COVID-19 vaccines. Version 7, October 3, 2021

COVID-19 vaccines have been developed, tested, and approved with an unprecedented speed with the aim to control the pandemic. Four vaccines are approved for use within the EU. Two of these based on mRNA technology (Pfizer/BioNTech and Moderna and two using non-replication competent adenovirus vectors (Oxford AstraZeneca and Johnson & Johnson/Jansen. There are also other vaccines in use in some European countries such as the Gamaleya's Sputnik V vaccine in Russia, Serbia, and Hungary and the Sinopharm inactivated vaccine in Hungary. Additional vaccines are being evaluated by the EMA. The rates of infections, hospitalizations, and deaths have decreased in most countries in Europe although some increases have been seen again after the summer mainly caused by the widespread circulation of the Delta variant of SARS-CoV-2

Efficacy data

We focused on mRNA vaccines (BNT162b2; Comirnaty®, Pfizer/BioNTech; Spikevax®, Moderna mRNA-1273), due to the too scarce experience in HSCT patients with replication-incompetent vector vaccines licensed in Europe (Vaxzevria®, Oxford-AstraZeneca; and Janssen/Johnson & Johnson). Results from the phase III study of Pfizer/BioNTech vaccine including 43500 subjects have been published[1]. This showed 94.6% protection after two doses of vaccine given three weeks apart. When results were split by age, the protective efficacy was 94.6% in adults 18 – 65 and 92.9% in adults > 65 years of age. More information can be obtained at the FDA (www.fda.gov) and CDC (www.cdc.gov) websites. BNT162b2 has also been approved for children 12-15 years old in both the EU, the US and in several other countries [2] whereas the result of a phase II-III study with a reduced dose of 10 µg in children 5-11 years old are expected by this year (https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-biontech-announce-positive-topline-results.

The results from the phase III study with mRNA-1273 vaccine have been published as well[2]. This included 30400 subjects each receiving two doses of vaccine or placebo given 4 weeks apart. The protective efficacy was 94.1% (95.1% in adults 18 – 65 and 86.4% in adults above the age of 65). This vaccine has also been approved by the EU and the US FDA for use in children 12 years old and older and studies in younger children are ongoing.

In “real world use”, both mRNA vaccines were shown to reduce asymptomatic SARS-CoV-2 infection, COVID-19 related symptoms, hospital admissions, and mortality in adults[3-6]. Several studies have reported lower rates of immune responses in solid organ transplant recipients [7-15] as well as in patients with some hematologic malignancies such as CLL, multiple myeloma, lymphoma, and myeloproliferative malignancies with the mRNA vaccines compared to healthy individuals[15-25]. The response rates are lower in SOT and onco-hematologic patients compared to healthy individuals. Particularly poor responses were seen with the use of anti-CD20 in the 12 months prior to vaccination, patients under treatment with BTK inhibitors or with daratumumab[15,19,22-24]. Furthermore, the responses after one dose are very poor, leaving the majority of patients unprotected. The second dose improves the serology response. For this reason, prolonging the interval between doses is not recommended for onco-hematologic[20] or HCT patients. There is conflicting data regarding the elicitation of T cell responses especially in patients treated with anti-CD20 antibodies and also the information about the protection induced by T cells alone in the absence of an antibody response is limited. Due to the lower serological response after vaccination in SOT and haematological malignancies, it is highly recommended that patients maintain masks and social distancing regardless of vaccination status, and their cohabiting family members receive vaccination to reduce the risk of transmission.

There have been several studies of varying designs in allogeneic HCT patients[15,26-30]. The response rates (defined according to the authors of the papers) to two doses of mRNA vaccines have varied between 69 – 85% with patients vaccinated earlier after HCT and those with ongoing or recently discontinued immunosuppression having a lower response rate (identified in at least two of the reports). The data regarding CAR T cell patients is more limited. Three small studies have reported response rates between 0 – 36% [15,26,29]

Safety information

For both the mRNA-based vaccines, there have been reports of anaphylaxis although considering the number of individuals vaccinated, these seem to be rare and one third have occurred in individuals with a history of anaphylactic reactions. In addition, there have been reports on Bell’s paresis in a slightly higher frequency in the vaccinated cohorts comparable to what is found with other viral vaccines. More recently rare cases of myocarditis and pericarditis

occurring in particular in younger adults have been reported after vaccination with either of the mRNA vaccines[31]. However, since both vaccines now have been used in a very large number of individuals, a general assessment can be made of a high degree of safety from serious side effects. The safety of mRNA vaccines in non-HCT patients with haematological malignancies seems to be similar as in healthy individuals[15,19,20]. However, three studies have reported a risk for eliciting or worsening GVHD after COVID-19 vaccination of allogeneic HCT recipients[15,28,29].

