ENGAGe
ESGO | European Network of Gynaecological Cancer Advocacy Groups

RECOMMENDATIONS

for gynaecological cancer patients and their relatives

in dealing with the COVID-19 pandemic and other viral infections

A European initiative to improve patient information and education by ENGAGe

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ENGAGe would like to thank its Executive Group members for their constant availability
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Dear patients, relatives, and readers,

The coronavirus, or COVID-19, pandemic has massively changed the whole world, including our everyday lives, both in society and in the health system.

Cancer patients are the focus of special attention, on one hand because they belong to the high-risk patient group and on the other hand because their cancer treatment usually requires very complex and high quality conditions.

Cancer patients are generally considered to be at risk for infections of all kinds, including COVID-19 infections, which can sometimes lead to very serious complications.

But how can a balance be found between this fear for their health and the progression of cancer?

The focus should always be on the best possible treatment of the cancer, even in a pandemic situation. Some steps have to be specially considered and sometimes even adapted as part of the general anti-coronavirus strategy. Most current treatment measures can and should be continued regardless of the pandemic.

The COVID-19 pandemic has posed a great challenge to physicians, medical staff, patients, and their families. The necessary rules and restrictions in society, and also in the health care system, also affect all of them.

A recent European survey of women with gynaecological cancers, including ovarian cancer, breast cancer, and cancer of the uterus, was able to highlight the great uncertainty among patients during the pandemic. Almost one in four patients was more afraid of COVID-19 infection than of cancer progression. We also received many inquiries, which underscored the great uncertainty. Therefore, we decided to write this brochure. Of course, it cannot replace a conversation with your physicians, but it should motivate you to proactively seek a conversation with your medical team.

In addition to the general aspects of the COVID-19 infection, we refer to the various situations that might occur in the clarification of cancer, and also to the surgical and drug treatment of cancer, maintenance therapy, and aftercare. In addition, we deal with other viral diseases such as influenza and colds.

This brochure is a translation of a German version from the German Foundation Ovarian Cancer, a member of the European Network of Gynaecological Advocacy Groups (ENGAGe), and has been modified to this present European version. Please understand that this information and its recommendations must be adapted to your local rules and recommendations and that this brochure is not a substitute for dialogues with your doctors and the medical staff.

We hope very much that you will find our brochure helpful and that it will support you in your medical therapy.

We would be very pleased to receive your feedback and suggestions.

Yours sincerely,

Jalid Sehouli

Contents

1. ACKNOWLEDGEMENTS AND THANKS 2
2. Dear patients, relatives, and readers 3
3. A new virus is in the world 5
4. Virus—what is it exactly? 6
5. Specific and general risk factors for corona inflammation 8
6. General instructions and hygiene rules for cancer patients 9
7. Vaccinations 11
8. What is the difference between a flu and a flu-like infection? 12
9. Which preventive measurements are useful for everyone? 14
10. 3 QUESTIONS, 3 ANSWERS in case of planned clarification of a cancer disease 14
11. 3 QUESTIONS, 3 ANSWERS to surgery / operation 15
12. 3 QUESTIONS, 3 ANSWERS for drug therapy 17
13. 3 QUESTIONS, 3 ANSWERS about radiotherapy 19
14. 3 QUESTIONS, 3 ANSWERS about hormone therapy 20
15. 3 QUESTIONS, 3 ANSWERS on maintenance therapy 21
16. 3 QUESTIONS, 3 ANSWERS for aftercare / follow up 23
17. 3 QUESTIONS, 3 ANSWERS on clinical studies 24
18. Travel as a cancer patient—the rules 26
19. Vaccination, vaccines, immunity 27
20. CONTACTS 35

A new virus is in the world

This novel coronavirus was most likely transmitted from animals to humans. And this virus can lead to severe disease progression in humans. We describe it as a zoonosis. This term is derived from the Greek words zoon (living being) and nosos (disease). Zoonoses are infectious diseases caused by bacteria, parasites, fungi, prions (degenerated proteins), or viruses and can be transmitted between animals and humans.

There are various other coronavirus species, including MERS (Middle East Respiratory Syndrome) and SARS (Severe Acute Respiratory Syndrome). The latter caused an epidemic with about 800 deaths in 2002/2003. During these epidemics and pandemics (2002/2003), bats most likely transmitted the pathogen to humans via an intermediate host—the path that researchers now suspect is also being used for SARS-CoV-2.

The new virus called COVID-19 (SARS-CoV-2)

is different from anything previously known.

It spreads in humans by „droplet infection", i.e., via components from the air we breathe and as well directly from person to person. Since you do not notice whether you already have the virus or whether another person has it, it spreads wherever people are in close contact with each other.

Another important point is the incubation period—the time from the admission of the virus up to the first signs of illness—is on average 4–6 days but can last up to 14 days. During this time, an infected person without symptoms can infect many other people. It is often not noticed and brings few and/or mild symptoms. Meanwhile, other people don't notice anything at all either, because the viruses are so tiny that they can neither be seen nor felt.

Another special feature of the coronavirus is that not everyone becomes ill when they are infected. But unfortunately, this person can still act as a carrier. Thus, these viruses are transmitted very quickly. The sick person is recognised so late that it is often not possible to trace the path of infection.

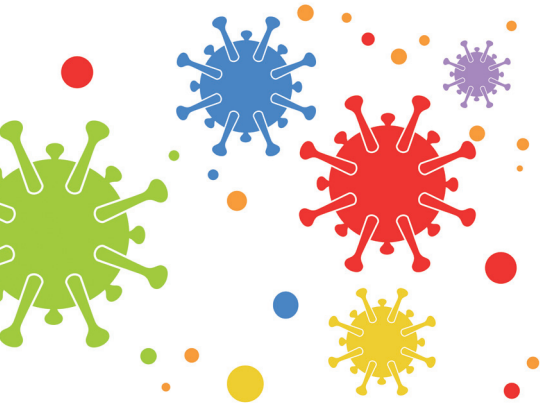
Virus—what is it exactly?

Viruses are not living beings! They have no cell nucleus and no metabolism of their own.

Therefore, they are fundamentally different from bacteria. While bacteria have a cell nucleus and can reproduce independently, viruses always need a host. This means they need a living cell into which they can implant their genetic material (RNA or DNA). Only then can a virus spread with the help of their host—plant, animal, or human.

But one more thing is important to know: Viruses are very small. Smaller than bacteria or cells. Therefore, they can only be recognised with the help of specific scientific methods.

Bacteria, however, are very different in size. Thus, the diameter of a bacterium is usually between about 0.1 and 1.0 µm. Viruses on the other hand are usually 15–400 nm (nanometers) small.



VIRUSES ARE NOT LIVING BEINGS!

They have no cell nucleus and no own metabolism and are usually 15 to 400 nm (nanometers) small.

But as small as they are, they can be very

DANGEROUS!

This is because in humans they search for certain cells in which they can spread. Once in the cell, they insert their genetic material and can multiply.

For the reasons described before, no antibiotics are effective against viruses like they are against bacteria. Special vaccines must be developed against viruses, which, with the help of the virus' own genetic information, enable our bodies—our immune systems—to recognise viruses and eliminate them from the body. This is a long and complicated process.

The model for successful vaccines against viruses is, above all, the new flu vaccines developed every year. These vaccines have been established for decades and protect millions of people from infection with the dangerous influenza viruses year after year. Various research groups are currently working on the development of a vaccine.

