

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

Version 6; 15<sup>th</sup> January 2021

General status of SARS-CoV-2 in the UK.

By December 2020 a new variant, VUI-202012/01 (B.1.1.7), was identified in the UK and subsequently in other countries which is more infective than variants present during the initial pandemic phase. By late December 2020 it became clear that the UK was experiencing a rapidly increasing incidence of SARS-CoV-2 in the general population arising from the second wave of the pandemic. This 'third wave' has been driven by the emergence of the new variant and may also have been increased by population behaviour during the holiday period. HSCT recipients and donors remain at considerable risk. In the absence of proven effective treatments it is important that transplant teams continue to advise patients and their families on social distancing behaviour to minimise exposure to the virus\*.

The positive results for several vaccine trials offers hope that the pandemic will be controlled by mid- to late 2021. However, it remains unclear whether all HSCT recipients will respond to the vaccine. This will be an important and urgent area of investigation. A more detailed description of the current status of SARS-CoV-2 vaccine is posted on the BSBMT&CT website. However, as it is as yet unknown how patients will respond to vaccination, transplant teams must remind patients that they remain at risk even after receiving one of the available vaccines.

It is likely that the current severe levels of infection will last until late January into early February but hospitals will remain under pressure for many weeks more.

Although there are no definitively proven effective treatments, considerable experience of patient management has been gained during the first outbreak and survival from COVID-19 is possibly improving.

The recommendation to reduce transplant activity at the onset of the pandemic was based on two concerns;

- 1) **Capacity:** The capacity within transplant centres to manage patients, bed capacity in the units, ICU bed availability and staffing reduction due to illness, self-isolation and transfer to non-transplant activities.
- 2) **COVID-19 risk:** The risk of COVID-19 in this vulnerable patient group.

Many centres may have returned to pre-COVID-19 levels of transplant activity. The 'third wave' of the pandemic is having an even greater impact on NHS services and centres will need to carefully consider their ability to manage patients over the next 4-6 weeks. Continuation of transplant activity will depend on the local availability of bed capacity and staffing levels. Although capacity pressures will fluctuate, the risk from COVID-19 will remain for some time. It is these risks that transplant teams will need to address before beginning the recovery of transplant activity.

The following recommendations are based on the guidance obtained from several sources including the EBMT, ASTCT, WMDA, Anthony Nolan and NHSBT but with interpretations for the situation in the UK. More importantly it represents a consensus from UK transplant teams and disease groups. Individual centres should 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 changes in the UK.

Transplant teams are advised to carefully read the latest guidance from the EBMT, ASTCT and for donor issues, the Anthony Nolan, NHSBT and WMDA on their websites.

EBMT guidance, updated 22<sup>nd</sup> December 2020:

<https://www.ebmt.org/sites/default/files/2020-12/EBMT%20COVID-19%20guidelines%20and%20summary%20v.13.pdf>

ASTCT guidance (regularly updated):

<https://www.astct.org/communities/community-home/librarydocuments?communitykey=d3949d84-3440-45f4-8142-90ea05adb0e5&tab=librarydocuments&LibraryFolderKey=&DefaultView=>

WMDA web link:

<https://share.wmda.info/pages/viewpage.action?pageId=344866320>

Anthony Nolan COVID-19 link, updated 30<sup>th</sup> October 2020:

<https://www.anthonynolan.org/patients-and-families/understanding-stem-cell-transplants/coronavirus-and-your-stem-cell-transplant>

NHSBT link:

<https://www.nhsbt.nhs.uk/news/coronavirus-update/>

NICE Guideline NG164, updated 29<sup>th</sup> July 2020 - COVID-19 rapid guideline: haematopoietic stem cell transplantation

<https://www.nice.org.uk/guidance/ng164>

## UK Myeloma Forum COVID-19 Guidelines:

<https://www.ukmf.org.uk/guidelines/covid-19-guidance/>

### BSBMT&CT Collaborative Group advice.

Changes since the last set of recommendations:

- 1) Addition of recommendations for maintaining transplant activity.
- 2) Updated links to other HSCT organisations.
- 3) Updated advice on cryopreservation of donor cells
- 4) Adjustment in prioritisation of patients.
- 5) Update of the recommended periods of strict self-isolation post-transplant
- 6) Change in the period of deferral for donors testing positive for SARS-CoV-2 or if in contact with an individual testing positive to align with the EBMT guidelines.
- 7) SARS-CoV-2 vaccination.

