

## **AOFOG Statement on COVID-19 (Gynaecological Oncology)** **(Updated on 7<sup>th</sup> Feb, 2022)**

COVID-19 pandemic has become a global problem. Cancer patients are found to be more susceptible for deterioration from COVID-19 than those without cancer. Patients and their carers should be educated with the knowledge about the signs and symptoms of COVID-19, as well as the general hygienic measures.

New patients should be triaged according to severity of symptoms, nature of the disease, availability of shared care with family physician, chance of cure, and physical fitness of the patients. Medical care providers have to be equipped with qualified protection.

Operations should be triaged where resources are restricted, and should be based on patients' symptoms, biology of the diseases, expected life expectancy, intent of the operations, complexity of the operations and the likelihood of intensive care unit (ICU) / high dependency unit (HDU) requirement.

Hypo-fractionation (increase dose per day and reduce the number of fractions) might be considered instead of conventional radiotherapy, to reduce the number of times necessary for patients to visit the hospital for treatments.

Patients receiving certain anti-cancer treatment are at risk of neutropenia and immunosuppression. Replacing parenteral medications with oral drugs and use shorter treatment regimens should be considered.

The decision should be fully discussed in multidisciplinary team and communicated to the patients and their family. The situation is evolving from time to time and different centres have different capacity, the management has to be individualised and well-documented.

Patients who are in disease remission should be deferred from routine follow-up, and those with stable active disease should have less frequent hospital visits. Follow-up by phone or video should be considered.

The number of active clinical trials should be limited and priority should be given to those trials that are curative intent, and those that offer drugs where there are limited effective therapies. The local ethics committee and sponsors should be informed about the potential deviation of the study drugs and monitoring from study protocol.

A summary of the management approach in gynaecologic cancers are as follow.

Diseases	Alternative strategies
<b>Cervical cancer</b>	
Early stage	Defer those potentially long operations like radical hysterectomy till resources become available. Neo-adjuvant chemotherapy can also be considered.
Locally advanced	Consider hypo-fractionation.
Recurrent	Consider carboplatin / paclitaxel instead of cisplatin / paclitaxel. Consider delaying non-curative treatment.
<b>Endometrial cancer</b>	
Early-stage low risk	Defer operations for 1-2 months and use progestagen at the meantime.
Early-stage high risk	Hold radiotherapy unless this is for curative intent.
Advanced stage	Consider to use chemotherapy first instead of upfront surgery. Hold radiotherapy unless this is for curative intent or severe symptoms like heavy bleeding.
Recurrent	Consider to use megestrol acetate, or megestrol acetate alternating with tamoxifen if estrogen/progesterone receptors are positive. Consider delaying non-curative treatment.
<b>Ovarian cancer</b>	
Early-stage low risk	If restaging surgery is required, it should be deferred from 1–2 months. Hold chemotherapy for controversial histology groups, such as stage 1c1 mucinous carcinoma.
Advanced stage	Consider neoadjuvant chemotherapy instead of upfront surgery, and administer 6 cycles instead of 3. Choose 3-weekly carboplatin / paclitaxel instead of dose-dense therapy. Reduce the use of HIPEC or intraperitoneal chemotherapy. For those BRCA / HRD positive and platinum sensitive patients, consider to use oral PARPi instead of bevacizumab for maintenance. For those not eligible for PARPi, need to balance the benefit of bevacizumab and the need of frequent hospital visit and risk of COVID-19.
Progressive / Recurrent	For those BRCA / HRD positive and platinum sensitive patients, consider to use oral PARPi instead of bevacizumab for maintenance. For those not eligible for PARPi, need to balance the benefit of bevacizumab and the need of frequent hospital visit and risk of COVID-19. Consider delaying non-curative treatment.
<b>Rare tumors</b>	
Uterine leiomyosarcoma	Hold chemotherapy for stage I disease. Choose doxorubicin, or oral aromatase inhibitors if estrogen receptor is positive, or pazopanib, instead of combination chemotherapy
Gem cell tumor	Hold bleomycin in dysgerminoma.
Low grade serous CA ovary	Consider aromatase inhibitor monotherapy instead of chemotherapy in advanced / recurrent patients.
Gestational trophoblastic neoplasia	Low risk: Consider pulse actinomycin-D instead of methotrexate. High risk: Consider immunotherapy instead of combination chemotherapy.
Vulvar cancers	Postpone treatment for a few weeks if a tumor is not progressing much in elderly patients. Consider neoadjuvant chemo-irradiation in advanced diseases.