Our urgent recommendation:
IF YOU CAN, GET A FLU VACCINATION!

Does the vaccination work when I am undergoing cancer therapy?

As studies show, the immune response to a vaccination at the beginning of a chemotherapy cycle is limited, but usually still sufficiently good. In addition, for some vaccinations, you can check the success of immunization with a blood titre test.

What is a “live” vaccine and what is a “dead” vaccine?

The live vaccine contains living pathogens that have been modified in the laboratory and have been greatly attenuated. Because they are alive, they can multiply in the body of the vaccinated person.

Examples: The measles, mumps, rubella vaccination; the vaccine against rotavirus; and chickenpox (varicella) vaccination.

In contrast to this, dead vaccines contain „killed“ pathogens or fragments of pathogens or certain surface proteins or inactivated bacterial toxins. Therefore, dead vaccines cannot multiply.

Examples: vaccines against tetanus, diphtheria, whooping cough, polio, meningococcus, pneumococcus, hepatitis B, hepatitis A)

Can vaccination take place even if someone has already started cancer therapy?

After a cancer diagnosis, it is generally recommended to check the vaccination status of the patients at an early stage and preferably to refresh the respective vaccinations before starting the therapy.

Live vaccines, such as measles, mumps, rubella; yellow fever; or varicella should not be administered during ongoing cancer therapy (chemotherapy) as the immune system may be weakened.

In general, dead vaccines are allowed during an ongoing cancer therapy (chemotherapy).

Examples of dead vaccines are vaccines against tetanus, diphtheria, whooping cough (pertussis), polio, meningococcus, pneumococcus, FSME, influenza.

The annual influenza vaccination is generally indicated for all cancer patients.
ASK YOUR DOCTOR ABOUT IT!

Specific and general risk factors for corona inflammation

Some cancer patients are at real risk.

SPECIFIC RISK FACTORS for patients with blood and cancer diseases

In general, the risk for cancer patients of suffering from pneumonia due to an infection with respiratory viruses is higher than for non-cancer patients. This may also apply to infections caused by SARS-CoV-2.

Potential risk factors that play a role in other SARS infections include:

- Severe immunosuppression
- Neutropenia phase
- Lymphocytopenia < 0.2 x 109/L.

Patients with hereditary immunodeficiencies or who are currently receiving cancer therapies are also classified as at-risk individuals.

Especially in view of the fact that many patients who have experienced severe COVID-19 disease are older and lymphocytopenia has frequently been observed, these risk factors should be given special attention.

GENERAL RISK FACTORS, including for patients with blood diseases and cancer

Many cancer patients also have one or more of the common risk factors for a severe course of COVID-19, including:

- Age ≥65 years
- Living in a care home

SPECIFIC DISEASES, especially with pronounced symptoms:

- Chronic lung disease or moderate or severe bronchial asthma
- Severe heart disease
- Immunosuppression
- Adiposity / being overweight (BMI ≥40)
- Diabetes mellitus
- Chronic renal insufficiency under dialysis/kidney dysfunction or liver diseases
- Current cancer therapies

Summarised assessment:

If patients belong to one of these risk groups, the treating physicians will pay special attention to the usual hygiene measures. If necessary, the patients concerned must then be treated in separate rooms under increased protective measures. An interruption of cancer therapy is generally only considered in case of severe infections.

LOOK AHEAD WITH COURAGE AND CONFIDENCE!

General instructions and hygiene rules for cancer patients

Protect yourself—keep physical distance from others!

As described above, coronaviruses are mainly transmitted by droplet infection. Tiny components of the droplets, called aerosols, can also infect other people via the air. However, it is still unclear whether viruses can also be transmitted via smear infection, such as through door handles, shopping carts or other surfaces that have been touched by someone infected. Therefore, it is very important to follow the hygiene rules developed by the government, scientists, and physicians. This especially applies to cancer patients and their relatives and friends.

The most important rules to be observed by cancer patients under all circumstances follow:

- Avoid close encounters with people, especially with people who do not come directly from your home environment.
- If you have to leave your home, please keep a distance of at least 1.5 meters between you and other people.
- Avoid large groups of people.
- Pay attention to the hygiene concepts of the organisers and ask for detailed information about them.
- Wear mouth protection consistently.
- Pay close attention to good body and hand hygiene:
- No shaking hands!
- No hugs!
- Fully disinfect all items that you are going to touch before and after you touch them.
- Regularly wash hands with soap for at least 30 seconds. When you are in medical facilities, use other types of hand disinfection as well. Inform yourself about the hygiene measures available!

Important appointments

Please inform your doctor, physiotherapist, friends, etc. that you belong to a risk group and must have any appointments by yourself and at a distance.

- When visiting the doctor, all persons in the clinic should pay particular attention to observing all hygiene measures.
- The medical staff wears masks and/or other barriers over their mouths consistently and will ensure the highest possible level of hygiene.
- If possible, cancer patients should be separated from other patients and their relatives or specially protected, i.e., special areas (e.g., registration and waiting areas) should be set up and physical distancing (at least 1.5 meters) should be observed.
- When possible, take a telephone or video consultation instead of an in-person visit.
- Pay attention to hand and surface disinfection and cover your mouth.
- Please disinfect your hands and cover your mouth before going to the doctor or contacting medical personnel.
- Always keep physical distance when possible. Of course, this is not always possible during physical examinations. But in these circumstances, the medical staff should strictly observe all rules and regulations.
- If you have cold-like symptoms or think you have had contact with a person with a COVID-19 infection, please do not go directly to the doctor or clinic and instead inform your doctors by telephone and ask for advice.
- Persons who have entered your country from abroad and have been in a risk area for SARS-CoV-2 infection over the last 14 days before entering the country have to be quarantined if necessary.

Please make sure to inquire before every trip that cannot be postponed:

- What is classified as a risk area for infections with SARS-CoV-2? This is generally defined by the National Ministry of Health or other governmental department.
- Obtain up-to-date travel information, as the classification of countries and regions can change very quickly.

Vaccinations

- It is a fact that vaccination is the only effective prevention against many viral infections. Of course, this is only true if special vaccines exist, such as those for the seasonal flu viruses. Since these viruses change constantly, patients must be inoculated again each year!
- For the coronaviruses (SARS-CoV-2), research groups worldwide are working on the development of an effective and safe vaccination protection.
- You can also carry out further vaccinations: This is especially true for all people who have either chronic diseases or acute diseases of the immune system.

Recommendations for Vaccination

Please take care that these recommendations can be different in your region and have to be adapted.

According to a study published in the Journal of Clinical Oncology[1], the influenza inoculation can be recommended to patients with cancer illnesses.

Vaccination against COVID-19

Several vaccines' are currently approved and under development, the approval process depends on the specific regional and national situations.

As already in this brochure, described, patients with cancer have in general an increased risk of severe COVID-19 and should be vaccinated against SARS-CoV-2 regardless of any other indications (i.e. age, other comorbidities).

Based on the ESMO recommendation**, the time-point for vaccination after allogeneic stem cell transplantation should follow general recommendations – usually, in the absence of graft-versus--host disease (GvHD), the vaccine can be applied 6 months post stem cell transplantation [].

Patients within clinical trials should not be deprived of COVID-19 vaccination, therefore, efforts should be placed for clinical trial protocols to allow concurrent COVID-19 vaccines and has to be discussed with the principle investigators and specific sponsors.

