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POSITION PAPER

Australia and New Zealand consensus position statement: use of COVID-19 therapeutics in patients with haematological malignancies

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Abstract

Despite widespread vaccination rates, we are living with high transmission rates of SARS-CoV-2. Although overall hospitalisation rates are falling, the risk of serious infection remains high for patients who are immunocompromised because of haematological malignancies. In light of the ongoing pandemic and the development of multiple agents for treatment, representatives from the Haematology Society of Australia and New Zealand and infectious diseases specialists have collaborated on this consensus position statement regarding COVID-19 management in patients with haematological disorders. It is our recommendation that both patients with haematological malignancies and treating specialists be educated regarding the preventive and treatment options available and that patients continue to receive adequate vaccinations, keeping in mind the suboptimal vaccine responses that occur in haematology patients, in particular, those with B-cell malignancies and on B-cell-targeting or depleting therapy. Patients with haematological malignancies should receive treatment for COVID-19 in accordance with the severity of their symptoms, but even mild infections should prompt early treatment with antiviral agents. The

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issue of de-isolation following COVID-19 infection and optimal time to treatment for haematological malignancies is discussed but remains an area with evolving data. This position statement is to be used in conjunction with advice from infectious disease, respiratory and intensive care specialists, and current guidelines from the National COVID-19 Clinical Evidence Taskforce and the New Zealand Ministry of Health and Cancer Agency Te Aho o Te Kahu COVID-19 Guidelines.

Introduction

We are currently living with high rates of transmission of SARS-CoV-2 in the community. Although the high rate of vaccination has resulted in reduced overall hospitalisation and intensive care unit (ICU) admissions, the risk of severe disease or death from SARS-CoV-2 infection (COVID-19) remains unacceptably high for immunocompromised patients with haematological malignancies.[1] This is because of impaired humoral and cellular vaccine responses, the underlying disease and/or associated therapy, age and comorbidities.[2]

Before the availability of widespread vaccination, a meta-analysis of patients with haematological malignancies and COVID-19 revealed that the risk of death among adult patients was 34%, with patients >60 years of age having a significantly higher risk of death than those <60 (relative risk (RR), 1.82; 95% confidence interval (CI), 1.45–2.27; $N = 1169$).[1] Although vaccination rates have increased dramatically since these data were collected, numerous studies have reported lower rates of seropositivity following COVID-19 vaccination in patients with haematological malignancies and lower antibody titres among those who do achieve a response.[3–7] Adding to the concerns is the issue of prolonged viral shedding in immunocompromised patients and its associated complications, including recurrent illness, challenges in de-isolating patients and psychosocial implications for patients who remain isolated for prolonged periods of time.[4,8] Effective management requires multidisciplinary care and educating the public, patients, community and hospital clinicians.

This position statement, achieved by group consensus, is intended to highlight relevant clinical issues specific to patients with haematological malignancies, but excluding those who are planned for or have received haemopoietic stem cell transplantation or CAR T-therapies, whose needs are addressed by the Australia and New Zealand Transplant and Cellular Therapies (ANZTCT) position statements on vaccination and treatment.[9,10] Given the limitations in current data, the relevant literature has been reviewed and selected by the expert authors. The authorship group includes malignant haematology experts in Australia and New Zealand, who have previously collaborated on guidelines on how to manage these diseases during the pandemic and vaccination.[2,11] Input was sought from key stakeholders, including the Australasian Society of Infectious Diseases, the Haematology Society of Australia and New Zealand, Leukaemia Foundation, Lymphoma Australia, Myeloma Australia and Leukaemia and Blood Cancer New Zealand. Geographic representation, sex balance and diversity of backgrounds and disciplines were considered where possible. This position statement will be regularly reviewed and updated as further data on COVID-19 therapeutics emerge. Updates will be made on the HSANZ website www.hsanz.org.au.