Safety has become a major issue with the Oxford-AstraZeneca and Janssen/Johnson & Johnson vaccines. There have been well-documented reports of Vaccine Induced Thrombosis and Thrombocytopenia (VITT) syndrome related to unusual site thrombosis, raised D-dimer and anti-platelet factor 4 (PF4) antibodies in some individuals. Clinical and laboratory diagnosis are covered in recent reviews[32]. Although relatively rare, this serious complication has resulted in countries deciding to stop using these. Several cases of capillary leak syndrome (CLS) have been reported with Oxford-AstraZeneca and Janssen/Johnson & Johnson vaccine. Their use is contraindicated in people with a known history of capillary leak syndrome. Guillain-Barré syndrome has also been reported after Oxford-AstraZeneca and Janssen/Johnson & Johnson vaccine vaccination. A high index of suspicion is recommended in order to diagnose and treat this complication as soon as possible. Current safety updates of all vaccines are presented at the EMA website: (https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines/vaccines-covid-19/covid-19-vaccines-authorised#safety-updates-for-authorised-covid-19-vaccines-section). .

A major concern for possibly reduced efficacy of the vaccines is the rapid spread of mutated variants of SARS-CoV-2. The most prominent of these is currently the Delta variant that now cause most SARS-CoV-2 cases in several countries. In Israel, after a period with very low transmission rate, the number of cases started to rapidly increase after approximately six months from when the majority of Israeli adults had received two doses of BNT 152b2 vaccine[33]. The protection against severe disease waned also after > 6 months. One possible reason is the widespread circulation of the Delta variant. However, a recent publication by Thomas et al reported a gradual decline in vaccine efficacy against infection through six months after vaccination but the protection against severe disease was retained at 96.7%[34]. Both the BNT162b2 and the ChAdOx1 nCoV-19 have lower clinical efficacy against the Delta variant (88.0% and 67%, respectively)[35]. Kehner et al reported increasing rates of breakthrough SARS-

CoV-2 infection in a vaccinated cohort of health care workers[36] strongly supporting the need for infection control measures when dealing with HCT and CAR T cell patients.

This waning of immunity and increased risks for reinfections has resulted in that some countries starting administration of a booster dose to high-risk populations and to persons above the age of 60 years. Preliminary data show that the level of neutralizing antibodies increased and individuals, who had received a booster dose had lower rates of infection and severe illness[37]. It has also been reported that a 3rd dose of BNT162b2 given to healthy volunteers increased the neutralization titers 4-7 times and neutralization extended to the Delta variant[38].

Several studies of additional doses have also been performed in immunocompromised individuals mainly those after SOT showing increased possibility of seroconversion as well as higher antibody levels in those, who had already seroconverted after a 2rd dose [39,40]. There is only one study of a 3rd dose performed in 42 HCT patients, who had responded poorly after the 2nd dose [41]. A 3rd dose resulted in a significant increase in SARS-CoV-2 antibodies but only 48% reached the antibody levels the authors had defined as protective. No severe adverse event was noted. Currently several countries are recommending a 3rd dose to immunosuppressed patients including HCT and CAR T cell recipients. The most effective schedule to induce good and long-lasting immunity using a three-dose program has not been determined but it would be logical to in the severely immunocompromised host to plan for a three-dose program up-front.

FDA on 22 September 2021 authorized a booster dose of Pfizer-BioNTech COVID-19 Vaccine, administered at least six months after completion of the primary series, for certain populations (individuals ≥ 65 years; individuals 18 through 64 years of age at high risk of severe COVID-19; and individuals 18-64 years whose frequent institutional or occupational exposure to SARS-CoV-2 puts them at high risk of serious complications of COVID-19 including severe COVID-19 (https://www.fda.gov/news-events/press-announcements/fda-authorizes-booster-dose-pfizer-biontech-covid-19-vaccine-certain-populations). Several other countries have introduced similar policies.