1) Source: Blanchette PS et al Influenza Vaccine Effectiveness Among Patients With Cancer: A Population-Based Study Using Health Administrative and Laboratory Testing Data From Ontario, Canada. Journal of Clinical Oncology, online pre-release on August 29, 2010,DOI:10.1200/JCO.19.00354

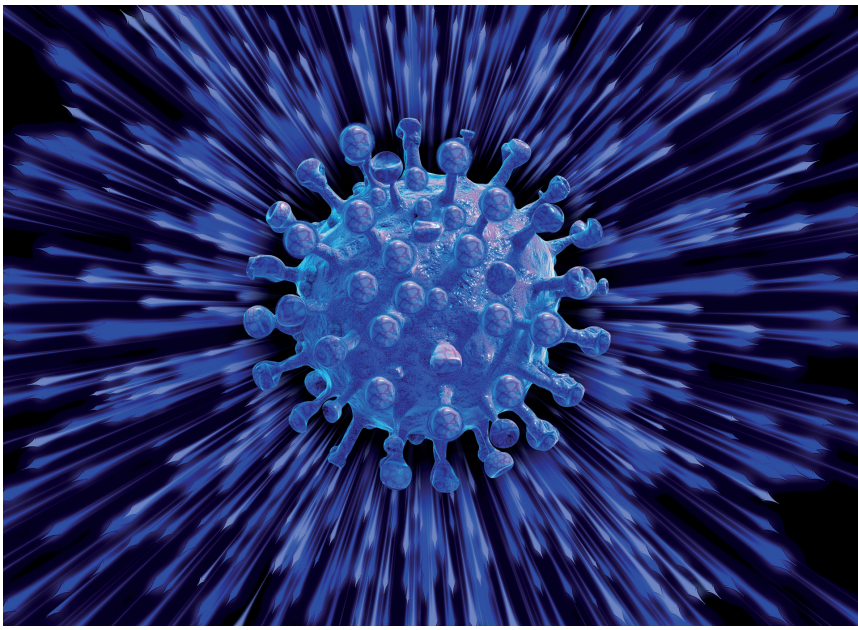
Despite vaccination close surveillance and monitoring of patients with cancer is required and should follow all general recommendations, such as physical distancing and masks, for cancer patients who have been not vaccinated

Although no obvious safety concerns are evident, there is a clear need to generate data on preference of vaccine technology and interaction of SARS-CoV-2 vaccines with antineoplastic therapies in patients with cancer, potentially impacting on efficacy, dosing or toxicity, via in-trial, post-trial and registry monitoring [V].

***https://perspectives.esmo.org/news/covid-19-vaccination-in-patients-with-cancer--esmo-releases-ten-statements**

Study highlights:

- The data of 26,463 cancer patients older than 18 (average age, 70) was evaluated. Almost a quarter of the patients received chemotherapy, and 45% had been vaccinated against influenza.
- The flu vaccination proved to be efficient: Especially in patients with malignant organ tumours, the vaccine reliably protected them from infection with the flu pathogens and prevented them from needing hospital treatment for influenza. It was less effective in patients suffering from leukaemia, a blood cancer. Chemotherapy was not shown to influence effectiveness.
- According to the study authors, flu vaccination can be recommended to all patients with cancer. But the strategies for preventing influenza among cancer patients should be improved.

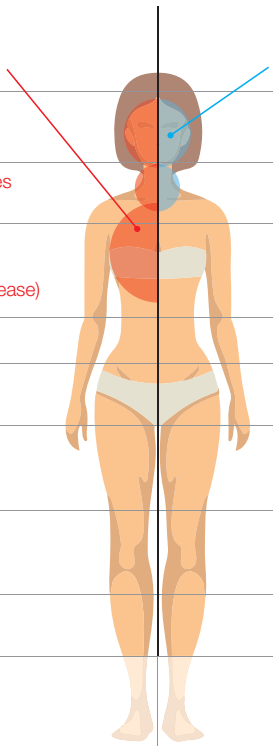


What is the difference between a flu and a flu-like infection?

Influenza viruses infect not only the upper airways but also the lower ones. This course of the disease is much more drastic than with a flu-like infection. The illness begins suddenly and the symptoms usually start with a high fever and a dry, irritable cough.

A flu infection or a cold can be caused by many different pathogens. The infection is usually limited to the upper respiratory tract. The symptoms usually begin slowly with a cold, while later a slight fever may develop.

SYMPTOMS	FLU (INFLUENZA)	FLU (INFLUENZA)
Start of disease	Comes on suddenly with severe symptoms	Gradually feeling worse
Fever	The body temperature rises to 38° to 41°	Only a small temperature increase
Cough	Dry, irritable cough, often painful (mostly at the beginning of the disease)	Low irritation causing a cough, often with phlegm but no chest discomfort
Appetite	Loss of appetite	Appetite mostly still present
Tiredness	Exhaustion, feeling of weakness	Mattiness
Muscle ache	Intense headaches, muscle and joint pain in the whole body	Possibility of a headache and aching limbs, but not the whole body
Sniffles	Blocked and/or runny nose	Frequent sneezing, a blocked and/or runny nose (mostly at the beginning of the disease)
Date	Occurs during flu season (December to April)	Can occur all year round, even with no flu cases in the surrounding area
Pathogen	Influenza-Vieren	Caused by more than 200 different pathogens



The illustrations are for orientation only.
The exact distinction between COVID-19,
influenza, and a cold can only be made by a physician.

Differences in typical symptoms of an infection

Another vaccination recommended for people with tumour diseases is the pneumococcal vaccination, which should be repeated only every 5 years. It protects against pneumonia caused by bacteria.

Other vaccinations, e.g., tetanus, HPV, etc., are also important and helpful for the immune system. This is because they can strengthen the immune system and thus generally improve the body's own defences.

COVID-19, cold, and flu

The most important differences in symptoms are:

SYMPTOMS	CORONA-VIRUS	EXPLANATION	GROUP
Tiredness	sometimes	sometimes	frequently
Sneezing	no	often	no
Sniffles	rarely	rare	sometimes
Headache	sometimes		frequently

Handling relatives and friends

- Of course, the public recommendations and rules apply here as well: keep physical distance, wash your hands frequently, avoid sick people, and avoid risky surgery.
- During chemotherapy and before and after surgery, it is strongly recommended only to meet with people who live in your own household.
- Please postpone contact with all other relatives and friends until after the end of your cancer treatment.

Important information in connection with the risk of viral infection, and the increased risk of more serious disease progression

- People with weakened immune systems may be more quickly and severely affected by infection with SARS CoV-2 or other viruses.
- In cancer patients, the immune system can be weakened for various reasons. However, there is so far no specific information about cancer patients who have been infected with SARS-CoV-2.

Which preventive measurements are useful for everyone?

The virus can be transmitted from person to person by droplets when speaking, coughing, or sneezing. It is also possible that viruses are transmitted from surfaces or when shaking hands (smear infection) if you touch your face afterwards. Therefore you should primarily follow these rules:

- Wash your hands regularly and thoroughly
- In case of contact with other people or objects, disinfect your hands—preferably before contact.
- Coughing and sneezing into the elbow or a disposable handkerchief
- Do not touch the face after contact
- Avoid shaking hands

All authorities generally recommend that contact with other people outside of one's own household should be reduced to a necessary minimum. Wherever possible, a distance of at least 1.5m should be kept from people outside the household.