Vaccine responses in haematology patients

Widespread vaccination has been crucial in reducing the morbidity, mortality and community impacts of COVID-19 infection. However, seropositivity or seroconversion following the administration of a COVID-19 vaccine, generally defined as SARS-CoV-2 spike IgG levels above a detection threshold or predefined serum antibody concentration, as opposed to the term seroprotection, which is a more accurate surrogate for clinical protection, can be significantly reduced in patients with haematological malignancies.[3,12] A systematic review including 7064 patients with haematological malignancies after two doses of the COVID-19 vaccine showed that overall the seropositivity rates were 62–66%.[12] There was a discrepancy in pooled vaccine responses based on the underlying disease, 51% in chronic lymphocytic leukaemia (CLL), 52–55% in lymphoma, 76–80% in myeloma, 87% in myeloproliferative neoplasms (MPNs), including chronic myeloid leukaemia (CML) and 93% in acute leukaemia.[12] These results were similar to those found in another systematic review of 2834 patients which reported serological response was seen in 42% with CLL, 52% with lymphoma, 66% with plasma cell dyscrasias, 83% with MPNs and 86% with acute myeloid leukaemia.[3,7,13]

It is important to note that seropositivity rates also vary with specific treatment and timing of treatment. During active treatment, seropositivity rates have been reported as low as 28% compared to 62% when patients are not on active treatment.[12] Patients with myelofibrosis on ruxolitinib have a reported seroconversion rate of 24% that improves with repeated vaccination.[14] The most vulnerable patient groups are those vaccinated within 12 months of CD20 antibody therapy who had a seropositivity rate of 19% (compared to 61% when vaccination occurred >12 months after treatment).[12] Similarly, patients who had received targeted therapy such as a Bruton kinase inhibitor (BTKi) had a seropositivity rate of 35%.[12] In patients with follicular lymphoma and Waldenström macroglobulinaemia receiving therapy, vaccine responses were reduced compared to treatment-naïve and healthy controls.[13] Only 5 out of 29 poor initial responders demonstrated seroconversion after a third vaccine dose.[13]

CLL patients are inherently vulnerable, with 36.6% of the treatment naïve failing to seroconvert after two COVID-19 vaccine doses. Those who do have low titres of anti-spike antibody and 75% fail to achieve neutralising activity against COVID-19.[5] In one study, those who were seronegative after two vaccine doses, only 23.8% seroconverted after a third dose.[15] A pooled estimate of seropositivity among those who had received anti-B-cell therapies (anti-CD20 antibodies, BTKis or venetoclax) was 13% compared to the initial two doses of vaccination.[5] A large study of 215 patients with CLL showed repeated vaccination could ultimately seroconvert 94.2% of patients. Of those who were seronegative after two doses and 39.7% were seroconverted after three doses. For those who remained seronegative, 40.6% responded after the fourth dose, 46.2% after the fifth dose and 16.7% after the sixth dose.[7] Furthermore, in those who achieve a response, multiple vaccine doses result in a progression rise in anti-spike antibody levels more capable of viral neutralisation activity.[7] Those who do not achieve increments typically fail to respond to additional doses and rely on either passive immunisation or antiviral therapy.[7,16] In a follow-up study of CLL patients with COVID-19, almost all those requiring hospitalisation had anti-spike antibody levels <5000 AU/mL.[16]

Patients with plasma cell dyscrasias have suboptimal COVID vaccine responses compared to normal controls (57% vs 81%).[17] Patients with monoclonal gammopathy of uncertain significance do not have significant differences compared with healthy controls; however, patients with smouldering myeloma and active myeloma do, regardless of treatment.[17] Factors associated with vaccine response include no active treatment (for >6 months) and a complete or partial remission with normal uninvolved immunoglobulin levels.[17] Factors associated with suboptimal vaccine responses include grade 3 lymphopenia, active treatment, those who had received over three lines of previous therapy and those receiving balantamab mafodotin, anti-CD38 or B-cell maturation antigen-targeted therapy.[12,17,18]

Assessment of vaccine responses in MPN is complicated by the heterogeneity of disease (essential thrombocythemia, polycythaemia vera, CML and myelofibrosis) and by differential effects of treatment. In a study of vaccine responses in patients with haematological malignancies, the most profoundly impaired responses were seen with the JAK inhibitor ruxolitinib and the BTK inhibitor ibrutinib.[19] In contrast, the response of CML patients treated with tyrosine kinase inhibitors and MPN patients treated with interferon-α was unaffected (compared to untreated individuals), whereas hydroxycarbamide was associated with reduced antibody titres (approximately 30% of the levels in untreated patients). An adverse impact of JAK inhibitor therapy on immune responses has been shown in several studies and appeared to be most significant in those with myelofibrosis.[20,21]

Serological responses to vaccines directed against seasonal influenza, diphtheria-tetanus-pertussis and haemophilus influenzae B are impaired in recipients of anti-CD20 therapy but improve with time elapsed since anti-CD20 therapy, with the best responses seen beyond 12 months. For example, seroconversion rates for influenza vaccination within 6 months of anti-CD20 therapy were significantly impaired in comparison to disease controls (relative benefit ratio of 0.22 (95% CI, 0.09–0.56) and 0.44 (95% CI, 0.23–0.84) respectively). However, by 6–12 months from anti-CD20 therapy, the difference between groups narrowed, and by 12 months after anti-CD20, the response to vaccination was close to that of controls.[1,3] The profound impact of anti-CD20 therapy on serological response to vaccines is relevant when counselling patients, as they may be at elevated risk of developing severe COVID-19 disease even if fully vaccinated.