Patients with cancer, especially those receiving treatment, are more vulnerable to COVID-19 and its complication due to the immunocompromised status. The European Society of Medical Oncology (ESMO) proposes RT-PCR SRAS-CoV-2 testing to all patients undergoing surgery, radiotherapy, chemotherapy or immunotherapy, ideally before each treatment / cycle. If the availability of RT-PCR SRAS-CoV-2 testing is limited, it should be considered in patients with symptoms suggestive of COVID-19 infection like fever, cough and sore throat.

Although cancer patients are generally excluded from COVID-19 vaccine clinical trials, recent data demonstrated that most vaccines were safe and effective in cancer patients. The ESMO and the National Comprehensive Cancer Network (NCCN) advocate COVID-19 vaccination in all cancer patients, except those who are undergoing stem cell transplantation or CAR T-cell therapy who should delay the vaccination after 3 months. The NCCN also suggests patients who have just had major surgery should delay the vaccination a few days to up to 2 weeks so that the clinicians can determine any complications like fever are due to surgery or vaccines.

Currently there is no strong evidence to recommend one vaccine over the others. Patients with cancer can achieve a clinically relevant seroconversion rate comparable to the general population after full COVID-19 vaccination [1, 2]. Nevertheless, the seroconversion rate appeared to be lower for those receiving cytotoxic chemotherapy [3]. The United States Centres for Disease Control and Prevention (CDC) recommends a 3<sup>rd</sup> dose of either the Pfizer / BioNTech or Moderna vaccine for people who are immunocompromised, who received cancer therapy within 1 year of their 1<sup>st</sup> dose of the COVID-19 vaccine, and who have newly diagnosed or recurrent cancer who will receive cancer therapy. And patients should get the 3<sup>rd</sup> dose as soon as 4 weeks after the 2<sup>nd</sup> dose. They should wear masks, avoid crowds and maintain good hygiene. Their carerers and close contacts should adopt the same preventive strategies.

Meta-analyses showed that COVID 19 infection did not have any interaction with surgery, immunotherapy and targeted therapy. There is no evidence that the use of immune checkpoint inhibitors can increase the risk or worsen the prognosis of COVID-19 infection [4, 5]. However, the interaction with chemotherapy is inconclusive [6-8]. The American Society of Clinical Oncology (ASCO) recommends initiating or resuming anti-cancer therapy once transmission-based precautions are no longer necessary, which the latter is based on the CDC recommendations. The United Kingdom National Institute for Health and Care Excellence also suggests treatment to be initiated or resumed after one negative SARS-Cov-2 test. Therefore, there is no need to routinely withhold or interrupt anti-cancer treatment.

## **Resources**

### **American Society of Clinical Oncology**

<https://www.asco.org/asco-coronavirus-information/care-individuals-cancer-during-covid-19>

### **Asian Society of Gynecologic Oncology**

<http://www.asiansgo.org/News/News/view.asp?seq=32&pagec=1&find=&searchword=>

### **British Gynaecological Cancer Society**

<https://www.bgcs.org.uk/public-information/covid-19/>

### **European Society of Gynaecological Oncology**

<https://www.esgo.org/esgo-covid-19-communication/>

### **European Society of Medical Oncology**

<https://www.esmo.org/for-patients/patient-guides/cancer-care-during-the-covid-19-pandemic>

<https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic/gynaecological-malignancies-epithelial-ovarian-cancer-in-the-covid-19-era>

<https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic/gynaecological-malignancies-endometrial-cancer-in-the-covid-19-era>

<https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic/gynaecological-malignancies-cervical-cancer-in-the-covid-19-era>

<https://www.esmo.org/guidelines/cancer-patient-management-during-the-covid-19-pandemic?page=1>

