ASH-ASTCT COVID-19 Vaccination for HCT and CAR-T cell recipients: Frequently Asked Questions (v2.0)


Introduction
The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic continues to cause excess morbidity and mortality in the US and worldwide. Hematopoietic cell transplant (HCT) and chimeric antigen receptor T cell (CAR T) recipients are at higher risk for serious complications from the virus, including hospitalization, ICU admission and death from COVID-19 (1-4). These patients are also burdened with other comorbidities associated with COVID-19-related mortality, including older age, cardiovascular disease, renal dysfunction and high-level immunosuppression among many others, which further deepen and drive worse outcomes.

In the US, two novel messenger RNA (mRNA) vaccines and one novel adenovirus vector-based vaccine have been approved through the Food and Drug Administration’s Emergency Use Authorization, these are listed in table 1. The BNT162b2 (Pfizer/BioNTech) and the mRNA-1273 COVID-19 vaccines (Moderna), have both been shown in large phase 3 clinical trials to be over 90% effective at preventing lab confirmed COVID-19 illness and severe infections (5, 6). The single dose recombinant, replication-incompetent adenovirus serotype 26 vector-based vaccine (Ad26.COV2.S) (Johnson& Johnson/Janssen) reduced the incidence of symptomatic COVID-19 with a reported overall efficacy of 66.1% (72% in the USA) based on data from the phase 3 clinical trial. The overall lower efficacy was thought to be due to newly emerging SARS-CoV-2 variant arising from South Africa [20H/S01Y.V2 variant (B.1.351)] which was the predominant strain circulating in South Africa at the time of the clinical trial and accounted for 95 % of the sequenced isolates.

Despite varied approaches to local allocation of vaccines among states and US territories, HCT and CAR T cell recipients should be amongst the first patients to receive vaccination, when available, although data on vaccine efficacy are not yet available within the HCT or CAR T cell recipient populations and the vaccine immune response are likely to be blunted compared to healthy individuals. However, despite the lack of data, the high level of protection afforded to those vaccinated in the clinical trials and overall safety of the vaccine in clinical trials and post EUA experience, the American Society of Transplantation and Cellular Therapy (ASTCT) and the American Society of Hematology (ASH) fully support early access to vaccines for these vulnerable patients, their caregivers, family and household contacts when and if vaccine supply permits.

This document will be updated periodically when new data becomes available. All current guidance and responses are based on opinions of the ASTCT/ASH COVID-19 Vaccine expert panel. Furthermore, the expert panel recognizes that vaccine supply varies between states due to federal and state allocation, and our opinion is not meant to supersede vaccine eligibility as determined by the state or federal government.
Table 1: List of currently approved COVID-19 vaccines under Emergency Use Authorization in the US

<table>
<thead>
<tr>
<th>Platform</th>
<th>Vaccine</th>
<th>Manufacturing Company</th>
<th>Age limit (years)</th>
<th>Number of doses/intervals (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mRNA</td>
<td>BNT162b2</td>
<td>Pfizer and BioNTech</td>
<td>≥ 16</td>
<td>2 doses/ 3 weeks apart</td>
</tr>
<tr>
<td>mRNA</td>
<td>mRNA-1273</td>
<td>Moderna</td>
<td>≥ 18</td>
<td>2 doses/ 4 weeks apart</td>
</tr>
<tr>
<td>Recombinant adenovirus vector</td>
<td>Ad26.COV2.S</td>
<td>Johnson &amp; Johnson/Janssen</td>
<td>≥ 18</td>
<td>1 dose</td>
</tr>
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Subsection A: Recommendations on timing of COVID-19 vaccine in HCT and CAR T cell recipients, and considerations for delay

When is the recommended time to administer the available COVID-19 vaccines to autologous HCT, allogeneic HCT and CAR T cell recipients?