There may be discordance between cellular (T-cell) responses to vaccination and humoral (serological) responses. In CLL patients, over 80% of patients had SARS-CoV-2-specific T-cell responses in the normal range,[5] the immune deficit being primarily humoral. This has also been reported in other low-grade lymphomas.[13] A study evaluating serological and T-cell responses after mRNA vaccination in patients with CLL, B- or T-cell lymphoma and myeloma showed that T-cell responses were detected in 86% of patients, as opposed to an overall seroconversion rate of 64.6%.[22] Seventy-four per cent of the patients who were seronegative

demonstrated a T-cell response, and only 13.1% had absent humoral and cellular responses.[22] In myelofibrosis, repeated vaccination improved serological responses but did not overcome the defective T-cell response.[14] The correlation between T-cell responses and risk of severe COVID-19 disease is not well established. Despite this potential preserved cellular protection, it has been observed that over 40% of those who are fully vaccinated and hospitalised with COVID-19 are immunocompromised.[23,24] Finally, there are limited data on the durability of vaccine response among those with haematological malignancies who do respond to vaccination.

Risk mitigation strategies

This group has published consensus position statements on risk mitigation strategies, underlying disease management and vaccination of patients with haematological malignancies during the COVID-19 pandemic.[2,11] Advice in this area is likely to change with infection rates, emerging variants and contemporaneous evidence of immune response durability. If possible, haematology patients should be vaccinated at least 2 weeks before immunosuppressive treatment.[11] However, urgent treatment must not be delayed in order to facilitate COVID-19 vaccination. There is no evidence to support treatment interruptions to avoid vaccination response attenuation, for example, those on oral therapies. Patients should be counselled regarding their risks of COVID-19 disease, including at initiation of treatment. We recommend that patients be provided with clear instructions regarding what to do if diagnosed with COVID-19 in the community.

Pre-exposure prophylaxis

Patients at the highest risk of severe COVID-19 disease are those unable to generate an immune response to vaccination. For these individuals, passive immunotherapy with long-acting monoclonal antibodies was thought to provide much needed additional protection.

A long-acting dual monoclonal antibody, tixagevimab and cilgavimab (Evusheld®), binds to the SARS-CoV-2 spike protein at two sites, to prevent viral entry into host cells. It was reported to reduce the risk of developing symptomatic COVID-19 infection by 77% (95% CI, 46.0–90.0) versus placebo ($P < 0.001$) when tested in patients who were not vaccinated against COVID-19 and who were at increased risk of severe disease because of comorbidities including immune compromise, obesity and COPD.[25] Tixagevimab/cilgavimab may offer up to 6 months' protection following two intramuscular doses, which can be given simultaneously at two different intramuscular sites.[26] However, the data to support the use of tixagevimab/cilgavimab were produced prior to the emergence of B1.1.529 as the dominant variant. The newer variants, including BA.1, BA.2 and XBB, have acquired mutations in the spike glycoprotein, which have reduced the effectiveness of tixagevimab/cilgavimab, as demonstrated by *in vitro* studies.[27] There is some evidence that the neutralising activity of tixagevimab/cilgavimab against the BA.5 variant may be improved[28]; however, this is an area of evolving data, and at the time of publication, monoclonal antibodies, such as tixagevimab/cilgavimab, are not recommended for the prevention or treatment of COVID-19 infection by the national regulatory bodies in Australia and New Zealand, US Food and Drug Administration, Infectious Diseases Society of America and NICE guidelines UK.