Since there have recently been scientific reports that, in addition to dangerous droplets, tiny components of viruses in the form of aerosols can remain in the air of closed rooms for longer periods of time, cancer patients should avoid staying in closed rooms with many people.

It is also not advisable to participate in larger events of any kind until the cancer treatment is completely finished.

SAFETY FIRST—PLEASE PROTECT YOURSELF CONTINUOUSLY!

3 QUESTIONS, 3 ANSWERS
in case of planned clarification of a cancer disease

QUESTION 1:

During a pandemic or epidemic, do I have to cancel/postpone planned diagnostics?

ANSWER 1: NO! If cancer is suspected, clarification—i.e., targeted diagnostics—is always very important! This also applies to cancer prevention. The medical staff knows the precautionary measures and rules. They will treat their patients carefully and safely, even in times of crisis. If cancer is suspected, they will make sure that you are physically separated from other patients.

QUESTION 2:

Do I have to stop contacts with other people if I suspect that I have cancer?

ANSWER 2: The usual precautionary rules announced by the public authorities apply. A person is not likely to be immunocompromised at the time of diagnosis, unless certain previous illnesses are already known.

Thorough examination—consider the risks

QUESTION 3:

Will my body be harmed or otherwise endangered by the different diagnostic measures?

ANSWER 3: The measures such as blood sampling, X-rays, CT or MRT scans do not represent an intervention that endangers the immune system.

What you can do is vaccinate. Against influenza, pneumococcus, tetanus and others (see above). Your doctor will advise you about this. Vaccination strengthens the immune system and also protects you during cancer therapy.

3 QUESTIONS, 3 ANSWERS to surgery / operation

OPERATIONS ARE INDISPENSABLY IMPORTANT. Should I postpone my planned surgery?

In most cases of cancer, surgery cannot be avoided and should not be postponed. The goal is always to completely remove the tumour in addition to securing the diagnosis.

For many tumours, this is one of the most important prognostic factors, so that if possible, there should be no significant postponement.

However, this may not be optimal if cold symptoms have not yet subsided and, for example, pneumonia is present. Please discuss this with your physicians. In most clinics, a COVID-19 test (smear from the nose and throat) is also performed a few days before the surgery. The planned surgery will take place only if the test result is negative.

Otherwise, COVID-19, like all other viral diseases, is subject to the same strict hygiene measures that are otherwise applied. In the case of a proven COVID-19 infection, additional measures are taken during surgery to protect medical staff. For example, so-called FFP-3 masks should be used. Otherwise, the classical surgical masks are sufficient.

For the affected patients, there are certainly some questions in connection with SARS-CoV-2. The most important questions are the following:

QUESTION 1:

In connection with this coronavirus pandemic or other waves of infection, is it necessary to postpone necessary surgery?

ANSWER 1: Generally and especially in gynaecological cancer, NO! There is only one exception: If you are currently suffering from an infection, the surgery must be postponed until the recovery from infection. However, if you are not infected, the surgery can—and should—be performed as planned.

QUESTION 2:

Is it dangerous to have an operation during a wave of infection?

ANSWER 2: So far, nothing is known about this. Since the entire surgical staff and the operating rooms themselves are thoroughly disinfected before every operation, there is no risk of infection. If you have an active COVID-19 infection and surgery should not be postponed, special additional measures are taken during ventilation and surgery.

QUESTION 3:

What happens if my planned surgery has to be postponed because of coronavirus?

ANSWER 3: Your doctors will only do this very rarely and only if postponement of the operation is possible for you without any risks. Also, in your hospital, a massive outbreak of infection may lead to restrictions in the capacity of the operating room and intensive care unit. However, this will be discussed with you in detail.

Where should I have surgery?

This question is very important for women with ovarian cancer. And with good reason—ovarian cancer is a difficult disease to operate. Only those with a lot of experience will achieve the best possible results and the patient's entire future prognosis depends on the outcome of this surgery. That is why we advise you to inform you properly and widely.

In any case, it is advisable to seek treatment in a certified centre for gynaecological tumours. This applies within the pandemic period as well as otherwise.

Surgery is a specialist's job—do not shift it during the coronavirus pandemic.

3 QUESTIONS, 3 ANSWERS for drug therapy

Postpone chemotherapy or immunotherapy? BETTER NOT!

Treatment with drugs that directly target the cancer has long been standard practice. The indication for chemotherapy varies depending on the type of tumour and tumour situation. Regardless of the pandemic, this measure should be discussed very carefully with your physicians. There are various medication alternatives. The timing of the start of therapy is also decisive. When a course of chemo- or immunotherapy has to be started depends on various factors: These include the general condition of the patient, many laboratory parameters, and the disease symptoms (e.g., abdominal fluid, shortness of breath). If chemotherapy is performed after surgery, it is generally true that chemotherapy can be performed within a period of about 3 to 8 weeks without worsening the prognosis. Please discuss this with your physicians.

Many cancers can recur despite surgery, chemotherapy, and targeted therapies (e.g., as maintenance therapies). Here too, the principle clearly applies: Always identify the best therapy and initiate it!

Treatment with innovative drugs—immune therapies

In addition to classical chemotherapy, many new things have happened in recent years. For example, the use of so-called PARP inhibitors and angiogenesis inhibitors has found its way into various therapy schemes. These targeted molecules/therapies have become more and more important and have become standard in many cases, especially in maintenance therapy.

Further studies are now investigating the effectiveness of new antibodies and so-called „small molecules". The results are not yet available because the studies are ongoing.

In any case, all important oncological therapies should not be delayed or discontinued, not even during the pandemic.

The most important questions about chemo- and immunotherapy:

QUESTION 1:

Am I more susceptible than other people to infection during ongoing drug therapy?

ANSWER 1: In principle, this is true. Every treatment with anti-cancer drugs also weakens the immune system. The body perceives these drugs as an external intervention. This is also true. And our immune system cannot help but notice that this attack is actually only directed against cancer. So there is a situation where our immune system uses all its power against the dangerous cancer cells. Through cancer and chemo- or immunotherapy, the immune system is weakened and cannot work as effectively as it does normally against other invaders such as certain viruses or bacteria.

QUESTION 2:

What do I have to do as a cancer patient during chemotherapy if an acute viral infection occurs or is already present in my personal environment?

ANSWER 2: Talk to your doctors about this immediately and tell them what to do:

- Who is the sick person?
- What infection does this person have?
- How close are you to this person?
- Do you yourself already have the feeling that you are been stuck?

Depending on the public health situation at the time, your doctors will decide whether chemotherapy can be started or continued. Everything depends on your personal circumstances and must be clarified with each patient individually.

QUESTION 3:

Is a delayed start or interruption of chemotherapy dangerous for me?

ANSWER 3: This question cannot be answered easily. In principle, there can always be a delay before the start of chemotherapy. This also applies if you suddenly develop an infection or other acute illness. In this case, cancer treatment must be postponed until you are fit again, because you need all your strength for chemotherapy.

The interruption of an ongoing chemotherapy is only useful or necessary if you are suffering from an acute infection. This must then be discussed and decided by the specialists, depending on the situation and the cancer.

Chemo- and immune therapies are important and they should always be administered according to plan.

It is also important from the patient's side that the medicine should be taken in accordance with the instructions and the prescribed laboratory tests should not be delayed! Reaching the institute or the doctor can be more difficult in these times, but don't give up trying!