HCT or CAR T cell recipients are often immunosuppressed for months afterwards due to conditioning regimens, maintenance therapy, immunosuppressive therapy, hypogammaglobulinemia or development of graft versus host disease (GvHD, in allogeneic HCT recipients); these factors may lead to a blunted immune response and affect vaccine efficacy (7-9). Yet by delaying immunizations, these patients are at risk of severe and life-threatening COVID-19 if they acquire the infection (1-4). Based on prior antigen-based vaccine trials in allogeneic HCT recipients, initiating vaccination series 3 months versus 6 months after transplantation did not affect induction of immunogenicity (8, 10-12). Clinical trial data to determine the optimal time to initiate vaccinations in HCT and CAR T cell recipients is unfortunately lacking but is of high priority. One potential concern is the efficacy of the Ad26.COV2.S (Johnson & Johnson/Janssen) vaccine in patients with prior adenovirus infection. This was noted with the use of recombinant adenovirus serotype 5 (Ad5) (13). As adenovirus serotype 26 (Ad26) does not commonly circulate in the general population, preexisting antibodies to this strain is unlikely. It was also reported in the phase 1 trial for Ad26.COV2.S (Johnson & Johnson/Janssen) vaccine that levels of Ad26 neutralizing antibodies did not correlate with vaccine efficacy (14). On another note, the different currently available COVID-19 vaccines were not evaluated head to head with each other, making it improper to compare vaccines effectiveness based only on phase 3 trial data that compared each vaccine to a placebo.

Based on the current evidence of high efficacy and safety in the general patient population including individuals with underlying conditions, the current mRNA SARS-CoV-2 vaccines could be offered as early as 3 months to HCT and CAR T cell recipients to prevent infection and severe disease although efficacy may not be optimal as suggested in situations of influenza community outbreaks (11). At this time, no preference of vaccine formulation is recommended and patients are encouraged to receive whichever formulation is available.
When should delay of vaccination be considered in HCT or CAR T cell recipients?

Cytotoxic or B-cell depleting therapies after HCT or CAR T cell therapy are often used for maintenance therapy but may contribute to poor vaccine immune response (15). Patients planned for such therapy should complete their SARS-CoV-2 vaccination when feasible prior to initiation or in between cycles of cytotoxic or B-cell depleting therapies if possible. Based on phase 1 trial for the mRNA SARS-CoV-2 vaccines, peak neutralizing antibodies developed 7-14 days after the second dose of the vaccine series, in patients without prior infection (16). Similarly, a rise in neutralizing antibodies was seen 15 days after a single dose recombinant, replication-incompetent adenovirus serotype 26 vector-based vaccine in phase 1 studies (14, 17). HCT and CAR T recipients who are planned to undergo cytotoxic or B cell depleting therapies could be offered the COVID-19 vaccine prior to therapy and allowed at least 2 weeks to pass after the second dose to allow memory T cell formation prior to giving cytotoxic or B-cell depleting therapies if feasible.

Human intravenous immunoglobulins (IVIGs) are often given to patients with hypogammaglobulinemia due to poor B cell function. As SAR-CoV-2 becomes more widespread, immunoglobulins to SARS-CoV-2 may be detectable in pooled IVIGs. Theoretically, the immunoglobulins would mask the antigens and dampen the immune response to the vaccines and cross react with serologic testing; for this reason, IVIG recipients were excluded from the phase 3 mRNA COVID-19 vaccine trials (5, 6, 18). However, based on recent CDC recommendations, no delay in vaccination is recommended for patients who are receiving IVIGs. These recommendations may change when more data is available.

When should HCT and CAR T cell recipients receive their 2nd dose of the mRNA COVID-19 vaccine if they become infected with SARS-CoV-2 in between doses?

If COVID-19 vaccinees become infected prior to the 2nd dose, the CDC recommends delaying the 2nd dose of either the Moderna or Pfizer series (17). However, these patients were originally restricted from receiving the second dose in the phase 3 clinical trials (5, 6). Further analysis of patients with asymptomatic infection between doses is ongoing. Based on data of patients previously infected with COVID-19 prior to mRNA vaccination series, HCT and CAR T cell recipients infected with COVID-19 between the 1st and the 2nd dose of vaccine series could be offered the second dose of their respective vaccine once symptoms have resolved and isolation precautions are discontinued as there is no indication so far of vaccine-associated enhanced disease (VAED) or other serious adverse events.