Given the reduced efficacy of vaccination in patients with haematological malignancies, monoclonal and polyclonal antibodies preparations may play an ongoing role, and future development will be focussed on targeting epitopes which are less likely to change with variant evolution. The groups which would benefit most from effective prophylactic therapy are:

(in order of least to more likely to respond to vaccination):

- Patients on BTKi, BCL2 inhibitors and JAK2 inhibitors and patients who have received anti-CD20 therapy in the last 12 months.
- Patients who have received anti-CD38, anti-antibody drug conjugates and bispecific agents in the past 6 months.
- Patients with CLL, other lymphoid malignancies and multiple myeloma who are considered clinically unlikely to respond to vaccination.
- Patients with acute leukaemia or myeloid disorders who are considered clinically unlikely to respond to vaccination.

During community COVID-19 spread, selection of an appropriate facility for the delivery of this treatment may require consideration of both patient exposure risk and resource constraints. Haematology units need to consider implementation strategies to ensure patients are informed of their eligibility and to facilitate equitable access.

Treatment

This group supports treatment guidelines by the National COVID-19 Clinical Evidence Taskforce and the New Zealand Ministry of Health and Cancer Agency Te

Aho o Te Kahu COVID-19 Guidelines.[29,30] The authors acknowledge that, at the time of writing, the efficacy of monoclonal antibodies is limited, and the emerging SARS-CoV-2 variants may render some products unsuitable. Furthermore, the data supporting the treatments discussed below do not include younger children.

Mild to moderate COVID-19

Anti-SARS-CoV-2 monoclonal antibodies

Sotrovimab is a targeted recombinant human monoclonal antibody, which was previously found to reduce the risk of disease progression, emergency department (ED) presentations and ICU admissions in mild to moderate disease.[31] The activity of this agent depends on the underlying variant of SARS-CoV-2 and has been shown *in vitro* to retain neutralising activity against BA.1 but significantly reduced activity against BA.2 and BA.5.[27] Given the current viral landscape, Sotrovimab is no longer recommended for routine use.[30]

Antiviral agents

Nirmatrelvir plus ritonavir (Paxlovid): Nirmatrelvir is a protease inhibitor, and ritonavir, when used in combination, inhibits its CYP3A metabolism. Paxlovid is indicated in patients with mild COVID-19 disease and no oxygen requirement who are within 5 days of symptom onset. The treatment course is nirmatrelvir 300 mg (2 × 150 mg) plus ritonavir (100 mg) po bd for 5 days. It is contraindicated in severe liver disease and in those with severe renal impairment (eGFR <30 mL/min/1.73 m^2). Dose reduction (nirmatrelvir 150 mg + ritonavir 100 mg) is recommended in patients with eGFR 30–60 mL/min/1.73 m^2. There are multiple drug interactions to be aware of with the use of Paxlovid. The ritonavir component is a strong CYP3A inhibitor and can increase concentration and toxicity risk of many cancer therapies, including BTK inhibitors, venetoclax, brentuximab, vincristine, ruxolitinib and prednisone. Paxlovid increases serum concentrations of these drugs and therefore the risk of their adverse effects. Avoiding the combinations or dose reductions of these agents with clinical monitoring is recommended if combined. Of particular concern is the increased concentration of venetoclax; this combination should be avoided during the venetoclax dose escalation phase of venetoclax because of the elevated risk of tumour lysis syndrome. Supportive agents, including azole antifungals such as voriconazole and immunosuppressants such as ciclosporin, are also affected by ritonavir and are likely to require dose modification and/or close therapeutic drug monitoring.

Remdesivir is a direct-acting nucleotide prodrug inhibitor of the SARS-CoV-2 RNA-dependent RNA polymerase. This agent is an option in non-hospitalised patients with mild to moderate COVID-19 who are at high risk of progressing to severe disease. It should be started within 7 days of symptom onset. It is administered intravenously for 3 days (200 mg dose on day 1, then 100 mg daily on days 2 and 3). Hospitalised patients should receive remdesivir for 5 days or until hospital discharge, whichever comes first. It should also be administered in a monitored setting because of the risk of hypersensitivity reactions. It is contraindicated in severe liver disease (ALT >5 × upper limit of normal, or ALT >3 × upper limit of normal and bilirubin >2 × upper limit of normal) and in those with severe renal impairment (eGFR <30 mL/min/1.73 m^2) unless receiving dialysis. It is recommended to test liver function, including synthetic function with a prothrombin time and kidney function prior to initiation, and to repeat during treatment if indicated. *In vitro*, remdesivir is a minor substrate of cytochrome P450 (CYP) 3A4 and a substrate of the drug transporters organic anion transporting polypeptide (OATP) 1B1 and P-glycoprotein, so therapy should be monitored in patients on amiodarone as it enhances the hepatotoxicity of remdesivir.