### Maintaining transplant activity:

The previous guidelines were issued as the UK entered into a period of relatively low SARS-CoV-2 incidence following recovery after the initial outbreak and transplant centres were advised to create 'COVID-safe' treatment pathways for patients and to re-start activity. The NHS is now generally better prepared for dealing with the fluctuating incidence of infection in the population but as the anticipated second wave started transplant teams began to experience periods of staff shortages, reduced capacity and heightened levels of anxiety in their patients and for staff. This has worsened since the emergence of the new variant. It is expected that transplant programs continue to follow the NICE Rapid Guidelines NG164 which provide advice on establishing and maintaining 'COVID-19 safe' treatment pathways.

The main patient groups that have been affected by the deferral of transplantation are those requiring autologous HSCT for myeloma and lymphoma. The BSBMTCT have worked closely with the UK Myeloma Forum in preparing the recovery recommendations.

### Capacity

- It is essential that centres are able to confirm sufficient capacity to manage planned activity. This includes:
  - Bed capacity in the transplant unit and ICU.
  - Staffing on BMT unit. Repatriation of staff if possible.
  - Stem cell laboratory capacity to manage donor cells for cryopreservation.
  - Associated services – pharmacy, renal support, physiotherapy.
  - Laboratory testing for SARS-CoV-2 in patients and staff.
  - Safe access to critical investigations such as endoscopy, bronchoscopy and radiology.
- Establish 'COVID-19 safe' patient treatment pathways, from clinics, during in-patient stay and post-transplant care. How this will be achieved will depend on the circumstances in each transplant centre, in some cases restarting transplant activity may not be possible and the NHSE BMT regional networks may be required to allow patients to be transferred to nearby centres that are able to provide COVID-19 safe care.
- Reduce out-patient visits by establishing telephone or video-clinics.
- Minimise visitors to hospital.
- Continued review of ambulatory transplant operations; the decision should be patient-focussed and ratified by the relevant MDT. Prevailing levels of SARS-CoV-2 in the catchment area of the centre should be considered, if rising then safe ambulatory pathways may not be appropriate.

### Case selection

As patients are deferred the balance of risks from COVID-19 infection and the delay to proceeding with transplantation begins to change. It is recommended that every case is assessed by local teams at MDTs. The priorities table remains a useful tool, patients deferred at the onset of the pandemic may now be considered to be in the clinical high-risk category. Case-by-case decision making will be essential to safe re-starting of transplant activity.

- Continue to follow NICE Rapid Guideline NG164 for COVID-19 in HSCT for guidance with prioritisation for patients with high risk disease based on disease characteristics and period of deferral.
- Refer to disease specific professional groups for guidance.
- Case-by-case decisions based on MDT discussions.
- Consult disease specific organisations which may provide guidelines to inform MDT decisions.
- Patients should be informed of the potential risks from SARS-CoV-2 infection as this may influence their decision regarding proceeding to transplant.

## **SARS-CoV-2 surveillance**

It will be important to develop and maintain robust policies and procedures to protect HSCT patients from SARS-CoV-2. These should be incorporated into existing Quality Management plans. The virus will remain within the community and will continue to be a major risk to patients until the pandemic is controlled. Programs must work with their local infectious diseases and infection control teams to create safe operational environments for patients. How this will be achieved will have to be determined at a local level but policies that include regular staff screening by symptom awareness, viral swab tests, serology to determine immunity are likely to be required. The emergence of more infectious variants underlines the need to maintain 'COVID-19 safe' pathways.