When can the current COVID-19 vaccines be given after therapy with SARS-CoV-2 monoclonal antibodies or convalescent plasma (CCP) in HCT and CAR T cell recipients?

No safety and efficacy data have been published on the use of mRNA SARS-CoV-2 vaccines after receipt of SARS-CoV-2 monoclonal antibodies or convalescent plasma by patients as part of their COVID-19 treatment; these patients were specifically excluded from the phase 3 mRNA COVID-19 vaccine trials (5, 6). CDC guidelines recommend delaying vaccination for 90 days based on half-life of the COVID-19 specific antibodies and based on the evidence that reinfection after natural infection is uncommon.
within 3 months (19-21). Currently, we recommend delaying COVID-19 vaccination for 90 days in HCT and CAR T cell recipients if they received either SARS-CoV-2 monoclonal antibodies or CCP, in alignment with the CDC recommendations.

Can SARS-CoV-2 monoclonal antibodies be given to HCT and CAR T cell recipients who develop COVID-19 after receipt of mRNA SARS-CoV-2 vaccines?

Efficacy of mRNA vaccines in HCT and CAR T cell recipients is unknown as clinical trials did not include this patient population. However, if SARS-CoV-2 infection is diagnosed after receiving the COVID-19 vaccine, these patients are still eligible for monoclonal antibodies under EUA guidance or convalescent plasma as part of treatment of COVID-19.

Subsection B: COVID-19 vaccine safety in HCT and CAR T cell recipients

Has the mRNA SARS-CoV-2 and adenovirus vector vaccine platforms previously been investigated in the immunocompromised patient population?

While there are no licensed mRNA vaccines in the US, the use of mRNA-vaccine platforms have been studied for the treatment of cancer and other infections, such as influenza, Zika, rabies, and cytomegalovirus (CMV) (22, 23). While adenoviral vectors have been tested in far more people than the mRNA vaccines, prior to COVID19, no adenoviral vector vaccines had demonstrated prevention of disease in humans, nor any are licensed for use in the USA. There is limited data regarding adenovirus vector-based vaccines in immunocompromised patients. Further investigation is warranted to study the immunogenicity and durability of the response of mRNA and adenovirus-based vaccine platforms in this population. The adenovirus vector (Ad26) used in the Janssen vaccine is replication incompetent and should not pose a safety concern for immunocompromised hosts.

What is known about the safety of mRNA SARS-CoV-2 vaccines?

The mRNA SARS-CoV-2 vaccines were administered to nearly 70,000 study participants, and the safety profile at 2 months median follow up has not raised any significant concerns (6, 24-27). HCT and CAR T cell recipients were excluded from these trials; however, individuals with well controlled HIV infection and CD4>350 were included. Similar to other vaccines, short-term side effects included local injection site reactions, fever, fatigue and headache typically resolved within 1 to 2 days. Adults >55 years of age experienced decreased frequency and severity of local injection site reactions and systemic side effects. Serious adverse effects were seen in 0.5-1.5% of study participants across the three reported trials with similar distribution in control and vaccine arms. Although extrapolation of safety data in the HCT and CAR T cell recipients can be challenging, significant side effects beyond the early post vaccination period are not anticipated and the benefits from vaccines may outweigh any short-term or long-term side effects. Close monitoring for early and late post-vaccination effects is warranted.

What is known about the safety of the recombinant Adenovirus vector SARS-CoV-2 vaccine?
The three recombinant adenovirus vector vaccines in clinical trials make use of different adenovirus serotypes; Ad5-nCoV (CanSino) vaccine uses the human derived serotype 5 (Ad5), ChAdOx1 (Astra Zeneca) vaccine uses the chimpanzee derived serotype AZD1222 and the AD26.COV2.S (Johnson& Johnson/Janssen) vaccine uses human derived serotype 26 (Ad26). To date, only AD26.COV2.S (Johnson& Johnson/Janssen) has received emergency use authorization (EUA) by the FDA. Provided information is limited to the AD26.COV2.S vaccine.

