on treatment intent and risk:benefit ratio of treatment**
1	Urgent allogeneic HSCT if delaying the procedure presents a high risk of disease progression, morbidity or mortality. This will mainly be malignant cases with a small number of urgent, non-malignant conditions.
2	High-grade lymphomas and other urgent cases needing autologous HSCT.
3	Chronic conditions including most non-malignant indications and low-risk malignant indications for allogeneic HSCT (most should be deferred).
4	Allogeneic HSCT recipients with predicted survival of less than 20-30% at 5 yrs based on pre-transplantation characteristics
5	Autologous HSCT for myeloma, low-grade lymphoproliferative diseases and non-malignant indications should be deferred until the risks associated with the COVID-19 pandemic have passed.

Consider using transplant outcome predictive tools such as the refined disease risk index[1] and HCT-CI[2] (link to on line calculator at HCT-CI) to inform decision-making for patients but also consider the limitations of using these scales.

SARS-CoV-2 positive patients:
Any patients testing positive for SARS-CoV-2 prior to SCT should be delayed by at least 3 months (ECDC recommendations), 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 achieved three virus PCR negative tests at least one week apart (deferral of 14 days minimum). In patients with low risk disease a three-month HCT deferral is recommended.

Autologous transplant recipients
- Emerging consensus that when possible autologous transplants should be deferred by at least 3 months, with case-by-case decisions. Advice may be available regarding which patients to defer and how to manage patients during the deferral period from the disease specific specialist groups, UK Myeloma Forum and Lymphoma Specialist Interest Group.
- Asymptomatic recipients should be screened for respiratory viruses and SARs-CoV-2 at least once 72 hrs prior to the start of conditioning.
- Minimise the use of chemotherapy priming, use GCS-F alone.
- Autologous SCT for non-malignant indications should be deferred until the peak of COVID-19 passes.

Allogeneic transplant recipients

- Careful planning required for the preparative regimen as donor cells may need to be cryopreserved prior to starting condition (see donor section).
- Asymptomatic recipients should be screened for respiratory viruses and SARs-CoV-2 at least once 72 hrs prior to the start of conditioning.
- Defer transplantation for any non-urgent indications. This will require allo-SCT MDT discussion on a case by case basis. Examples would be for MDS, MPD.
- Patients and relatives should receive instructions regarding isolation and preventative measures, this should be repeated and supported with written information.
- If close contact with COVID-19 individual immediately prior to transplant defer transplant for 3 weeks if possible (EBMT guidelines), test if symptomatic following local infection control guidelines.
- Patients who test +ve pre-SCT should be deferred where possible by at least 3 months until asymptomatic with viral throat swab negative x 3 tests, 1 week apart (EBMT guidelines). In patients with high risk disease HCT should be deferred until the patient is asymptomatic and has achieved three virus PCR negative tests at least one week apart (deferral of 14 days minimum).

Allogeneic donors

- Advise sibling donors to avoid crowded public places, practise good hygiene and avoid large group gatherings for 28 days prior to donation (EBMT Guidelines). Screen donors if symptomatic and prior to starting conditioning. Advice may change soon to screen at the medical and again 2 days prior to donation. Consider harvesting sibling and cryopreserving stem cells prior to conditioning.
- Anthony Nolan now strongly recommend moving to shipping and cryopreserving stem cells before starting conditioning because of the risk of donor becoming ill and being unfit to donate plus growing uncertainties regarding transport. Liaise with local processing laboratories to warn them of each donation and whether to cryopreserve or not.
- Anthony Nolan will arrange SARS-CoV-2 testing of donor at the medical and repeated at harvest. Results should be available by the time product is cryopreserved. If not the processing laboratory may need to quarantine cryopreserved cells until results available.
- Sibling donors should also be screened twice, once at the medical and again on the day of donation.
- Donors will be excluded from donation for 3 months if proven COVID-19 or for 4 weeks if in close contact with COVID-19 case. Screening for SARS-CoV-2 will be required. If no suitable alternate donors and SCT urgent, perform risk assessment and lease with registry. In this situation the recipient should be involved in the discussion and be informed of the donor situation.
- 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.
- Identify back-up donor from different country or cord in case harvesting/transport of 1st donor problematic (Anthony Nolan will facilitate).
- Consider the option of a haplo-identical donor as a back-up.
- There have been concerns that SARS-CoV-2 may be passed via blood products. Although viral RNA has been detected in blood samples of patients with COVID-19 there have been no reports of transmission of infection by blood products.
- Consider avoiding bone marrow as the stem cell source as access to theatres may be limited and prone to sudden cancellation.
- Donors should be contacted approximately 14 days post-harvest to determine if they have experienced any symptoms suggestive of COVID-19.

Peri and Post-transplant:

- Minimise the number of family members that visit patients. Educate all family members on hand hygiene, and how to avoid potential contact risk behaviour.
- Patients should be managed in strict protective isolation; risk assess the need for any investigations and procedures that remove the patient from their isolation room, there may be a greater risk from exposure to SARS-CoV-2 than from not having the investigation.

- Patients who are known to be SARS-CoV-2 +ve should be isolated in negative pressure cubicles wherever possible, failing this in a neutral pressure cubicle. When seeing such patients, healthcare professionals should wear full PPE including gowns, FFP3 masks, gloves and visors.
- At present it is unlikely to be feasible to screen ward staff in contact with patients routinely because of availability of testing and the pick-up rate in asymptomatic individuals is unknown.

After discharge:

- **This will be the time of greatest risk to transplant recipients.**
- At discharge reinforce need for self-isolation of the transplant recipient and if possible the immediate carer.
- Minimise clinic visits, consider how patients travel to the centre and try to reduce risks from public transport. Hospital transport may become limited.
- Set up telephone follow-up clinics, explore ways for patients to have blood tests away from busy areas in hospitals.

Staff:

- Healthcare professionals with cough/SOB/fever should not come to work. Current NHS policy does not mandate viral testing of staff prior to returning to work but this should change in the very near future.
- HCP who are coryzal without fever should avoid coming to work and self-isolate for at least 7 days. They should ideally be screened for respiratory viruses and SARS-CoV-2. These recommendations need to be discussed with your local Infection Control Team.
- There is evidence that healthy individuals can continue to shed virus for up to 12 days from the onset of symptoms. Therefore it is strongly recommended that staff should be *symptom free* for 7 days before working directly with patients.
- Switch meetings/MDTs to telecons as much as possible and consider splitting workforce to mitigate risk of large proportion of team being affected at same time
- Avoid work related international travel/ large meetings

CAR-T therapy:

As yet no clear consensus. Patients are at increased risk peri- and post-treatment. Additional risk from interruption in the manufacturing chain. The pharmaceutical companies involved in the manufacture of CAR-T should be contacted directly.

Continue to check the most up to date guidelines from the donor registries and EBMT.

BSBMTCT Executive
27th March 2020

Refs:

1. Armand P et al, Blood 2014; 123:3664-3671
2. Sorror M et al, J Clin Onc 2014; 32:3249-3256