- Screening protocols – symptoms, naso-pharyngeal and throat swabs.
- The role of serological testing is unclear but may be available in some centres.
- Screening of asymptomatic BMT unit staff (including non-medical staff) and in-patients with viral swabs at a minimum on a weekly basis.
- Pre-admission screening by symptoms checks and viral swabs, ideally within 72hrs of planned admission prior to the start of conditioning.
- Patient triage and quarantine policies in clinics, in hospital, in ambulatory treatment pathways.
- Currently the EBMT recommend a nucleic acid based test such as PCR rather than the antigen rapid test due to the relatively lower sensitivity of the latter (EBMT COVID-19 guidelines, version 13, December 22<sup>nd</sup> 2020).

## **Prophylaxis and treatment:**

Transplant units will be familiar with the prevention and 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, shortness of breath. SARS-CoV-2 appears to mainly cause fever, dry cough and sore throat with coryza occurring in only a minority of cases but other symptoms may occur. Any patient pre, peri or post-transplant with respiratory symptoms should be isolated and tested for respiratory viral pathogens *including but not only* 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.

It is very important that staff responsible for taking viral swabs, including self-swabbing, follow correct procedures to avoid false negative results. Recommend formal training and documented evidence of correct technique, ideally as part of the JACIE quality management system within the transplant program.

At this time there are no proven effective anti-viral agents recommended specifically for SARS-CoV-2, early positive results with remdesivir have recently been questioned<sup>1</sup>, however anti-microbial therapy should be optimised with treatment directed according to any positive isolates. There is convincing 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 now used particularly dexamethasone. Tocilizumab has also been proven to be of benefit. The EBMT provide some guidance on treatment options and teams are strongly recommended to work with multidisciplinary teams including specialists from infectious disease, infection control, respiratory medicine and intensive care. When possible COVID-19 patients should be entered into clinical trials.

**Due to the higher infectivity of the new variant BMT teams should liaise with their Infection Control teams on the use of enhanced PPE rather than simple surgical masks when working with transplant patients.**

## **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.
- Wearing face masks to provide protection when outside of their home.
- 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).
- Any planned transplant should be reviewed and deferred if possible following the NICE Rapid Guidance.

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, ideally 1 week apart or as a minimum >24hrs apart, but practice and availability of testing may vary between institutions. However, it would be vital to test transplant patients prior to the start of conditioning if they have a history of recent contact with symptomatic individuals. It is strongly advised to use PCR rather than an antigen based testing method.

**Psychological and emotional support:**

Patients will be under considerable additional psychological and emotional stress due to the risks associated with COVID-19. Ensure that sufficient support processes and staff are available to provide support for patients and their families. Staff are also experiencing increasing levels of stress and may need support.

The following table may help in determining transplant prioritisation:

Priority level	Categorisation based on treatment intent and risk:benefit ratio of treatment
1	<p>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.</p> <ul style="list-style-type: none"> <li>- High cure fraction or other clinical and long-term effectiveness</li> </ul>
2	<p>HSCT procedures where there is risk of disease progression or clinical complications if delayed significantly (e.g. &gt; 6 months)</p> <ul style="list-style-type: none"> <li>- Intermediate cure fraction or effectiveness</li> </ul> <p>For example:            High-grade lymphomas and other urgent cases needing autologous HSCT for curative intent (for example diffuse large B-cell lymphoma and Hodgkin lymphomas) based on clinical risk assessment.            Myeloma cases identified as clinical high risk due to disease characteristics or prolonged deferral.</p>
3	<p>HSCT procedures where the risk of disease progression or clinical complications if significantly delayed is low (e.g. over 6 months). This group also includes:</p> <ul style="list-style-type: none"> <li>• procedures where the risks associated with undertaking an HSCT procedure within the current environment are deemed to be higher than the benefits of the procedure</li> <li>• procedures that are not of curative intent or limited long-term effectiveness</li> </ul> <p>For example:            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).            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.</p>

Advise using transplant outcome predictive tools such as the refined disease risk index<sup>2</sup> and HCT-CI<sup>3</sup> (link to on line calculator at [HCT-CI](#)) to inform decision-making for patients.

