Vaccination against SARS-COV-2 (COVID-19) for Patients with PID

IPOPI will revise and update these recommendations as new evidence is compiled and analysed.

Latest update: 26 Jan 2021

Disclaimer: Please note that all PID patients should consult their PID expert physician before receiving vaccinations.

What is vaccination?

Vaccination (or immunisation) is the administration of a vaccine that contains components of an infectious organism. These stimulate the immune system to make antibodies or T cells that provide protection against subsequent infections by that organism (adaptive immunity). Vaccines are produced using micro-organisms that have been killed (inactivated) or altered (attenuated) in some way so that they resemble the normal bacteria or virus but should no longer cause disease. Attenuated vaccines are also known as live vaccines. Importantly, most patients with primary immunodeficiency (PID) should not be given live-attenuated vaccines as they may cause them to have infections. (*More info on vaccinations here*.)

Vaccination has always been a part of prevention of severe infection not only for the general population but for also for patients with PID. Vaccination protects people against preventable diseases that can be serious and life-threatening. It also helps preventing infectious diseases from spreading easily when a large percentage of the population is vaccinated. This statement gathers the latest information concerning the current vaccination programmes against SARS-CoV-2, the causative agent of COVID-19.

The first vaccines are becoming available

COVID-19 vaccination is an important tool to help stop the pandemic and the first vaccines are now becoming increasingly available (Pfizer/BioNTech, Moderna, AstraZenica/University of Oxford, Sputnik V, Sinopharm…). There are several types of vaccines in development and all of them teach our immune systems how to recognize and fight the virus that causes COVID-19. Sometimes this process can cause side effects, that are generally mild. All COVID-19 vaccines that are in development are being carefully evaluated in clinical trials and will be authorized or approved only if they make it substantially less likely for the recipient to get COVID-19 and they are reasonably well tolerated.

There are several platforms such as: Protein subunit, Viral Vector (non-replicating), DNA, Inactivated Virus, RNA, Viral Vector (replicating), Virus Like Particle, VVr + Antigen Presenting Cell, Live Attenuated Virus and VVnr + Antigen Presenting Cell (*More info here*.) There are currently over 60 vaccines in clinical development. At least an additional 170 vaccines are in pre-clinical development.

Vaccines based on the new mRNA based technologies (*"mRNA vaccines"*) and other types of vaccines have been granted a conditional marketing authorisation (CMA) by the EMA and emergency use authorisation by the FDA in the US and by MHRA in the UK

as well another several countries. The Comirnaty® COVID-19 mRNA vaccine from Pfizer/BioNTech has also received an Emergency Use Listing (EUL) from World Health Organization (WHO), opening the door for countries to expedite their own regulatory approval processes to import and administer the vaccine.

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Currently, there is not enough validated data to establish the mid-term to long-term efficacy and tolerance/side effects for the recently approved COVID-19 vaccines in the population, including patients with PID. However, the general recommendation is that all patients with PID should be vaccinated (provided that they are not live attenuated viral vaccines), especially the ones with known risk factors for COVID-19. It is also recommended that their close contacts should get vaccinated. All PID patients should consult their PID expert physician before receiving vaccinations.

Patients who do not respond to vaccines by measurable antibody titers (such as patients with an antibody deficiency including patients with a profound hypogammaglobulinemia or agammaglobulinemia) should still be considered for vaccination, as the vaccines have been shown to activate the cellular immunity via T-lymphocytes, which may provide a partial protection against COVID-19. This also applies to patients who received a therapy against B-Lympocytes (such as *rituximab*).

Patients (including children) with specific PIDs such as: AIRE deficiency (APS1/APECED), NFkB1 or NFkB2 deficiency as well as diseases leading to alterations of the interferon pathways should be highly prioritised for this vaccination.

Patients who already had COVID-19 and recovered still need to get vaccinated with a COVID-19 vaccine. Current evidence suggests that reinfection is uncommon within 90 days after the initial infection and vaccination may be postponed until the end of this period.

To avoid a co-infection with the influenza virus and COVID-19, it is also recommended that all PID patients and their close contacts be vaccinated against seasonal flu (please refer to your PID expert in order to choose between inactivated vaccines or live attenuated ones).

Two dose schedules

Most COVID-19 vaccines currently being developed require two doses, with varying intervals between the first and second dose (Pfizer-BioNTech: 21 days, Moderna: 28-42 days, Sputnik V: 21 days…).

Side effects

It is normal to have certain reactions after a vaccination. There may be redness, swelling, pain around the injection site and/or fever myalgia. These vaccine reactions are usually mild and last only a few days. So far, severe side effects have been very rarely reported.

Risks associated with COVID-19 vaccines for parts of the population (excl. allergies)

Children: The vaccines from *Pfizer-BioNTech, Moderna* and *AstraZeneca/University of Oxford* have not been tested on children. Vaccination is therefore not indicated for children below the age of 16 for Pfizer-BioNtech, and below the age of 18 for Moderna.

Individuals with COVID-19 risk factors (severe chronic lung disease, diabetes, obesity (body mass index ≥30kg/m^2), high blood pressure, cardiovascular disease, old age): Until now, phase 2/3 clinical trials of mRNA vaccines have not shown any significant adverse effects in this group. This did not include citizens under age 16 and over 85 years.

Immunocompromised persons: In *Pfizer-BioNTech's* phase 2/3 trials, approximately 4% of the people who received the vaccine had a history of HIV infection (without this infection necessarily being accompanied by immunosuppression) or malignancy diseases. Data on efficacy, immunogenicity, or safety specific to this group is not yet available. No data is available on patients with PID. There is no reason to believe that immunosuppression will promote the occurrence of adverse effects, the problem is rather that the vaccine may be less effective.

Immunosuppressed people may receive RNA vaccines if they have no contraindications to vaccination. According to CDC Advisory Committee on Immunization Practices (ACIP; U.S.) and the Joint Committee on Vaccination and Immunisation (JCVI; U.K.) recommendations, patients should be counselled about the unknown vaccine safety profile and effectiveness in immunocompromised populations, as well as the potential for reduced immune responses. It is strongly recommended that patients continue preventive anti-infection measures, as the level of protection after vaccination is not known for an immunodeficient individual.

In the phase 3 trial of the *AstraZeneca/University of Oxford* chimpanzee non-replicant adenoviral vector-based vaccine, immunosuppression was an exclusion criterion for participation.

For *Janssen's* adenoviral vaccine trial, immunosuppression was not an exclusion criterion, the first results of which are expected in Q1 2021. Regarding adenovirus-based vaccines, there might be some degree of immune response against the adenoviral vector that could hamper the specific immune responses to vaccination.

General word of caution: vaccination during an active autoimmune manifestation (such as severe autoimmune cytopenia, glomerulonephritis, inflammatory flare of the Central Nervous System…) should be avoided as this might lead to a risk of flare-up.

Other recommendations

Given the lack of vaccine coadministration studies, it is recommended to avoid concomitant vaccination within 2 weeks of the COVID-19 vaccine dose.

Continued follow-up is advised in order to generate more data on vaccine efficacy and safety in PID population.

Off-label use of the non-LAV COVID19 vaccine can be envisaged by PID experts for high-risk groups as defined above < 18y of age. This off-label use will need approval from the national authorities and from the Ethical Committees involved.

Further reading

- COVID-19 Vaccines: Key facts – by the European Medicines Agency
- Vaccine schedule for members of the European Union
- Eight ways in which scientists hope to provide immunity to SARS-CoV-2
- COVAX: Working for global equitable access to COVID-19 vaccines