

COVID-19 vaccines. **Version 8, January 3, 2021**

It is now exactly one year since the EBMT IDWP produced the first set of vaccination recommendations regarding COVID-19. During this year, COVID-19 vaccines have been developed, tested, and approved with an unprecedented speed with the aim to control the pandemic but we are now seeing failures of long-term protection at least against SARS-CoV-2 infections although the protection against severe disease seemingly holds up better. Five vaccines are approved for use within the EU. Two of these based on mRNA technology (Pfizer/BioNTech and Moderna, two are using non-replication competent adenovirus vectors (Oxford AstraZeneca and Johnson & Johnson/Jansen, and one is a recombinant nanoparticle protein-based vaccine (NVX-CoV2373; Novavax) based on the Spike protein and includes an adjuvant. 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 hospitalizations, and deaths have decreased in most countries in Europe but infections have increased during recent months and the arrival of a new variant, Omicron, has resulted in rapidly rising infection rates and new restrictions in several European countries.

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) or the recombinant nanoparticle protein-based vaccine (NVX-CoV2373; Novavax). Results from the phase III study of Pfizer/BioNTech vaccine including 43500 subjects have been published¹. BNT162b2 has also been approved for children 5 years and older in both the EU, the US and in several other countries with a vaccine efficacy of 90.7% for the ages 5-11 and 100% for the age 12 – 15 years^{2,3}.

The results from the phase III study with mRNA-1273 vaccine have been published as well⁴. This vaccine has also been approved by the EU and the US FDA for use in children 12 years old and older with a vaccine efficacy of 93.3%⁵.

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 adults⁶⁻⁹. Several studies have reported lower rates of immune responses in solid organ transplant recipients¹⁰⁻¹⁸ 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 individuals¹⁸⁻²⁸. 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^{18,22,25-27}

There have been several studies of varying designs in allogeneic HCT patients²⁹⁻³⁹. The response rates (defined according to the authors of the papers) to two doses of mRNA vaccines have varied between 69 and 85%. Different studies have identified different risk factors for poor response with patients vaccinated earlier after HCT, lower lymphocyte counts, GVHD, and those with ongoing or recently discontinued immunosuppression reported as having poorer responses in several of these reports. The data regarding CAR T cell patients is more limited. Three small studies have reported response rates between 0 – 36%^{18,29,32}

No data exist yet regarding the NVX-CoV2373 effect in immunocompromised individuals but the pivotal studies showed a 90.4% reduction of symptomatic COVID-19 cases seven days after the second dose (<https://www.ema.europa.eu/en/medicines/human/EPAR/nuvaxovid>). The side effects reported have been mild to moderate and consisted mainly of classic vaccine side effects including local or systematic symptoms including headache, muscle or joint pain, and tiredness.

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-hematologic²³ 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.

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 very rare. More recently rare cases of myocarditis and pericarditis occurring in particular in younger adults have been reported after vaccination with either of the mRNA vaccines⁴⁰. The reported incidence is higher for mRNA-1273 than for BNT152b⁴¹ and therefore several authorities recommend the PfizerBioNech vaccine for individuals < 18 years. The safety of mRNA vaccines in non-HCT patients with haematological malignancies seems to be similar as in healthy individuals^{18,22,23}. However, three studies have reported a risk for eliciting or worsening GVHD after COVID-19 vaccination of allogeneic HCT recipients^{31,32,34}.

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 reviews⁴². 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-authorized#safety-updates-for-authorized-covid-19-vaccines-section>).

Durability of protection and the impact of SARS-CoV-2 variants

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 although the number of cases with the recently identified Omicron variant is rapidly increasing 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 vaccine⁴³. The protection against severe disease waned also after > 6 months.

However, a 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%⁴⁴. This has also been translated into a lower overall mortality in patients who has received a booster dose⁴⁵. Both the BNT162b2 and the ChAdOx1 nCoV-19 have lower clinical efficacy against the Delta variant (88.0% and 67%, respectively)⁴⁶. Kehner et al reported increasing rates of breakthrough SARS-CoV-2 infection in a vaccinated cohort of health care workers⁴⁷ 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 that most European countries are recommending a booster dose not only to high-risk populations but more broadly. It has 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 variant⁴⁸.

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 2nd dose^{49,50}. The efficacy and safety of giving a 3rd dose is still limited. One study was performed in 42 HCT patients, who had responded poorly after the 2nd dose⁵¹. 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. As a subset of a large French cohort study, 181 patients received a 3rd dose at a median of 54 days after dose 2. The results showed that among 70 patients without a previous response, 41% mounted a detectable response. Furthermore, among 46% with a weak prior response, 85% achieved a good response and finally all 65 patients, who had a good response the antibody level either increased or reached the highest antibody level of the used assay³⁷ However, no data was reported about the risk for GVHD after a 3rd dose. 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 in the severely immunocompromised host to plan for a three-dose program up-front with an interval between the 2nd and 3rd doses being between 4 weeks and 5 months depending on the epidemiological situation.