Molnupiravir (Lagevrio): Molnupiravir is a ribonucleoside analogue that inhibits SARS-CoV-2 replication. It is no longer recommended for the treatment of COVID-19 infections. Based on the outcome of the PANORAMIC trial, which demonstrated that there was no reduction in hospitalisations or death in high-risk patients who acquired COVID-19 and were treated with Molnupiravir.[32]

Steroids: Inhaled budesonide and systemic dexamethasone are adjunctive treatments, the latter indicated in patients who have developed an oxygen requirement. Prolonged and high steroid use in patients with haematological malignancies should be supported with PJP and antiviral and antifungal prophylaxis as clinically indicated.

Moderate to severe disease

Patients with haematological malignancies and moderate to severe disease because of COVID-19 infection should receive multidisciplinary care from experts in intensive care, infectious disease and respiratory medicine in collaboration with the treating haematologist. In addition to standard COVID-19 management strategies such as anticoagulation, prone nursing and oxygen supplementation, the haematologist can assist in providing guidance regarding the level and duration of anticoagulation and immunosuppression of the patient depending on the treatment and

underlying disease. Haematologists can oversee bleeding risk in the context of cytopenias, manage therapeutic drug monitoring, for example, in patients on antifungal prophylaxis and viral reactivation risks and can suggest the escalation of care or adjuncts specific to the needs of patients with haematological malignancies such as blood product support, intravenous immunoglobulin (IVIG) for patients with hypogammaglobulinaemia or granulocyte colony-stimulating factor (GCSF) for neutropenic patients. Although the specific role of IVIG or GCSF in COVID-19 infection is unknown, it is the expert opinion of this group that these adjuncts should be used as per standard of care for immunosuppressed haematology patients with severe infection.

Monitoring of patients with COVID-19

We recommend that patients with COVID-19 receive standard-of-care monitoring through their local hospital COVID-19 pathway, as well as regular review, by Telehealth where appropriate, by a haematologist or clinician experienced in managing immunocompromised patients, to advocate in the event of deterioration, to monitor disease resolution and to ensure that disease-related follow up is not overlooked. If patients are on ongoing treatment for their underlying haematological malignancy, close follow-up to screen for recurrence of symptoms that may necessitate re-testing and retreatment is needed.

Prolonged viral infection, issues with de-isolation and viral reactivation

Immunocompromised individuals can also have prolonged COVID-19 infection and viral shedding,[33–35] which in part may relate to the development of T-cell exhaustion.[2] Consequently, this can cause difficulty in de-isolating patients following infection, as well as delayed manifestations of COVID-19. Anecdotally, there have been several cases of patients experiencing re-infection or failure to clear infection within the first few months of infection. There is mixed guidance regarding surveillance testing and re-treatment. Increasingly, the use of PCR cycle threshold (Ct) and viral cultures may be used to guide management and de-isolation of patients with persistent PCR positivity.[36,37] Cycle threshold on PCR testing correlates inversely with viral load and is a surrogate marker proposed for clearance testing. Assays vary in sensitivity, making identification of a universal Ct cut-off difficult; however, higher Ct values are thought to be associated with a low risk of infectivity. Haematologists should liaise with local infection control, microbiology and infectious diseases teams to interpret local values. Viral culture is also useful if positive; however, test accuracy is dependent on specimen quality, so negative results should be interpreted with caution and in conjunction with Ct values. Correlation between high Ct and negative viral culture has been established. Viral culture may not be readily available at all centres. If viral culture is not available, then high Ct, symptom resolution and negative rapid antigen test could be relied on to determine the safety of de-isolation. Importantly, symptom recurrence following the resolution of symptoms should prompt re-testing.

COVID-positive patients who remain SARS-CoV-2 culture positive, have low Ct values or have declining Ct values after a course of treatment should be evaluated for additional or continuing antiviral therapies in consultation with their haematologist and a medical virologist infectious diseases/microbiology specialist with expertise in managing COVID-19. No recommendation to de-isolation can be made, whereas there is evidence of ongoing replication-competent viral shedding; however, additional psychosocial support should be offered if this resource is available given the impacts of prolonged isolation in this patient population.[7] In a persistently positive patient who remains SARS-CoV-2 culture positive or who has falling Ct values following treatment, the decision to release from isolation should be made by the treating clinician and local infectious diseases/infection prevention teams.