### **SARS-CoV-2 positive patients pre-transplant:**

There are two considerations regarding the decision to proceed to transplant in patients who develop SARS-CoV-19 infections prior to the start of transplant conditioning:

- 1) The risk from the underlying haematological condition
- 2) The severity of the SARS-CoV-2 infection

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). This differs from the EBMT guidance but in practice assumes that after two negative tests patients would start pre-transplant assessments including organ function with a final test immediately prior to the start of condition. There is growing evidence that some patients may remain PCR positive for many weeks following infection with SARS-CoV-2, possibly because of a limited immune response due to their treatment or disease. Patients that remain PCR positive for SARS-CoV-2 but who are otherwise well will need to be carefully assessed on the risk vs benefit of proceeding to transplant or for any transplant related procedure such as autologous stem cell harvest and they will need to be counselled appropriately.

Patients that experienced moderate to severe COVID-19 symptoms should have sufficient time to allow recovery of critical organ function and general performance status to those similar to pre-COVID-19 infection levels.

In patients with low risk haematological disease a three-month HCT deferral is recommended if they experienced moderate to severe COVID-19 symptoms, with negative SARS-CoV-2 PCR tests and critical organ function tests and performance status similar to pre-COVID-19 levels.

In cases of asymptomatic or mildly symptomatic infection, a deferral of a minimum of 14 days, preferably 21 days, with three negative swab test results, similar to the EBMT guidance.

### **Autologous transplant recipients**

- Programs should review all cases and consider carefully the risk from COVID-19 in their area and the pressures on resources within their hospital.
- Advice will continue to be produced by the disease specific specialist groups, UK Myeloma Forum and Lymphoma Specialist Interest Group.
- Decisions on which patients to prioritise should be based on clinical risk assessments, decided in MDT settings.
- Patients should be advised to practice strict self-protective measures and if at all possible self-isolate for 14 days prior to admission.
- Asymptomatic recipients should be screened for respiratory viruses and SARs-CoV-2 at least once, ideally 24-72 hrs prior to the start of conditioning. Some units may require a negative swab prior to admission to the transplant unit and a repeat sample prior to the start of conditioning.
- If clinically appropriate, GCSF alone mobilisation should be used.
- If chemotherapy priming or GCSF alone, test by SARS-CoV-19 swabs *prior* to start of treatment.
- Autologous donors *do not* require repeated SARS-CoV-19 testing on the day of stem cell harvest unless required to maintain 'COVID-19 safe' patient pathways.
- Autologous SCT for non-malignant indications should be deferred until the current peak of COVID-19 passes.
- Continued suspension of ambulatory transplant operations unless the risks of frequent hospital visits can be mitigated by patient benefit and the decision should be patient-focussed and ratified by the relevant MDT and regional NHSE network.

### **Allogeneic transplant recipients**

- Careful planning required for the preparative regimen as the need to cryopreserve donor cells prior to starting condition may continue (see donor section).
- Patients should be advised to practice strict self-protective measures and if at all possible self-isolate for 14 days prior to admission.
- 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 low risk 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 14 days if possible (EBMT guidelines), test if symptomatic following local infection control guidelines.
- Patients who test +ve pre-SCT should be managed as detailed in the section 'SARS-CoV-2 positive patients pre-transplant'.

## Allogeneic donors

- Advise sibling donors to avoid crowded public places, practise good hygiene and avoid large group gatherings for 14 days prior to donation (EBMT Guidelines).
- Screen by viral swabs donors if symptomatic. If asymptomatic, screen as indicated below.

### Cryopreservation:

The situation regarding the cryopreservation of donor stem cells, either prior to transport or after transfer to the receiving transplant centre, is complex and rapidly changing. There is a growing concern that cryopreservation may reduce the number of viable stem cells following thawing and infusion. Factors that need to be considered are: donor age, stem cells source (BM may be at greater risk of stem cell attrition), country of origin (incidence of SARS-CoV-2 and transport of cells), disease indication for transplant (some indications have higher risk of graft failure). Also consider that donor cells, when cryopreserved, may be prepared in a large number of separate cryobags which may further complicate the transplant.