3 QUESTIONS, 3 ANSWERS about radiotherapy

If possible, radiotherapy should not be postponed or interrupted even during COVID-19 pandemic.

Radiation therapy facilities should carry out curative therapies as completely and without interruption as possible, even in the event of bottlenecks such as those caused by coronavirus-related staff shortages and quarantine measures. Rays are sometimes necessary—they can heal.

The situation with gynaecological tumours is different. Women with breast, cervical, and uterine cancers are relatively often treated with radiotherapy after surgery and chemotherapy. Its main purpose is to combat any residual tumour.

Radiation therapy plays only a minor role in the treatment of ovarian, fallopian tube, and peritoneal cancer. It is only used if distant metastases have occurred in rare cases. This can happen in the brain region, for example. Today, there are very specific (stereotactic) irradiation techniques available for this purpose. For most patients, radiation is not necessary.

But there can always be some questions.

QUESTION 1:

If irradiation is necessary for me, can it be performed despite the pandemic?

ANSWER 1: In principle, there is no reason to delay or interrupt radiation therapy. An infectious event has no influence on this, according to what we know so far.

QUESTION 2:

Do the rays have an aggravating effect on an acute infection?

ANSWER 2: This has not been proven anywhere so far. As has been seen so far, the radiation therapies used today have no effect on what happens during an infection.

QUESTION 3:

Where is the best place to receive radiation therapy during a pandemic or epidemic?

ANSWER 3: Talk about this with your medical care team. They will certainly be able to recommend an experienced centre.

For irradiation, consult only with experts experienced in oncology.

3 QUESTIONS, 3 ANSWERS about hormone therapy

Hormones control the human being and sometimes cancer.

Hormones often play a major role in women's cancer—but in a negative sense. Many female tumours, primarily breast tumours, are caused by the hormones oestrogen and/or gestagen. For this reason, anti-hormonal therapies are often used for these types of cancer.

Hormones do not play a major role in ovarian, fallopian tube, and peritoneal cancer. After surgery and chemotherapy, the production of oestrogens and progestins usually stops or is greatly reduced. This makes it clear that drugs that work against these hormones are not used here.

Antihormonal therapies are only used for very rare low-grade carcinomas to the application.

QUESTION 1:

What should be done if, after surgery and chemotherapy, the hormone products are no longer available? Does this mean that the process comes to a standstill and normal life is impaired?

ANSWER 1: Talk openly to your doctor about everything you observe in yourself. This can range from general disturbances of well-being to problems with sexuality and partner problems. It is important that your doctors understand how you feel. And then they will look for and find ways and means to help you.

QUESTION 2:

After ovarian cancer therapy, can hormones be taken to replace decreasing hormone production?

ANSWER 2: Your doctors have to decide this individually. Under certain circumstances, locally applicable preparations can be given. In the case of classic ovarian, fallopian tube, or peritoneal cancer (high-grade carcinoma), hormone replacement therapy can certainly be administered. Please discuss this with your physicians. Above all, you should never let yourself be influenced by self-proclaimed healers and other non-specialists!

QUESTION 3:

What can you do to rebuild your body after surgery and chemotherapy without further medication?

ANSWER 3: There are many ways to help women get better. Above all, these include exercise, moderate sport, healthy nutrition, and positive thinking. Being integrated into a good environment of family and friends can be especially helpful and valuable.

The goal—strengthening health.

3 QUESTIONS, 3 ANSWERS on maintenance therapy

Do the same rules apply to maintenance therapies as to chemotherapy?

In gynaecological oncology there are different types of maintenance therapies. All of them have the goal of preventing a recurrence of the tumour or at least postponing it for a long time: Today, the following are used:

- Anti-angiogenesis inhibitors
- PARP therapies (intervene in the repair mechanism on)
- Anti-hormonal therapies (for breast cancer).

For all these therapies, it should be noted that additional medical visits may be necessary at the start of maintenance therapy to check for effects and tolerability. But after only a few weeks this also leads to normalisation and maintenance therapy becomes a part of normal life.

AS MANY PATIENTS SAY: „I GOT USED TO 'MY' PILLS A LONG TIME AGO."

Maintenance therapy can take a long time. And questions like the following arise in the process:

QUESTION 1:

Does maintenance therapy affect my immune system as intensively as chemotherapy?

ANSWER 1: In general, the immune-weakening effect is significantly lower than with classic chemotherapy. Some of them (e.g., PARP inhibitors) are administered directly after chemotherapy, so that the remaining effects of chemotherapy alone can weaken the immune system.

QUESTION 2:

If an acute infection occurs, do I have to stop or interrupt my maintenance therapy?

ANSWER 2: In the case of infections, changes in blood values, such as a drop in white blood cells (leukocytes) and red blood cells (erythrocytes, resulting in anaemia), can have a short-term effect on the immune system. A pause or a general dose reduction for fear of catching COVID-19 is possible. However, infection or other viral or bacterial diseases are not indicated according to current knowledge.

QUESTION 3:

How long do I have to take these drugs?

ANSWER 3: This cannot always be determined in advance. Most of these drugs are relatively new but have already been well tested. The duration of the effect—over months or years—has yet to be tested. This is mainly due to their effectiveness. And that can also be an important reason why the experts ask you to participate in an observational study on long-term effects. If you have a chance to take part in such a study, do so because it will be of great help to you and all future patients.

Maintenance therapy—the goal of long-term control.

3 QUESTIONS, 3 ANSWERS to surgery / follow up

QUESTION 1:

How do I find a self-help/support group/patient group that suits me?

ANSWER 1: Anyone—patients and family members alike—can contact one of these organisations directly. You can also contact fellow patients or ask your treatment team.

QUESTION 2:

Is aftercare the same as rehabilitation?

ANSWER 2: NO! Rehabilitation is a measure that immediately follows treatment in the clinic. It should be done by every patient if possible. Rehabilitation serves the direct recovery and helps to overcome the consequences of surgery and chemotherapy as quickly as possible.

QUESTION 3:

Who will accompany me during aftercare?

ANSWER 3: This is an important task for the general practitioners or specialists who normally treat you in your everyday life. For all women with gynaecological cancer, it is usually the gynaecologists who are in charge of the patient. What is important here is to ensure the communication between all doctors involved!

Please contact them in confidence.

As a general rule, it is also important that you talk to experts from the field of psycho-oncology or with other affected persons. For example, self-help groups can help many patients return to as normal a life as possible. You should also talk about this with your doctors. They can give you the most important tips and advice.

Recovery after cancer therapy is important and feasible.

Cancer is associated with many restrictions and changes in life for every person. But it is important to know: Today, well over 50% of all cancers are curable and tumour disease can be stabilised in many people. Your doctors and all employees in the clinic and practice will contribute their best to this. However, your active participation is also important to help you overcome your disease.

In our opinion, every patient has the right to experience these programs and to participate in them. Information is available to all oncological physicians, the health insurance companies, the cancer information service, and also the patient self-help groups. For many patients, it is valuable to contact a self-help group that is concerned with their illness.

Have a joint treatment plan with your doctor, in which you define the steps and the options available to you during the pandemic, including who, where and when you feel, and what to follow.

3 QUESTIONS, 3 ANSWERS on clinical studies

Participate—clinical studies are very important

There is always a lot of talk about participating in clinical studies. Often one hears negative opinions in these discussions. But they are wrong in principle. Participation in a clinical study led by experts ensures that every patient receives the best possible treatment. In these studies, which are conducted by experts and in = medical centres, no one is treated incorrectly. On the contrary: the best possible therapies are used. Patients are permanently under special observation by their doctors.