Our knowledge about the safety regarding the recombinant Adenovirus vector SARS-CoV-2 vaccine, AD26.COV2.S, is from the FDA Fact sheet (18). A total of 44,325 people were enrolled into the phase 3 trial for AD26.COV2.S from 8 different countries, including the USA; of those 22,174 received the vaccine (18). Patients with controlled HIV were included as well, but a separate analysis of this population was not released. Like the mRNA vaccines, the most common side effects were pain at the injection site, headaches, fatigue, muscle pain, nausea and fevers. Serious side effects were seen in 0.7% of people who received the vaccine (18). A hypersensitivity event was reported in one case, and no cases of anaphylaxis were reported initially. Yet 2 cases of anaphylaxis were subsequently reported to the FDA. Additionally, numerical imbalances were noted for certain unsolicited side effects, such as thromboembolic events, seizures and tinnitus (18). The FDA fact sheet also notes that the vaccine may have lower efficacy in immunocompromised patients, but no evidence is cited (18). It is again challenging to extrapolate safety to HCT and CAR T cell recipients from the available data, and prior to administration, potential risks and benefits should be weighed. Close monitoring for early and late post-vaccination effects is warranted.

What is the safety of mRNA and recombinant adenovirus vector SARS-CoV-2 vaccines in patients with unknown prior SARS-CoV-2 exposure?

Based on prior studies in Severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) and Middle East respiratory syndrome (MERS), there is a theoretical concern that formation of low titer neutralizing antibodies can precipitate a VAED (28). Although there were no HCT or CAR T cell recipients enrolled in the current clinical trials, there were no concerns for VAED among the general population including a small number of patients who had history of cancer (< 3%) and 1218 individuals with stable HIV. These trials included a subset of study participants who were seropositive for SARS-CoV-2 at time of study entry (9.6% had evidence of previous infection), and participants who developed COVID-19 in the vaccine arm.

What are the risks of serious allergic reactions from mRNA and recombinant adenovirus vector SARS-CoV-2 vaccines?

For individuals with history of anaphylaxis to other vaccines, counselling for a potential similar reaction is recommended and should be monitored for 30 minutes if vaccinated. All individuals who receive vaccine need to be monitored on site immediately following vaccination for at least 15 minutes. It is still recommended for individuals with drug or food allergies to receive the SARS-CoV-2 vaccines. The potential for anaphylaxis to either mRNA vaccines is 2-4.7 per million doses /100,000 (29).
The risk of anaphylaxis reported after the AdV26.Cov2.S (Johnson & Johnson/Janssen) vaccine is extremely low. The only contraindication to this vaccine is an immediate severe allergic reaction to one of the components of the AdV26.Cov2.S (Johnson & Johnson/Janssen) or known allergy to polysorbate. Individuals with history of anaphylaxis to other vaccines, drugs or foods can safely receive the vaccine with close monitoring. Patients who are allergic to ingredients of the mRNA vaccines or those with known allergy to PEG, should consider getting the recombinant Adenovirus vector SARS-CoV-2 vaccine or AD26.COV2.S, and vice versa (30). The CDC also recommends that those who cannot get the second dose of the mRNA SARS-CoV-2 vaccine due to contraindications (such as allergic reaction to the first dose), may consider the single dose recombinant Adenovirus vector SARS-CoV-2 vaccine after at least 28 days have passed after the first dose. The CDC website provides detailed guidance on vaccine ingredients and triaging candidates based on their history of allergic reactions (21).

Is it safe to combine routine post-transplant vaccines with SARS-CoV-2 vaccines?