- The decision to use fresh or cryopreserved stem cells from allogeneic donors must be made on a case-by-case manner as several factors need to be considered that will vary.
- The current rise in incidence of the new variant SARS-CoV-2 has now swung the balance of risk in favour of cryopreservation.
- Anthony Nolan, Welsh Bone Marrow Donor Registry and NHSBT currently continue to 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 the potential for problems regarding transport. However, the situation is extremely dynamic and advice may change and some national registries will check whether cryopreservation is planned. Check on the WMDA website which is frequently updated: <https://share.wmda.info/display/LP/COVID-19+-+Impact+on+Registry+Operations> for the recommendations in specific countries.
- Liaise with local processing laboratories to warn them of each donation and whether to cryopreserve or not.
- If fresh cells are to be used, it is strongly advised that 'back-up' donors including alternative unrelated donors, haplo-identical donors and cord blood stem cells are identified ahead of the start of conditioning. The Anthony Nolan has agreed to fully work up alternative donors.
- The BSBMTCT strongly encourage centres to return information on transplant outcomes following the use of cryopreserved allogeneic donor stem cells to the Anthony Nolan and BSBMTCT survey.

### Other allogeneic donor issues:

- Anthony Nolan and some other registries will arrange SARS-CoV-2 testing of unrelated donors at the medical and repeated on the first day of 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.
- Donors should be screened twice, once at the medical prior to start of GCSF and again on the first day of harvest.
- Donors will be excluded from donation for 14 days from the *resolution of symptoms* if they had confirmed COVID-19 or if PCR positive for SARS-CoV-2 at screening with or without symptoms. If no suitable alternate donors and SCT urgent, perform risk assessment and lease with registry for unrelated donors. In this situation the recipient should be involved in the discussion and be informed of the donor situation.
- Donors should be deferred for 14 days if in close contact with COVID-19 case (EBMT recommendations) and have at least 2 negative swabs prior to starting harvest procedure.
- Identify back-up donor from different country or cord in case harvesting/transport of 1<sup>st</sup> 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.
- Advise avoiding bone marrow as the stem cell source as access to theatres may be limited and prone to sudden cancellation depending on local circumstances.
- 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, ideally none except in exceptional circumstances.
- 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.
- There is evidence of prolonged viral PCR positivity in patients post-transplant. It is possible that these patients may be shedding viable virus. Such patients may remain relatively well but should be managed in ways to minimise transfer of virus to other patients and staff with strict viral isolation policies.
- Management of COVID-19 cases should involve a multidisciplinary team.
- In order to establish COVID-19 free environments and the evidence of asymptomatic carriage and possible transmission it is necessary to screen ward staff routinely in contact with patients. Regular screening of in-patients is also strongly recommended if not already in use. This will depend on local availability of testing but programs should work with their Infection Control and Infectious Disease teams to develop routine procedures.

### After discharge:

- **This will be the time of greatest risk to transplant recipients.**
- Evidence from several retrospective studies confirms the concern that HSCT recipients are at increased risk of severe COVID-19 and have a higher mortality rate than non-transplant individuals.
- At discharge reinforce the need for strict self-isolation of the transplant recipient and if possible the immediate carer(s). During periods of high SARS-CoV-2 incidence in the community advice similar to that given by the PHE at the onset of the first wave should apply:
  - o These apply to autologous SCT recipients who have received an autoSCT *within* the previous 6 months.
  - o These apply to allogeneic SCT recipients who have received an allo-SCT *within* the previous 12 months or for patients with continuing immunosuppressive therapy; with chronic GvHD or ongoing evidence of immunodeficiency based on insufficient CD4 count and/or hypogammaglobulinaemia.
  - o The risk of severe COVID-19 appear to be greatest in older patients, those with co-morbid conditions or with poor performance status irrespective of transplant type <sup>4</sup>.
  - o For newly transplanted patients, the period of rigorous self-isolation starts *from the time of discharge* for 12 weeks.

After the period of rigorous self-isolation patients should follow social distancing behaviour to minimise the risks of viral infections\*.