Of course, studies continue to take place in times of pandemics, such as the current COVID-19 pandemic. Please always ask the study centre whether there are any restrictions in ongoing studies.

QUESTION 1:

What is done in a clinical study?

ANSWER 1: There are many different questions. It starts with the comparison of several therapy options in large patient groups. Or new therapy strategies are tested against the currently valid standard therapies. The best possible treatment and intensive observation of each individual patient is always ensured.

QUESTION 2:

Am I a „guinea pig“ if I participate in a clinical study?

ANSWER 2: NO! The opposite is the case! There are no „trials“ in a clinical study on patients. These studies are only approved by the authorities and the ethics commissions when—for example, in the development of new drugs—all early stages of testing have been completed. It is then already certain that a new drug is effective. And in the clinical trial, the effectiveness of the new drug in comparison with the current standard therapy is now being tested.

QUESTION 3:

Should I expect more effort in the framework of a clinical study?

ANSWER 3: Basically, **YES!** The prescribed examinations of your state of health can be more intensive than in normal treatment. This means that there will be more appointments at the centre. There will also be more frequent physical examinations and special blood tests. All this is for the personal safety of the participants and requires a little more time.

Clinical studies—the best for patients.

Travel as a cancer patient —the rules

What do I have to consider when I want to travel?

If the cancer has been treated for a long time, there is usually no significantly increased risk of infection compared to non-cancerous or healthy people. Nevertheless, the officially recommended vaccinations and hygiene measures for the respective travel country should be observed. In general, it is also recommended to brush up on polio, rabies, and hepatitis B and A vaccinations.

Patients undergoing chemotherapy can have an increased risk of infection. In addition, certain recommended vaccinations (live vaccines such as yellow fever) may not be given. Therefore, please discuss this with your doctors in good time. In addition, there are usually other important aspects, such as blood checks, which must be considered during or after chemotherapy.

The urgent advice:

Please discuss all questions regarding travel with your physicians.

How do I know which of my symptoms are caused by cancer and which ones by COVID-19 or another viral disease?

IIt can be difficult to tell in individual cases, so we ask you to inform your doctors about all symptoms you are experiencing, even if they are not directly related to cancer, cancer therapy, or a viral disease.

Symptoms typical for infections can also occur due to tumour diseases (e.g., pleural effusions) or cancer therapies (e.g., polyneuropathy, taste disorders with paclitaxel). In addition, various other viral (influenza, flu viruses) and bacterial diseases (e.g., pneumococcus) can cause different forms of pneumonia. Therefore, please go to your physicians immediately so that they can initiate the appropriate treatment with the help of differential diagnoses.

Strengthen strengths—promote well-being!

These are the most important rules for all cancer patients. The treatments require a lot of strength from all people. Through good preparation, variety in life, and careful handling of oneself, each person can do a lot to ensure that the treatments work well and lead to the goal. Travel can also support this. One does not have to go on a trip around the world. There are many obvious destinations in our country where you can recover very well.

Your doctor will be happy to give you additional advice on travel.

Vaccination, vaccines, immunity

Introduction

Several vaccines have already been approved by the European authorities. In a short time, further vaccines will follow. Hopefully, broad sections of the world population will soon gain immunity against this dangerous virus, and severe cases of COVID-19 infection will be significantly reduced in number.

Of course, there are still many questions about vaccination and vaccines, but according to various expert panels, these questions do not refute the benefits of vaccination. Essential information for cancer patients will be explained in this chapter.

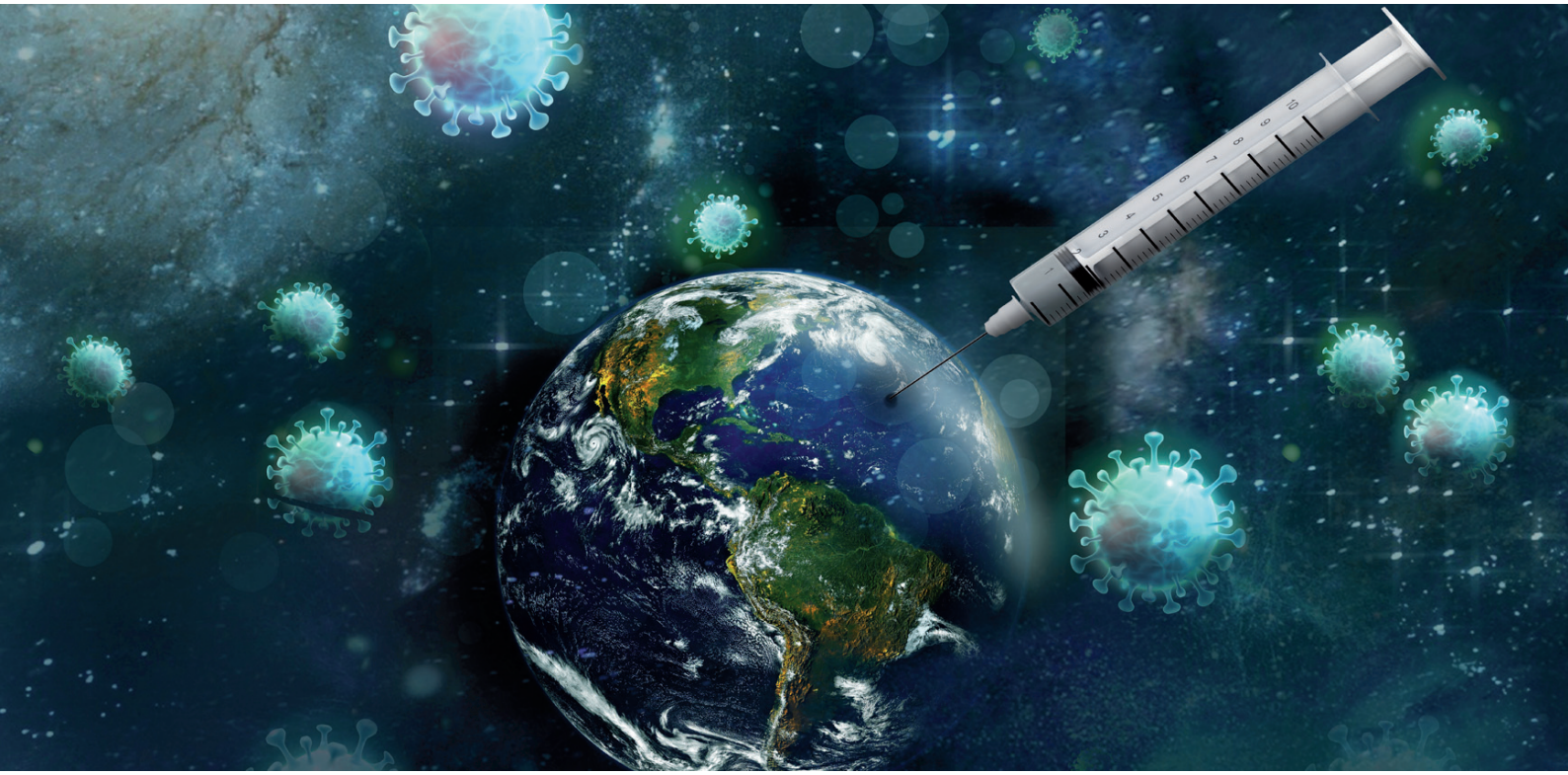
If you have further questions about vaccination, ask your doctors directly in order to prevent any misunderstandings.