If an HCT recipient has received COVID-19 vaccine before HCT or CAR T cell therapy, the procedures will most likely wipe out all immune memory as for other vaccines. In general, post-HSCT patients should be viewed as “never vaccinated” patients regardless of the pre-HSCT vaccination history of the patient or the donor Therefore, any previous COVID-19

vaccination should be considered discounted, and it is recommended that individuals are re-vaccinated as if they have never received a COVID-19 vaccine. This is in accordance with the situation for other vaccines given pre-transplant and where post-transplant revaccination is recommended[42].

Neither the mRNA nor the vector-based vaccine technology has been used previously in HCT recipients and it is difficult to deduce if one technique would be more likely to produce a more robust immune response in immunosuppressed individuals or would have different safety profiles. Further studies are needed to determine the risk for possible immune activation phenomena such as GVHD when using these vaccines. As a general rule, the vaccines that use SARS live attenuated virus or replicating viral vectored vaccines (vectored by measles, vesicular stomatitis virus, influenza virus, for example) are contraindicated in HCT or CAR T-T cell treated patients. Most of this live-attenuated virus or replicating viral vectored vaccines are currently only in phase 1-2 trials. Similarly, any BCG-approach vaccination is contra-indicated in immunocompromised patients.

National regulations and recommendations should be followed also when vaccinating HCT or CAR T cell treated patients. Prioritization for getting the vaccine will be made by the health authorities in each country. It is our belief that patients early after HCT or CAR T therapy, those on immunosuppression, and those with pulmonary compromise ought to have a high priority together with health care staff caring for these patient groups.

One important issue is regarding vaccination of donors. As always in case of donors, safety of the donor is paramount and there are recommendations to postpone donations in donors developing side effects. Use of live attenuated and replication-competent vaccines in the donors must result in delay of the transplantation according to recommendations by the ECDC. However, no such vaccine is currently licensed in Europe. There is currently no data supporting a transfer of protective or disease attenuating immunity from donors to HCT recipients and therefore HCT schedules should not be adapted to allow vaccination of the donor.

The use of a vaccine for SARS-CoV-2 modifies the interpretation of the serologic test. As the four EMA licensed vaccines induce antibodies against the spike glycoprotein, to evaluate for evidence of infection in a vaccinated individual, a test specifically evaluating IgM/IgG to the nucleocapsid protein should be used.

Since the immunity to SARS-CoV-2 seems to decrease over time and reinfections have been reported, vaccination should be offered to persons regardless of history of prior symptomatic or asymptomatic SARS-CoV-2 infection. In the general population, reinfection is uncommon in the 90 days after initial infection. Thus, immune competent persons with documented acute SARS-CoV-2 infection in the preceding 90 days may delay vaccination until near the end of this period. There is some information suggesting a more robust immune response to mRNA vaccines who had undergone SARS-CoV-2 infection, both in healthy individuals and immunocompromised patients[15]. However, there is currently no data on the duration of protection due to the resolved SARS-CoV-2 infection in the immunocompromised, but this period might be shorter than in the immunocompetent. Therefore, individuals with a resolved SARS-CoV-2 infection should receive the same vaccination program as seronegative individuals. If an individual has received one of the currently available anti-SARS-CoV-2 monclonal antibodies, it is recommended by the USA CDC that vaccination should be deferred for > 90 days as a precautionary measure as the antibody treatment may interfere with vaccine induced vaccine responses (available at https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html)

An interesting possibility is heterologous vaccination when two different vaccines are used to improve the immune responses. Studies are needed in populations such as HCT and CAR T cell treated patients, which are likely to have poor or short-lived immune responses to repeated doses of the same vaccine[43,44].

An important but difficult question is whether determining antibody levels against SARS-CoV-2 should be done before additional vaccine doses are planned or given. Most countries, which have recommended an additional dose to immunocompromised or older individuals do not recommend determining antibody status before an additional dose is given. The response rates to two doses and risk factors for poor response is described earlier in this document. Since the antibody level correlate of protection is not known and furthermore the speed of waning immunity is unknown, the use of serology to determine whether a patient should receive an additional dose vaccine is tentative at best. Such decisions could be taken on individual patient basis for example in CAR T cell treated patients, patients vaccinated early after HCT, or in patients with unstable GVHD. Therefore, no general recommendation for perming post-vaccination serology is recommended at this time.