The recently emerging Omicron variant has been shown to have several mutations in the SPIKE-protein of SARS-CoV-2. The knowledge is still limited but emerging data clearly suggest that double-vaccinated patients are vulnerable to infection with the Omicron variant

of SARS-CoV-2. There have also been several reports suggesting that this variant spreads much more easily than previous variants including the Delta variant and this is supported by that Omicron now is the dominating variant in several countries. So far, most Omicron patients have had mild symptoms and few cases of patients requiring ICU or who have died with this variant have been reported. Whether this is due to the populations so far infected being mostly younger and with less co-morbidities remains to be elucidated. The effects of booster doses on the protection against Omicron is also still unknown. Existing information in public databases suggest that antibodies induced by all vaccines are less effective *in vitro* against infections with the Omicron variant and also the neutralizing capacity of most monoclonal antibodies, the exceptions being sotrovimab and AZD7442 (tixagevimab / cilgavimab), are none to very low. Furthermore, also the neutralizing effect of hyperimmunoplasma is reduced (<https://covdb.stanford.edu/page/susceptibility-data/>).

Data from several studies suggest that a 3rd dose of the BNT162b2 or the mRNA-1273 vaccine can result in increased levels of neutralizing antibodies that possibly can mediate protection against severe disease but that vaccine effectiveness is likely to be lower against Omicron⁵²⁻⁵⁶ (please, see also preprint references at the end of the reference list). A preliminary meta-analysis suggested that a booster with an mRNA vaccine has the potential to raise efficacy to 86.2% against symptomatic infection and to 98.2% against severe disease (Khoury et al: Analysis: A meta-analysis of early results to predict vaccine efficacy against Omicron; <https://doi.org/10.1101/2021.12.13.21267748>).

Some countries are discussing the possibility that an additional (4th) dose either with the same vaccine, a modified vaccine to cover better new variants, or with a different vaccine is needed to protect high risk populations such as the elderly and patients having undergone HCT or CAR T cell therapy. However, there is currently no information regarding efficacy or safety of such an approach.

Post-HCT vaccination in patients vaccinated prior to HCT

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 recommended⁵⁷.

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.

Donor vaccination

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.

Serological assessments

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 patients¹⁸. 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 anti-SARS-CoV-2 monoclonal antibodies, it is recommended by the USA CDC that vaccination should be deferred (with the length of deferral based on the antibody half-life and the indication for monoclonal antibody administration) 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^{58,59}.

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. However, to know if a patient is seronegative could be useful in evaluating the potential benefit of administering monoclonal antibodies either as primary or post-exposure prophylaxis. Of note considering the reduced efficacy of some monoclonal antibodies against Omicron, knowledge about the distribution of SARS-CoV-2 variants in the patient's community is also very important. 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 performing post-vaccination serology is recommended at this time.

Currently our assumptions and recommendations are:

- 1) HCT patients above the age of 5 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 BNT162b2 vaccine is licensed for children 5- 11 years.**
- 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 but can be given together with standard dose inactivated influenza vaccine.** It is prudent to avoid other vaccines **7** 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) 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 < 5 years old

- 9) 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.
- 10) 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/sites/default/files/documents/Supply-SoHO-COVID-19--second-update-erratum-Feb-2021.pdf>). For non-replicating vaccines (mRNA or non-replication competent 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.
- 11) 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.
- 12) Healthcare workers should be vaccinated to protect the patients, **but strict infection control measures need to be maintained since break-through infections occur.**
- 13) **Household contacts above the age of 5 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.
- 14) 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 in HCT recipients. The best timing of a 3rd dose is currently unknown but can be considered 4 weeks – 5 months after the 2nd dose.**
- 15) 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**
 - **Five** vaccines are approved for use within the EU. Two of these based on mRNA technology (Pfizer/BioNTech and Moderna, two are using non-replication competent adenovirus vectors (Oxford AstraZeneca and Johnson & Johnson/Jansen) **and one is a recombinant nanoparticle protein-based vaccine (Novavax).**
 - 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.
- **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
- **Variants of SARS-CoV-2 and vaccines**
 - **Neutralization activity induced by vaccination**
 - **The rapidly spreading Omicron variant has been shown to have a lower sensitivity to neutralization by all vaccines as well as to most monoclonal antibodies and hyperimmune plasma.**
 - **Preliminary data suggest that a 3rd dose of one of the mRNA vaccine can increase neutralizing antibody levels.**

- A third dose of vaccine is now generally recommended by most countries.

Recommendations

1. HCT patients **from the age of 5 years** should be vaccinated against SAR-CoV-2. Only the two mRNA vaccines are licensed for children from 12 years and only the BNT162b2 vaccine is licensed for children 5-11 years.
2. **Vaccination against COVID-19 should take priority** over the regular vaccinations program.
 - **The vaccine should routinely be administered alone with the exception of standard dose inactivated influenza vaccine..**
 - **It is prudent to avoid other vaccines within 7 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.
3. **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
4. **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.
5. **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.
6. **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.
7. **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 < 5.**
8. **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

9. 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.
 - For non-replicating vaccines (mRNA or virus vector-based), it 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.
10. 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.
11. Healthcare workers should be vaccinated to protect the patients **and strict infection control measures need to be maintained since break-through infections occur.**
12. House-hold contacts **from the age of 5 years** 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.
- 13. Protection against COVID-19 wanes with time. New variants such as Omicron are also less sensitive to neutralization than previous variants. A third dose is recommended in HCT recipients**
14. No general 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.