Mitigating treatment delays because of COVID-19 positivity

Patients initiating chemo- or immunotherapy for a haematological malignancy in a hospital setting should be screened for COVID-19 by PCR or rapid antigen testing. If possible, we recommend delay of therapy until PCR negative and asymptomatic. Optimal delay between infection and treatment is unknown, and proceeding with treatment may need to be weighed against the severity of symptoms and the urgency of treatment. If patients are a close contact prior to treatment, we recommend a 14-day deferral period if possible, given the infection latency period. We recommend that patients who become positive following initiation of therapy should be treated as described above with COVID-appropriate treatment, and the decision to proceed with therapy should be based on clinical urgency and need.

Long COVID-19

Long COVID-19 is often a debilitating multisystemic illness encompassing myalgic encephalomyelitis/chronic fatigue syndrome, dysautonomia, impacts on multiple

organ systems, and vascular and thrombotic abnormalities.[38] Hypothesised mechanisms include viral persistence, neuroinflammation, hypercoagulability and autoimmunity.[38] Incidence in the general population is at least 10% of COVID-19 patients,[38] but the incidence and in patients with haematological malignancies has not been reported. In the era of recurrent COVID infections which are associated with an increased risk of long COVID-19, it is possible that patients may present with haematological malignancy and long COVID-19 and that one may precede or clinically obfuscate the other. Evidence based diagnostic and therapeutic options are yet to be established.[38] We recommend, where possible, considering multidisciplinary approaches, in collaboration with clinicians with relevant expertise. Local models for screening, assessment and management of long COVID-19 are emerging.

Summary of recommendations

Prevention

- Patients should be counselled regarding their increased risk of severe COVID-19 infection in the setting of sub-optimal vaccine responses (consensus opinion).
- Patients should ideally be fully vaccinated 2 weeks prior to treatment as per local guidance, but crucial therapy such as induction therapy for acute leukaemia must not be delayed (consensus opinion).
- Patients should be counselled regarding their risks of COVID-19, including at initiation of treatment (consensus opinion).
- Provide clear patient education regarding actions to take in the event of community COVID-19 diagnosis (consensus opinion)
- Patients should not be treated with pre-exposure or post-exposure monoclonal antibodies in the current viral landscape (current evidence and consensus opinion).

Treatment

- Patients with mild to moderate COVID-19 should be offered antiviral treatment as early as possible (current evidence).
- Remote care services to manage COVID-19-positive patients in the home and the hospital setting require oversight by a haematologist or clinician experienced in managing immunocompromised patients (consensus opinion).
- COVID-19 infection should be managed in accordance with best practice at the time of diagnosis, as advised by infectious diseases, respiratory and intensive care specialists, and in line with current guidelines from the National COVID-19 Clinical Evidence Taskforce and the New Zealand Ministry of Health and Cancer Agency Te Aho o Te Kahu COVID-19 Guidelines (consensus opinion).
- Site-specific treatment pathways in patients with haematological malignancies with COVID-19 are encouraged to ensure supply and facilitate timely administration of treatments (consensus opinion).
- Caution is recommended regarding potential drug interactions and renal and liver impairment when using nirmatrelvir plus ritonavir (current evidence).

Post-infection monitoring and de-isolation

- Guidelines in this area are rapidly evolving, and confirmation with local regulations is recommended.
- Consider the use of PCR Ct and viral cultures to guide management and de-isolation of patients with persistent PCR positivity (consensus opinion).
- Patients with persistent positivity, where viral culture is not available; Ct value and symptom resolution could guide de-isolation (consensus opinion).
- In persistently positive patients, discussion with local infectious disease specialist is recommended, and extended psychosocial supports should be offered where possible (consensus opinion).
- Symptom recurrence following resolution of symptoms should prompt re-testing (consensus opinion).
- Patients with long COVID-19 where possible should be managed in collaboration with clinicians with relevant expertise (current evidence and consensus opinion).

Mitigating COVID-related treatment delays

- Patients initiating chemo- or immunotherapy for a haematological malignancy in a hospital setting should be screened for COVID-19 by PCR or rapid antigen testing (consensus opinion).
- If positive, we recommend delay of therapy until PCR negative and asymptomatic if possible (consensus opinion).
- Optimal delay between patient infection and proceeding to treatment is unknown, but this needs to balance the urgency of treatment and severity of symptoms (consensus opinion).

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