Currently our assumptions and recommendations are:

1) HCT patients above the age of 12 years should be vaccinated against SAR-CoV-2. Patients could be given whatever vaccine is made available in their country as long as they are not live-attenuated or contain replicating viral vectors. However, only the two mRNA vaccines are licensed for adolescents.
2) Since the only studies so far reported have been performed with the mRNA vaccines, these vaccines seem preferable based on the currently existing information.
3) Response rates are lower than in healthy individuals especially if patients are vaccinated soon after HCT. Therefore, it makes sense to adapt the timing when vaccination should be initiated to the SARS-CoV-2 infection rate in the surrounding community.
    a. If the transmission rate in the surrounding community is high, vaccination could be initiated at the earliest three months after HCT. Whether an earlier start would give any protective effect is currently unknown.
    b. if transmission in the surrounding community is well controlled, it would be logical to wait until six months after transplantation to initiate vaccination
4) There is a risk for worsening/eliciting GVHD after allogeneic HCT. This risk needs to be considered when deciding about time for vaccination.
5) Although side effects are expected as with any vaccine, side effects other than GVHD have not been reported to be more common than in healthy individuals.
6) If an HCT recipient has received COVID-19 vaccine before HCT or CAR T cell therapy, the procedures will most likely wipe out all immune memory as for other vaccines. Therefore, any previous COVID-19 vaccination should be considered discounted, and it is recommended that individuals are re-vaccinated as if they have never received a COVID-19 vaccine.
7) Vaccination against COVID-19 should take priority over the regular vaccinations program. The vaccine should routinely be administered alone. It is prudent to avoid other vaccines 14 days before and after the administration of mRNA or replication-incompetent vector vaccines against SARS-CoV-2 unless the indication for the other vaccine(s) is strong.
8) If an HCT recipient has received COVID-19 vaccine before HCT or CAR T cell therapy, the procedures will most likely wipe out all immune memory as for other vaccines. Thus, they most likely need to be vaccinated as COVID-19 naïve patients post HCT.

9) Reasonable criteria to postpone COVID-19 vaccination based on our current knowledge are:
    a. Severe, uncontrolled acute GVHD grades III – IV.
    b. Recipients, who have received anti-CD20 antibodies such as rituximab or obinutuzumab during the past six months or other B-cell depleting therapy such as inotuzumab or blinatumomab .
    c. CAR T cell patients with B-cell aplasia earlier than six months after treatment.
    d. Recent therapy with ATG or alemtuzumab.
    e. Children < 12 years old
10) Studies of safety, efficacy and immunogenicity of COVID-19 vaccines are recommended, since there is limited information regarding what antibody levels (both to spike or nucleocapsid proteins correspond to clinical protection; and general preventive practices should be continued after vaccination.
11) It is likely that stem cell donors will have been vaccinated prior to donation and the ECDC has issued recommendations as have several registries. The ECDC recommendations state that there is no risk to vaccinate donors with mRNA or protein subunit vaccines and such individuals can donate as long as they are feeling well (https://www.ecdc.europa.eu/en/publications-data/coronavirus-disease-2019-covid-19-and-supply-substances-human-origin). For non-replicating vaccines (mRNA or virus vector-based), it might be reasonable to wait a few days (3-7) after vaccination before starting G-CSF for stem cell mobilization to avoid overlapping toxicities or before collection.
12) An urgent stem cell donation should not be delayed due to vaccination of the donor. If the need for transplant scheduling is not urgent, it makes sense that the donor is vaccinated before donating to decrease the risk for the donor contracting SARS-CoV-2 infection.
13) The ECDC also recommends that donors, who receive attenuated vaccines (virus vector-based or live-attenuated virus vaccines), have to be deferred for four weeks after vaccination.
14) Healthcare workers should be vaccinated to protect the patients, but strict infection control measures need to be maintained since break-through infections occur.
15) House-hold contacts above the age of 12 years old should be vaccinated, especially when the HCT recipient is early after transplant or receiving intensive immunosuppression, as such patients are unlikely to respond to COVID-19 vaccine.

16) Protection against COVID-19 wanes with time and it is probable that it will be shorter in immunocompromised patients than in healthy individuals. A third dose is recommended by several national authorities and should be considered in HCT recpients.
17) No recommendation for post-vaccination determination of antibody level can be given at this time. However, it can be indicated in subgroups of patients such as CAR T cell treated patients, patients vaccinated early after HCT, or in patients with unstable GVHD.

Other vaccines: Influenza vaccination is strongly recommended in HCT and CAR T cell treated patients. It is also logical to ensure that the patient's vaccination status against *S. pneumoniae* is up to date.