The safety and efficacy of mRNA SARS-CoV-2 vaccines have not been studied when combined with other vaccines. The mRNA SARS-CoV-2 vaccines should be administered alone, separate from routine post-transplant vaccines. The interval any SARS-CoV-2 vaccine and other vaccines should be at least 14 days both before or after its administration as per the CDC recommendations for the general population (30). COVID-19 vaccination should take priority to routine vaccination.

Is it safe to use COVID-19 vaccines for treatment of an acute COVID-19 in HCT and CAR T cell recipients?

Although data from vaccine clinical trials have demonstrated safety in patients previously infected with COVID-19 (5, 6), the mRNA SARS-CoV-2 nor the recombinant Adenovirus vector vaccines are a replacement for therapy. HCT recipients or CAR T cell therapy recipients with recent COVID-19 should be offered the vaccine once symptoms resolve. The vaccines should not be used for treatment of COVID-19.

What are some considerations or concerns post-COVID-19 vaccines among HCT and CAR T cell recipients?

A study in immunocompetent individuals (<56 years of age) showed that COVID-19 vaccine BNT162b1 elicits CD4+ and CD8+ T cell responses with TH1 cell responses and increased production of IFNγ, IL-2 and IL-12 (31). Similarly, the phase 1 data for the recombinant Adenovirus vector SARS-CoV-2 vaccine reported an increase in IFNγ ELISPOT responses, with no IL-4 response, favoring a TH1 cell response (17). As no transplant recipients were enrolled in the vaccine phase 2/3 trials, it remains unknown whether post-vaccination inflammatory reactions could incite risk for GvHD, hemophagocytic lymphohistiocytosis, and transplant-associated thrombotic microangiopathy. Close monitoring and reporting of such events are strongly advised.

What are the clotting risks associated with administration of the COVID-19 vaccine, in particular the AZD1222 (AstraZeneca) vaccine?
Recently, very few cases of thrombosis at unusual sites (e.g. sinus or cerebral vein thrombosis) and cases of disseminated intravascular coagulation have been observed within four to sixteen days after vaccination with the AZD1222 (AstraZeneca) vaccine in countries outside the US. Affected individuals were mostly women of less than 55 years of age. These thrombotic events were associated with thrombocytopenia, indicating an immunological mechanism as the pathophysiological correlate of these thromboses; the exact mechanisms are currently under investigation.

The overall risk is extremely low, and the German Paul Ehrlich Institute had previously reported 13 cases of sinus or cerebral vein thrombosis after more than 1.6 million AZD1222 (AstraZeneca) vaccine doses administered (https://gth-online.org). According to the current state of knowledge, there is agreement that there is no evidence of thromboses at typical locations (e.g. deep vein thrombosis or pulmonary embolism) to be more frequent after vaccination with AstraZeneca or any other vaccine. There is also agreement that the positive effects of vaccination outweigh possible adverse events, so that individuals should not be discouraged from being vaccinated. Individuals who report dizziness, headache or other neurological symptoms that could pinpoint to a sinus vein thrombosis or symptoms in accordance with other unusual thrombotic locations should undergo further medical evaluation to diagnose or rule out thrombotic events. These thrombotic events have not been noted with other COVID-19 vaccines. The FDA and European Medical Agencies continue to monitor for any additional signals. The AZD1222 (AstraZeneca) vaccine is not available in the USA currently.

**Subsection C: Recommendations for special HCT and CAR T cell recipient populations**

**What additional factors should be considered regarding COVID-19 vaccines for pediatric HCT and CAR T cell recipients?**

In the US, the age limit for current COVID19 vaccines available under emergency use authorization (EUA) are 16 years or greater for the BNT162b2 (Pfizer) vaccine, and 18 years or greater for the mRNA-1273 (Moderna) and Ad26.Cov2.S (Johnson & Johnson/Janssen) vaccines. Table 1 also lists the approved ages for the different COVID-19 vaccines. However, pediatric trials (age>12y) have completed enrollment to test the efficacy and safety of both the BNT162b2 (Pfizer) and Moderna mRNA vaccines; results are expected to be announced in the Spring-Summer of 2021. As in adults, there are no specific data on safety or efficacy available in pediatric HCT and CAR T cell recipients. Recommendations for timing of vaccine administration could be like those in adults. Considerations for vaccination of household contacts, use of serologic assays, use of monoclonal antibodies in the context of vaccination, and co-administration with other vaccines are the same as in adults.

