Australia and New Zealand Transplant and Cellular Therapies COVID19 Vaccination Consensus Position Statement

Australia and New Zealand have achieved very good control control of community spread of SARS-CoV-2 during the global pandemic due to highly effective public health interventions.(1, 2). Amongst autologous and allogeneic haematopoietic stem cell transplant and CAR-T cell (TCT) patients, there has been 1 death and <5 infections reported to date.

Haematology patients including bone marrow transplant patients are at high risk of complications and death from COVID-19 with an estimated mortality of up to 36%, which is comparable to the mortality rate of aged care residents (3-5). While mortality risk in paediatric patients (estimated at 4%) is lower, it is much higher than in healthy children (4). The rates of severe disease requiring ventiliation is estimated at 15% and 13% in allogeneic and autologosus stem cell transplant recipients respectively. Factors associated with a higher risk of mortality include age >50 years; male sex and development of COVID-19 within 12 months of transplantation (5). Furthermore, preliminary reports suggest that immunocompromised haematology patients have prolonged virus shedding and the potential for accelerated viral evolution (6-8). This data should inform future preventative efforts as both countries commence their vaccination campaigns.

At time of writing there are two vaccines of relevance in Australia and New Zealand. The Pfizer/BioNTech SARS-Cov-2 vaccine is a first-in-class mRNA vaccine which in an international phase 3 study was administered to 43,448 participants aged 16 or older in a two dose regimen 21 days apart. The vaccine was 95% effective against symptomatic COVID-19 from seven days after the second dose. Efficacy was consistent across age, gender and ethnicity, and no serious safety concerns were reported. This trial included a small number of patients (n=76) with leukaemia or lymphoma as a co-morbidity, 36 of whom received the vaccine (9). The AstraZeneca ChAdOx1 nCOV-19 vaccine is a replication-deficient chimpanzee adenoviral vectored vaccine given in a two dose regimen. In a pooled analysis across four studies with varying dosing, overall vaccine efficacy was 70.4% with no serious safety concerns reported.(10) In a subgroup of 8,895 participants who received two standard doses (as will be administered in practice), vaccine efficacy was 62%. Experience with viral vectored vaccines is limited with no evidence in haematology or TCT patients. An alternative vaccine available internationally is the Moderna mRNA SARS-CoV-2 vaccine (mRNA-1273) which is another two dose regimen vaccine administered 28 days apart, shown in a phase 3 study to have an overall efficacy of 94% (11). Other vaccines with potential future relevance in Australia and New Zealand include the Novovax vaccine NVX-CoV2373, the Janssen vaccine Ad26Cov2S and access to the COVAX facility.

None of these studies included immunocompromised participants or TCT patients. There are currently no studies specifically evaluating vaccine response or efficacy in TCT patients. Despite the lack of data, none of these are live vaccines and therefore pose no risk of COVID-19 transmission. While there is no specific data on patients with graft versus host disease, other vaccine products have not shown a risk of worsening acute or chronic graft versus host disease (12).

Given this paucity of data, representatives of all adult and paediatric allogeneic bone marrow transplant centres and cellular therapy centres as well as representatives from autologous only centres in Australia and New Zealand collaborated with Infectious diseases specialists with expertise in TCT on this consensus position statement regarding COVID-19 vaccination in TCT patients in Australia and New Zealand:

1. Given the high mortality risk associated with COVID19 in TCT patients, TCT patients and health care workers delivering care to these patients should be prioritised. (13)
2. The benefits of vaccination outweigh the unknowns in TCT patients without contraindications such as allergies to the vaccine.
3. Patients planned for TCT should be vaccinated as soon as feasible prior to TCT without deferral of TCT.

4. Where possible, vaccination should be completed at least two weeks before planned TCT procedures. (14)
5. It is acknowledged that optimal responses to the vaccine are more likely >6 months post TCT and when patients are off immunosuppressive therapy. Clinicians could consider vaccination as early as 3-6 months post TCT in patients aged ≥16 depending on local and community transmission and clinical factors. (13, 15)
6. The unknown risks in the setting of graft versus host disease (GVHD) are likely to be outweighed by the benefits, particularly in patients with lung GVHD. Therefore, in allogeneic HSCT recipients who remain on immunosuppressive therapy beyond 6 months, consideration should be given to the indication, intensity and expected duration of immunosuppressive therapy when deciding whether to vaccinate or defer. Especially if patients are close to weaning off immune suppressive therapy, a short period of deferral may improve immunogenicity to vaccination and would be appropriate in the context of well controlled community transmission. (13, 15)
7. TCT patients should be advised to continue to practice usual public health measures (e.g. masks, physical distancing, avoiding crowds, ensuring good indoor ventilation, and hand hygiene) in accordance with national and regional guidelines after vaccination as immunogenicity and efficacy in these patients is unknown. (15)
8. Patients with suspected or confirmed previous COVID-19 infection should be vaccinated as per international guidelines as immunity may wane (16, 17).
9. Available vaccines are not licensed for use in patients under the age of 16 years noting that trials are underway to answer this question. (15)
10. Healthy bone marrow transplant donors should be vaccinated as soon as possible prior to donation, preferably within 3 months prior to donation without deferral of donation.
11. Household transmission is one of the most common mechanisms of SARS-CoV-2 transmission. Therefore, vaccination of household members and/or carers of haematology patients with high efficacy vaccines should be prioritised (18).
12. Acknowledging the lack of data for efficacy and safety of COVID-19 vaccines in TCT patients, we recommend highly efficacious mRNA vaccines in TCT patients, health care workers delivering their care and household members. This preference, however, should not delay vaccination with more immediately available vaccines.
13. Where feasible, assessment of vaccine response with post vaccination serology testing should be performed in TCT patients.
14. Studies to determine the optimal vaccine, timing, number of doses and schedule in TCT patients are urgently needed. It is also important to consider the role of donor vaccination and the role of vaccination in paediatric TCT patients since this cohort was excluded from the pivotal above mentioned studies.

These statements will be regularly reviewed and updated as further data on vaccines emerge. Updates will be made on the ANZTCT website www.anztct.org.au.

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