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Table 1

General considerations

- **Available vaccines**
    - Four vaccines are approved for use within the EU. Two of these based on mRNA technology (Pfizer/BioNTech and Modena and two using non-replication competent adenovirus vectors (Oxford AstraZeneca and Johnson & Johnson/Jansen.
    - One important question is if any of the vaccines is preferable for use in HCT or CAR T cell treated patients
        - The choice of vaccine has become more difficult with the restricted use of some vaccines in some countries. Therefore, national regulations and recommendations should be followed also when vaccinating HCT or CAR T cell treated patients.
- **Preliminary results of phase III trials, not approved yet**
    - Gam-Covid-Vac (Sputnik V), recombinant adenovirus vaccine (first dose: ADV26; second dose: rADV5) showed an efficacy of 91.6% in preventing PCR-confirmed COVID19 disease (in patients > 60 years of age was 91.8%)
    - Novavax, recombinant prefusion spike protein nanoparticles vaccine, showed an efficacy of 95.6% against the original COVID-19 strain and 85.6% against the UK variant strain.
- **Vaccine data for HCT or CAR T cell treated patients**
    - **Neither the mRNA or the vector-based vaccine technology** has been used previously in HCT recipients and it is difficult to deduce if one technique would be more likely to produce a more robust immune response in immunosuppressed individuals or would have different safety profiles.
    - Several studies have been performed in patients with hematological malignancies and also in HCT and CAR T cell treated patients with the mRNA vaccines. Poorer responses are seen in patients vaccinated early after HCT or in those with ongoing immunosuppression
- **Vaccines safety**
    - The four vaccines now approved by EMA now have been used in a large number of individuals, **a general assessment can be made of a high degree of safety from serious side effects. Nonetheless, there are reports of anaphylactic reactions (**i.e 4.7 cases per million of doses of Pfizer/BioNTech vaccine and 2.5 cases/million dose of Moderna vaccine) and rare but potentially fatal vaccine-induced immune thrombotic thrombocytopenia cases (VITT).
    - There have been reports on GVHD developing or worsening in close temporal association with vaccination.
    - **Vaccines that use SARS-CoV-2 live attenuated virus or replicating viral vectored vaccines** (vectored by measles, vesicular stomatitis virus, influenza virus, for example) **are contraindicated** in HSCT or CART-T cell receptors. **Similarly, any BCG-approach vaccination is contra-indicated** in immunocompromised patients
- **Prioritization of HCT or CAR T patients for getting the vaccine**
    - It is our belief that patients early after HCT or CAR T therapy, those on immunosuppression, and those with pulmonary compromise ought to have a **high priority** together with health care staff managing these patient groups

- **Other vaccines**
    - **Influenza vaccination** is strongly recommended in HCT and CAR T cell treated patients. It is also logical to ensure that the patient's vaccination status against ***S. pneumoniae*** is up to date
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- **Variants of SARS-CoV-2 and vaccines**
    - **Neutralization activity induced by vaccination**
        - The rapidly spreading Deltavariant has been shown to have a lower sensitivity to neutralization by all vaccines.
        - This has also resulted in an increased risk for infection, hospitalization, and severe COVID-19 in patients having received only one dose of MRA vaccine.
        - Immunity is also waning over time and several countries are recommending an additional dose of mRNA vaccine to immunocompromised individuals and some also in the elderly and vulnerable populations.
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    - **Clinical efficacy of vaccines**
        - Emerging data shows protection from severe infection and death for Pfizer/BioNTech, Jansen/Johnson&Johnson, Novavax and CoronaVac/Sinovac vaccines in all settings, although the prevention of asymptomatic transmission and mild-to-moderate disease is more variable as shown in difference in protection when studies were performed in different regions of the world. The protection of Oxford-AstraZeneca vaccine against death and severe disease by B.1.351 is uncertain as it didn't prevent mild-moderate cases in a randomised trial.

Recommendations

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1. HCT patients above the age of 12 years should be vaccinated against SAR-CoV-2. Only the two mRNA vaccines are licensed for children. They could be given whatever vaccine is made available in their country as long as they are not live-attenuated or contain replicating viral vectors.