Basic information

The European Society for Medical Oncology (ESMO) and the Standing Committee on Vaccination at the Robert Koch Institute (STIKO) recommend that **all cancer patients be vaccinated against the pathogen SARS-CoV-2**, regardless of other conditions such as older age or concomitant diseases. Cancer patients generally have a higher risk of contracting COVID-19 and of suffering a more severe course of the disease.

For example, ESMO recommends that cancer patients who have received a stem-cell transplant should be vaccinated about six months after the transplant. This does not apply if a rejection reaction (GvHD) has occurred.

Cancer patients who are being treated as part of a clinical trial should also be offered a COVID-19 vaccination. However, this must be approved and authorised in the study protocol.



Even after vaccination, general coronavirus precautions must continue to be followed by all cancer patients. These include wearing a medical mask that covers the mouth and nose (i.e., surgical mask or, even better, an FFP2 mask or respirator) every day, disinfecting hands regularly, keeping a physical distance from others of at least 1.5 metres, and ventilating rooms regularly.

The experts are now investigating the efficacy and tolerability for cancer patients of different coronavirus vaccines in various studies. The effects for all phases of cancer therapy will be investigated—from initial treatment to long-term therapy and further monitoring after cancer therapy completion. A clear recommendation has also been made by ESMO for this.

Further important information

Antibiotics are not effective against viruses since viruses are not living organisms like bacteria or fungi. Viruses have to enter our body's cells so that they can multiply there and cause the disease. Vaccinations are one of the most important measures in the prevention of various viral diseases. Vaccinations are effective against many viral diseases, such as flu (influenza), pneumonia, childhood diseases (measles, mumps, rubella, chickenpox), hepatitis A and B, and other viruses. It is also effective against oncogenic human papillomaviruses (HPV), which can trigger cervical cancer and other types of tumours.

Modern vaccinations are safe and lead to immunity against the respective virus in humans.

The duration of vaccine-given immunity varies depending on the type of virus. For example, the flu vaccine must be repeated every year, as flu viruses can change rapidly (mutate) and completely new virus types can emerge. Most vaccines use components of the viruses—direct information from the virus—to generate a defence reaction in the immune system, which leads to immunity against this virus. In preventing the new coronavirus SARS-CoV-2, researchers have also used new technologies (mRNA vaccines) that are even more effective.

The following section explains in detail the interrelationships between immunity, the different vaccines, and possible side effects. If you as a patient have any further questions, please discuss them openly and directly with your doctors.

COVID-19 vaccines

In researching new active substances against these viruses, scientists have taken different paths in the development of vaccines. Due to the rapid worldwide spread of the virus—called a pandemic—new and highly effective treatment options had to be sought very quickly. In this chapter, we will look at the currently known vaccines, their advantages and disadvantages, as well as their effects and possible side effects and explain the special considerations for cancer patients.

Researchers are currently working on more than 170 possible vaccines. As of March 2021, three vaccines have been approved in the EU, while four more vaccines have been approved in China, Russia, and India. In addition to the conventional vaccines (vector-borne, inactivated viruses, virus components), new technologies are also being used for the first time. For example, the production of components of the SARS-CoV-2 virus in the form of the messenger substance mRNA. It is important to emphasise that no vaccines alter the genetic material (i.e., they are not DNA vaccines), and the changes in a patient's immune system will not be hereditary (not passed down to their children).

The first innovative vaccines—mRNA

mRNA vaccines contain gene segments of the pathogen SARS-CoV-2 in the form of messenger RNA (mRNA). Based on the mRNA, specific proteins are produced in the body's cells after vaccination, which then stimulate the immune system to form specific antibodies against SARS-CoV-2 and a cellular defence against SARS-CoV-2-infected cells. In this way, an immune response is generated. Proteins that stimulate an immune response are called antigens.

To enter the body's cells, the mRNA is coated with special lipid substances (mRNA lipid nanoparticles). These are stable even after intramuscular injection and enable the uptake of the mRNA into the patient's muscle and immune cells. Studies have shown that the lipid nanoparticles are not cytotoxic (harmful to cells) and do not pose any danger to the human body. (Source: RKI; 19.01.2021). The following manufacturers produce mRNA vaccines: BioNTech/Pfizer, Moderna, CureVac.

Vector vaccines

Vector-based vaccines consist of viruses that are harmless to humans and contain a genetic sequence in their genome with the blueprint for one or more components of the SARS-CoV-2 virus (antigen). The COVID-19 vector vaccines contain harmless, well-studied carrier viruses (e.g., chimpanzee adenoviruses, parainfluenza viruses) into whose genome a gene has been inserted that contains the blueprint for the SARS-CoV-2 surface protein, the spike protein. In the cells, the genetic information on the gene is read out and translated into protein.

There are vector vaccines that are capable of replication and vector vaccines that are not capable of replication but neither of these cause disease in humans. The vector viruses thus serve as „gene shuttles" for the spike protein gene. The spike protein formed from the transferred gene stimulates the body's immune system to produce antibodies against SARS-CoV-2 (humoral immune response). In addition, a T-cell response (CD4, CD8) can be triggered (cellular immune response)*. The following manufacturers produce vector vaccines: Oxford/AstraZeneca, Gamaleya National Centre of Epidemiology and Microbiology in Russia (Sputnik V), Johnson & Johnson (Janssen), and CanSino Biologics in China.

The restriction that pregnant women should generally not be vaccinated has to do with the fact that pregnant women were not allowed to participate in the first studies. However, the Standing Commission on Vaccination considers it unlikely that vaccinating the mother while breastfeeding is harmful to the baby. Further studies will follow soon.

However, according to the Standing Committee on Vaccination at the Robert Koch Institute, vaccination can be offered in individual cases with a high risk of severe COVID-19 disease, after weighing the risk-benefit ratio and after information.

*(*Source: https://www.rki.de/DE/Content/Infekt/Imp- fen/Materials/Faktenblaetter/COVID-19.pdf;jsessionid=43B340461264B1D44DBBACA0B0D9DF5A. internet061?__blob=publicationFile)*

Here you will find an educational leaflet on COVID-19 vaccination with vector vaccine: https://www.rki.de/DE/Content/Infekt/Impfen/Mate- rialien/COVID-19-Vektorimpfstoff-Tab.html

Inactivated (dead) vaccines with virus particles

mRNA vaccines contain gene segments of the pathogen SARS-CoV-2 in the form of messenger RNA For these vaccines, particles of the virus are killed and then multiplied in the laboratory. These killed virus particles can no longer trigger an illness in the body but they are able to arm the immune system against the viruses in question. This technique is mainly used for flu vaccines. The following manufacturers produce inactivated vaccines: Sinovac and Sinopharm in China, Novavax in the USA.

SIDE EFFECTS

No serious side effects have been observed after injecting the mRNA vaccines. What is known:

- There may be mild local reactions at the vaccination site (redness, pain, warm sensation). All vaccinations may trigger these reactions.
- In very rare cases (a few cases per 1 million people vaccinated), systemic allergic reactions have been observed. For this reason, the Paul Ehrlich Institute (a regulatory authority for vaccines) also recommends vaccinating people with allergies. However, it is recommended that doctors observe people with allergies for at least 30 minutes after vaccination.
- Allergy sufferers should inform the vaccination staff of their allergies before the vaccination. Then a special observation can be ensured on site (Position paper, Paul-Ehrlich-Institut (PEI), 05.01.2021).