**Should HCT or CAR T cell candidates receive the COVID-19 vaccination to prevent severe disease post HCT or CAR T cell therapy? Should stem cell donors receive the COVID-19 vaccination to prevent disease in transplant recipients?**

To enhance vaccine immune response in HCT recipients, some vaccination strategies have attempted to initiate the vaccine series prior to transplantation, which has shown some success in autologous HCT recipients who receive the first dose of a vaccine series prior to transplantation (32-34). However, these vaccine series included up to 3 doses after transplantation. The current EUAs for the COVID-19 vaccines restrict the use to two doses at specific alternative time only and attempts to deviate from the
established EUAs’ criteria are highly discouraged by the FDA and other societies (35). Additionally, studies in allogeneic HCT recipients receiving influenza vaccination prior to transplant had poor immunogenic responses. At this time, transplant candidates should not be offered the COVID-19 vaccine prior to transplantation nor CAR T cell therapy unless under a research protocol.

Vaccinating stem cell donors prior to stem cell harvesting has not been shown to benefit HCT recipients in prior studies (36, 37). It is also difficult and not feasible in cases of unrelated donors. Stem cell donors should not be offered the COVID-19 vaccine for the sole purpose of benefiting the stem cell transplant recipient unless under a research protocol. However, if the donor has been vaccinated, it may be desirable to wait at least 2 weeks after the second dose before stem cells donation (if possible) as it may provide some protective effect to the recipient.

**Subsection D: COVID-19 serologic testing post vaccination in HCT and CAR T cell recipients**

What is the appropriate timing and the role of serologic testing for COVID-19 after COVID-19 vaccination?

The neutralizing antibodies against receptor binding domain (RBD) of the spike protein are considered protective against reinfection, in contrast to antibodies against the nucleocapsid which are not thought to be protective (38). Available vaccines will only produce antibodies to the spike protein. In healthy individuals who had mild to moderate COVID-19 infections, high titers of neutralizing antibodies lasted up to 5 months after initial infection with robust antibody response occurring by day 30 post infection (39). However, the correlation between COVID-19 antibodies and development of subsequent illness is not clear. Similarly, antibody response is expected with COVID-19 vaccination. Durability of response to COVID-19 mRNA-1273 vaccine was assessed in a subset of vaccine’s recipients (40). Neutralizing antibodies levels were detected in the entire subset at day 119 and 90 days after first and second dose of the vaccine, respectively (40). Lower geometric mean titer was observed in vaccine recipients of age >71 years compared with those <70 years of age (40). However, the antibody response (titer and durability) to COVID-19 vaccine in the HCT and CAR T cell recipients is not known. As the role of serologic testing post vaccination in HCT and CAR T cell recipients is not clear, we do not recommend routine testing with serology unless done under a research protocol.

On the other hand, if serologic testing is desired by the patient or healthcare providers, we recommend testing for SARS-COV-2 antibodies against the spike protein anytime between 30 and 90 days after the second dose of the vaccine. Importantly, some of the commercially available serology assays test for antibodies for the nucleocapsid (N) protein which are markers of prior natural infection from SARS-CoV-2 and not an indication of immune response to COVID-19 vaccines; thus, understanding which serologic assays are available at your disposal is of utmost importance. Additionally, with increasing prevalence of SARS-CoV-2 infections and vaccinations uptake across the US, pooled immunoglobulin (IgG) may contain antibodies against SARS-CoV-2 the spike and nucleocapsid proteins; thus, if serologic testing is desired, we do not recommended testing for SARS-CoV-2 antibodies within 4 weeks of IVIGs infusion due to a possible false positive results.
Subsection E: Recommendations for the close contacts of HCT and CAR T cell recipients regarding COVID-19 vaccination.