- Minimise clinic visits, review how patients travel to the centre and try to reduce risks from public transport. Hospital transport may become limited.
- Set up telephone or video follow-up clinics, explore ways for patients to have blood tests away from busy areas in hospitals.
- As some patients will still require face-to-face visits for review centres must develop strategies to minimise risks to patients attending the hospital.
- There is some evidence that individuals with low vitamin D3 levels may develop more severe COVID-19 disease. It is recommended that patients receive vitamin D3 supplementation (EBMT recommendations), with regular checks on serum levels of the vitamin.

### Staff:

- Healthcare professionals with cough/SOB/fever and loss of taste and smell should not come to work. If possible they should obtain a SARS-CoV-2 swab test.
- Be aware of the less frequent symptoms that have been associated with SARS-CoV-2 infection, staff education and self-reporting procedures must be in place to increase awareness of these symptoms.
- HCP who are coryzal without fever should avoid coming to work and self-isolate for at least 7 days. They should be screened for respiratory viruses (if local arrangements allow) 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 staff should be *symptom free for 7 days and have a negative viral swab by PCR* before working directly with patients, consistent with NICE Guidelines.
- Switch meetings/MDTs to telecons as much as possible and if possible splitting workforce to mitigate risk of large proportion of team being affected at same time
- Avoid work related international travel/ large meetings

- Be aware of the additional psychological and emotional stress that staff will experience and identify measures to provide support.

### **CAR-T therapy:**

Patients are at increased risk peri- and post-treatment to a similar degree to allo-HSCT recipients. Delays in patients awaiting collection of MNCs or for immune-depletion therapy prior to infusion of CAR-Ts are at risk of progression of their underlying disease. This must be balanced against the risks from either acquiring SARS-CoV-2 and the probable high risk of severe COVID-19 if a patient with SARS-CoV-2 proceeds to treatment.

There are additional risks from interruptions in the manufacturing chain. The pharmaceutical companies involved in the manufacture of CAR-T should be contacted directly for up to date information.

### **CTAG**

COVID-19 Therapeutics Advice & Support Group (CTAG) was established through discussion between Drugs and Therapeutics Committees (DTCs) and specialists to provide advice and support in the management of COVID-19 whilst national guidelines evolve. CTAG primarily draws on advice from national sources (NHSE, MHRA, NIHR, CMO's office) and uses published literature with expert opinion when necessary. CTAG's outputs take the format of 'Position Statements'. Two priority statements have been developed:

- *Antivirals* <https://ctag-support.org.uk/docs/antivirals.pdf>
- *Immunomodulatory agents* <https://ctag-support.org.uk/docs/immunomodulators.pdf>

These may be of use in patients with evidence of COVID-19 related secondary HLH.

**Continue to check the most up to date guidelines from the donor registries, disease specific groups and EBMT.**

BSBMTCT Executive

15<sup>th</sup> January 2021

### **References:**

1. Piscocya A et al, Plos One Dec 2020 <https://doi.org/10.1371/journal.pone.0243705>
2. Armand P et al, Blood 2014; 123:3664-3671
3. Sorrow M et al, J Clin Onc 2014; 32:3249-3256
4. Ljungman P, et al, EBMT Annual Meeting; 29.08.2020; Madrid: BMT; 2020.

### **\*Social distancing behaviour examples:**

- Avoid contact with anyone displaying symptoms of coronavirus (COVID-19). These symptoms include high temperature, new and continuous cough, shortness of breath, loss of taste and smell.
- Work from home where possible.
- Avoid non-essential use of public transport, varying your travel times to avoid rush hour, when possible.
- Avoid large gatherings, and gatherings in smaller public spaces such as pubs, cinemas, restaurants, theatres, bars, clubs when these re-open.
- Avoid gatherings with friends and family. If they do need to visit, be extra cautious about hygiene, touching and hand-washing. Protective masks should be worn. Keep in contact using remote technology such as phone, internet, and social media.
- Wear protective masks when in public spaces.

Note: The updated BSBMTCT Vaccination Sub-Committee guidelines on COVID-19 vaccination is posted on the BSBMTCT website as a separate document.