2. **Vaccination in patients that have received convalescent plasma or anti-SARS-CoV2 monoclonal antibodies**
   - Both types of passive antibody therapies may influence immune response to COVID-19 vaccines SARS-CoV-2. If vaccination is considered despite that the patient has had COVID-19, it is recommended to defer vaccination for at least 90 days as a precautionary measure to avoid potential interference of the antibody therapy with vaccine-induced immune responses
3. **Vaccination against COVID-19 should take priority** over the regular vaccinations program.
   - **The vaccine should routinely be administered alone.**
   - **It is prudent to avoid influenza or pneumococcal vaccines within 14 before and after** the administration of mRNA or replication-incompetent vector vaccines against SARS-CoV-2 unless the indication for the other vaccine(s) is strong. With the currently approved two-dose vaccines, this means a postponement of approximately 6 – 8 weeks for other vaccines.

4. **If an HCT recipient has received COVID-19 vaccine before HCT or CAR T cell therapy,** the procedures will most likely wipe out all immune memory as for other vaccines. Thus, they most likely need to be vaccinated as COVID-19 naïve patients post HCT.
   - However, it should be recognized that the current labels for all the licensed vaccines do not include additional doses after the first vaccine series. Thus, it is off-label and this must be taken into consideration if additional doses are contemplated post-HCT

5. **Time after HSCT for vaccine administration**
   - If the transmission rate in the surrounding society is high, vaccination could be initiated at the earliest three months after HCT
   - If transmission in the surrounding society is well controlled, it would be logical to wait until six months after transplantation to initiate vaccination.

6. **Safety**
   - There is a risk for worsening/eliciting GVHD after allogeneic HCT. This risk needs to be considered when deciding about time for vaccination.
   - Although side effects are expected as with any vaccine, side effects other than GVHD have not been reported to be more common than in healthy individuals.

7. **Reaccination of previously vaccinated individuals**
   - If an HCT recipient has received COVID-19 vaccine before HCT or CAR T cell therapy, the procedures will most likely wipe out all immune memory as for other vaccines. Therefore, any previous COVID-19 vaccination should be considered discounted, and it is recommended that individuals are re-vaccinated as if they have never received a COVID-19 vaccine.

8. **Reasonable criteria to postpone vaccination** with our current knowledge are:
   - Severe, uncontrolled acute GVHD grades III – IV.
   - Recipients, who have received anti-CD20 antibodies such as rituximab or obinutuzumab during the past six months or other B-cell depleting therapy such as inotuzumab or blinatumomab .
   - CAR T cell patients with B-cell aplasia earlier than six months after treatment.
   - Recent therapy with ATG or alemtuzumab.
   - Children < 12.

9. **General preventive practices should be continued after vaccination**

- Studies of safety, efficacy and immunogenicity of COVID-19 vaccines are recommended, but positive antibody testing (both to spike or nucleocapsid proteins) is not equivalent with sufficient protection; and general preventive practices should be continued.
- Considering the rapid emergence and spread of SARS-CoV-2 variants with possibly higher risk of vaccine breakthroughs, HCT and CAR T cell treated patients should continue to follow recommendations with the aim to limit the risk for exposure

10. **Donor vaccination against SARS-CoV-2**
    - **It is likely that stem cell donors have been vaccinated prior to donation**
        - The ECDC recommendations state that there is no risk to vaccinate donors with mRNA or protein subunit vaccines and such individuals can donate as long as they are feeling well.
            - They also recommend that donors, who receive attenuated vaccines (virus vector-based or live-attenuated virus vaccines), have to be deferred for four weeks after vaccination.

11. For non-replicating vaccines (mRNA or virus vector-based), tt might be reasonable to leave a few days (3-7) after vaccination before starting G-CSF for stem cell mobilization to avoid overlapping toxicities or before collection.

12. An urgent stem cell donation should not be delayed due to vaccination of the donor. If the need for transplant scheduling is not urgent, it makes sense that the donor is vaccinated before donating to decrease the risk for the donor contracting SARS-CoV-2 infection.

13. Healthcare workers should be vaccinated to protect the patients.

14. House-hold contacts >12 Years old should be vaccinated, especially when the HCT recipient is early after transplant or receiving intensive immunosuppression, as such patients are unlikely to respond to COVID-19 vaccine.

15. Protection against COVID-19 wanes with time and it is probable that it will be shorter in immunocompromised patients than in healthy individuals. A third dose is recommended by several national authorities and should be considered in HCT recipients.

16. No recommendation for post-vaccination determination of antibody level can be given at this time. However, it can be indicated in subgroups of patients such as CAR T cell treated patients, patients vaccinated early after HCT, or in patients with unstable GVHD