Given the lack of published data on the safety and efficacy of the COVID-19 vaccines in immunocompromised patients, what is an effective vaccine strategy to reduce viral transmission to this group of patients?

Viral transmission from COVID-19 positive household contacts poses the highest risk of viral spread to any population (41), but especially to immunocompromised patients. Other close contacts include healthcare workers caring for immunocompromised patients, who are also at increased risk for exposure to COVID19 in the community (42). Vaccination of household members, close contacts and healthcare providers caring for immunocompromised patients, is a central strategy to reduce the risk of viral transmission to immunocompromised patients. All close contacts including healthcare workers are strongly encouraged to get vaccinated if they have access to COVID-19 vaccines.

When should family members, caregivers and/or household contacts who interact with HCT and CAR T cell recipients be administered COVID-19 vaccines?

Although nosocomial transmission can occur and is associated with higher morbidity and mortality (43), community exposure is the most common source for many infections among cancer and transplant patients including COVID-19. With the enhanced focus on infection control efforts in health care settings, including universal masking, social distancing, symptom screening, and frequent SARS-CoV-2 testing for these high-risk patient population, hospital and clinic-based transmission is less frequent. However, family members, caregivers, household contacts are more likely to be the source of transmission of SARS-CoV-2 in the context of being unmasked for prolonged periods of time when in contact with immunocompromised patients, especially in closed and/or poorly ventilated environment. In a recent meta-analysis of 54 studies with 77,758 participants, the estimated overall household secondary attack rate was 16.6%, although higher rates of transmission with a symptomatic household member (41). Models suggest that over 50% of all SARS-CoV-2 infections are a result of transmission from pre-symptomatic or asymptomatic infections (44). Therefore, efforts to separate symptomatic contacts from high-risk immunocompromised patients, although still recommended, may not prevent transmission particularly in-home environments. Furthermore, when infected, prolonged shedding among immunocompromised patients can potentially put other family members and other close contacts at increased risk (45). We recommend that all close contacts of HCT and CAR T cell recipients receive COVID-19 vaccines as soon as it is made available based on local allocation guidelines.

To date, currently available vaccines are known to reduce the severity of COVID-19 disease and its complications, but data on prevention of primary infection or even transmission from those vaccinated has not been adequately demonstrated. For this reason, family members, caregivers, other household members should continue to wear masks, practicing social distancing and follow all current recommendations for preventing SARS-CoV-2 exposure and acquisition.

Is there any foreseeable risk to HCT and CAR T cell recipients by vaccinating their close contacts with the available or soon to be available COVID-19 vaccines?
Currently, approved mRNA vaccines (Pfizer-BioNTech, Moderna), under the FDA’s EUA, do not contain live-virus; thus, these vaccines are safe to use in close contacts of immunocompromised patients.

Similarly, the Johnson & Johnson/Janssen COVID-19 vaccine, uses a replication deficient Adenovirus 26 vector, that is non-transmissible to others. Other candidate vaccines are still ongoing clinical trials or are under FDA review.

The Astra-Zeneca-Oxford Vaccine consists of live simian adenovirus vector ChAdOx1, containing the full-length structural surface glycoprotein (spike protein) of SARS-CoV-2; but the virus has been modified to be replication-deficient and it cannot be transmitted to others. This vaccine is currently not approved for use in the US (25). The Novavax vaccine candidate (NVX-CoV2373), a protein subunit vaccine delivered with an adjuvant (saponin-based Matrix-M™), is not a live-virus vaccine and not yet approved for use in the US (46). Therefore, when or if these vaccines become available for use in the US, there is no foreseeable risk of SARS-CoV-2 transmission to immunocompromised patients or their close contacts.

References
27. Vaccines and Related Biological Products Advisory Committee December 17, 2020 Meeting Announcement.

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