Immunity

The aim of every measure against pathogens is to build up protection against the invaders. This is called immunity. Immunity can be achieved in two different ways:

- Acquired immunity. This is achieved when the body has been through an illness.
  - It can last for different lengths of time
  - It can be effective against moderate pathogen mutations
  - It does not help against new types of viruses.
    This is why the flu vaccination must be repeated every year.
- Immunity through vaccination.
  - It effective against moderate viral mutations
  - It lasts for different lengths of time.

Immunity to SARS-CoV-2 lasts at least several months after infection or vaccination, and the vaccination may have to be repeated. As of March 2021, about 10–15% of people in Germany have antibodies against SARS-CoV-2, and many have been infected with SARS-CoV-2 without knowing it (this is called "asymptomatic infections"). Currently, a negative antibody test does not completely rule out that an infection has occurred. If you have had an infection, please discuss with your doctor which vaccination is advisable for you and when.

fungi, and viruses. During cancer therapy, and even for a certain time after therapy, the patient's immune system is severely weakened. Therefore, it is crucial to vaccinate cancer patients so that they can build up as much protection as possible. This applies to all known vaccinations, including those against flu viruses, pneumococci (which cause pneumonia), and other risks.

In addition to vaccination to reduce risk of COVID-19 infection for cancer patients, there is a high national and international consensus that all other precautionary measures, such as social distancing, hand disinfection, and compulsory masks, remain valid without restriction.

Thanks to a cooperation with the association Eierstockkrebs Deutschland e.V. (Ovarian Cancer Germany), we are able to answer the most important questions asked directly by patients:

QUESTION 1:

Can my cancer medication influence the effectiveness of the COVID-19 vaccination? (e.g., chemotherapeutic drugs such as carboplatin, paclitaxel, maintenance therapies such as bevacizumab, olaparib, niraparib, rucaparib, etc., or immunotherapies).

ANSWER 1: This is not yet known. It is generally recommended to start vaccination before or after an active cancer therapy.

If you are currently undergoing chemotherapy and the last cycle is not planned for many months, vaccination can also be considered during chemotherapy, after the blood values have recovered.

Please discuss this with your doctors.

Other cancer therapies, such as antibody or PARP inhibitor therapies, anti-hormone therapies, as well as radiotherapy, have no relevant restrictions for vaccination.

SARS-CoV-2 antibody tests and antigen tests

• The antibodies against the SARS-CoV-2 coronavirus in serum (anti-SARS-CoV-2) are versatile and differ in their ability to act against the virus. Neutralising antibodies, which are formed against the spike protein of the virus, are formed a few days to weeks after vaccination or infection and point to protective immunity. Other antibodies can only be detected in human serum after an infection.

• In contrast to the antibody in serum, PCR tests (viral RNA detection) and rapid tests (nucleocapsid antigen detection) in nasopharyngeal swabs confirm an acute infection and the risk of further spread of the SARS-CoV-2 virus. Self-tests are also available: A swab from the anterior nasal region (not from the nasopharynx) and the saliva test. These samples are less invasive and therefore more convenient for the patient, but they are less reliable and not sufficient for the medical field.

QUESTION 2:

Which vaccine is best for cancer patients? Are there differences between the various mRNA vaccines?

ANSWER 2: According to the information available so far, the effects and side effects are comparable.

QUESTION 3:

In which cases do I, as a cancer patient (< 70 years), have a particularly high risk of a severe course of the disease?

ANSWER 3: All cancer patients are considered at risk as long as they are receiving active cancer therapy. According to the recommendation of various professional associations, they should therefore be classified in an early vaccination group.

QUESTION 4:

The media have reported complications for patients with allergies who take the COVID-19 vaccine. I have hay fever. Can I still get vaccinated?

ANSWER 4: In individual cases, slight allergic reactions have been observed after vaccination. However, this applies to every vaccination.

So far, there is no official recommendation to skip the vaccine for people with allergies. Please discuss this with your doctors.

QUESTION 5:

During chemotherapy, I had a strong allergic reaction to paclitaxel. Is the coronavirus vaccination safe for me?

ANSWER 5: This has to be clarified on a case-by-case basis. However, an allergy to a cancer drug does not mean that the patient is also allergic to the COVID-19 vaccine, so this is not a criterion for exclusion.

QUESTION 6:

During my abdominal operation, the spleen had to be removed. Does this put me at increased risk for a severe course of COVID-19?

ANSWER 6: After splenectomy, the risk for certain pathogens is increased.

This is why vaccination against encapsulated bacteria such as pneumococci, haemophilus influenzae type B, and meningococci is so important for you.

The risk for a severe COVID-19 infection is not known so far.

QUESTION 7:

Are there plans to include cancer patients in the ongoing vaccine trials and, if so, when?

ANSWER 7: Cancer patients were also involved in the registration trials. However, no information is yet available on patients during ongoing therapies. New studies are being planned.

It can be assumed that there will be these specific studies in the near future.

QUESTION 8:

I have read that one vaccine contains a virus that is important for its effectiveness and harmless for healthy people. Can this „auxiliary virus“ be dangerous for cancer patients?

ANSWER 8: No. These virus components are inactive and thus harmless to humans.

They only serve as “gene shuttles” that introduce the antigens into the body.

QUESTION 9:

How important are booster vaccinations?

ANSWER 9: Each vaccine is different.

With the mRNA vaccines, a second vaccination (the “booster”) is necessary after about 21 days.

The question of whether a later booster or a complete omission of a second vaccination or the introduction of a third vaccination is necessary for cancer patients is being tested in new studies.

QUESTION 10:

Suppose I had already had a COVID-19 infection without knowing it. Can this cause the vaccination reactions to be more severe than expected?

ANSWER 10: According to the information available so far, the effects and side effects are comparable.

AND FINALLY

The COVID-19 pandemic has put everyone in exceptionally difficult situations. It is more than understandable that the topic of vaccination also raises many questions, so we would like to encourage you to discuss your questions and uncertainties directly with your doctors.

Far more than 100,000 people have been examined in the inclusion studies. The approval criteria of the drug authorities are very strict, and all studies have been independently analysed again for their safety and efficacy. The good tolerability and efficacy were the basis for the approvals in Europe and all over the world.

Many millions of people worldwide have already been vaccinated. So far, safety and tolerability have been confirmed. Therefore, the recommendation for all cancer patients is to be vaccinated according to the scientific recommendations. This is the best possible protection today, without forgetting the other important protective measures.

deutsche stiftung eierstockkrebs
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German version of this brochure is free for download on the website of Ovarian Cancer Foundation Germany:

https://stiftung-eierstockkrebs.de/wp-content/uploads/2020/08/Patientinnen--Manual_CovidAusgabe_RZ_20200631-print25.pdf

info@stiftung-eierstockkrebs.de

Internet community DIWA https://www.facebook.com/DIWA.community/

ENGAGe
ESGO European Network of Gynaecological Cancer Advocacy Groups

Contact information of ENGAGE

Webpage: https://engage.esgo.org/

Email: engage@esgo.org

Facebook: https://www.facebook.com/groups/155472521534076/about/

ENGAGe recommends contacting your local patient association!

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