<https://www.esmo.org/covid-19-and-cancer/covid-19-vaccination>

### **National College of French Gynecologists and Obstetricians**

<https://www.sciencedirect.com/science/article/pii/S2468784720300635>

### **International Federation of Gynecology and Obstetrics**

<https://www.igo.org/covid-19-management-gynecological-cancers>

### **International Gynecologic Cancer Society**

<https://igcs.org/covid-19/>

### **Society of Gynecologic Oncology**

<https://www.sgo.org/clinical-practice/management/covid-19-resources-for-health-care-practitioners/>

### **Society of Gynecologic Oncology of Canada**

<http://g-o-c.org/publications/goc-position-statements/>

### **National Comprehensive Cancer Network (NCCN)**

<https://www.nccn.org/covid-19/>

## **References**

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3. Thakkar A, Gonzalez-Lugo JD, Goradia N, Gali R, Shapiro LC, Pradhan K, et al. Seroconversion rates following COVID-19 vaccination among patients with cancer. *Cancer Cell*. 2021;39:1081-90 e2.
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6. Zhang H, Han H, He T, Labbe KE, Hernandez AV, Chen H, et al. Clinical Characteristics and Outcomes of COVID-19-Infected Cancer Patients: A Systematic Review and Meta-Analysis. *J Natl Cancer Inst*. 2021;113:371-80.
7. Liu Y, Lu H, Wang W, Liu Q, Zhu C. Clinical risk factors for mortality in patients with cancer and COVID-19: a systematic review and meta-analysis of recent observational studies. *Expert Rev Anticancer Ther*. 2021;21:107-19.
8. Park R, Lee SA, Kim SY, de Melo AC, Kasi A. Association of active oncologic treatment and risk of death in cancer patients with COVID-19: a systematic review and meta-analysis of patient data. *Acta Oncol*. 2021;60:13-9.

## COVID-19 vaccination and Cancer

COVID -19 has had devastating effects on patients with cancer, with many missed diagnosis and delayed treatments due to health systems under pressure and at times patients themselves are reluctant to seek medical care.

Unfortunately, there have been second and third waves of the pandemic globally, but the glimmer of hope is the rollout of vaccinations in countries albeit at a lower rate than anticipated.

Women with cancer are at an increased risk of contracting COVID-19, at greater risk of infection and death than the general population. (1) Even though there is limited evidence of the use of COVID-19 vaccines in people with cancer, some guidelines should be available for clinicians based on the evidence at hand.

### Should women with cancer receive COVID-19 vaccine?

Yes. There is no real data on vaccine immunogenicity and efficacy specifically for oncology patients but because of the high risk of severe infection from COVID in this vulnerable group the benefits are thought to outweigh the uncertainty.

International consensus that patients with cancer should be prioritised for vaccination include

- European Society of Medical Oncology (ESMO) <https://www.esmo.org/covid-19-and-cancer/covid-19-vaccination>
- National Comprehensive Cancer Network (NCCN) [https://www.nccn.org/covid-19/pdf/COVID-19\\_Vaccination\\_Guidance\\_V1.0.pdf](https://www.nccn.org/covid-19/pdf/COVID-19_Vaccination_Guidance_V1.0.pdf)
- UK Chemotherapy Board [https://b-s-h.org.uk/media/19241/clinician-faqs-and-guidance-on-covid19-vaccine-for-patients-receiving-sa\\_.pdf](https://b-s-h.org.uk/media/19241/clinician-faqs-and-guidance-on-covid19-vaccine-for-patients-receiving-sa_.pdf)
- American Society of Clinical Oncology (ASCO) <https://www.asco.org/asco-coronavirus-resources/covid-19-patient-care-information/covid-19-vaccine-patients-cancer>

Immunocompromised women might not mount a robust immune response compared to others so consideration should be given to the timing of vaccination.

### General Advice after Vaccination

- Encourage them to continue good infection prevention and control measures even after receiving the vaccine, including good hand hygiene and staying away from others who are unwell.
- Household and family members should be vaccinated when the vaccine is made available to them to reduce the risk of infection.

### Vaccination for those on chemotherapy

There is limited data on the optimal timing of vaccination in relation to chemotherapy (2)

If it is possible then the vaccination should occur at the furthest point from the immunosuppressing effect of the chemotherapy during any given cycle.

- If possible, for patients planned for but not yet on chemotherapy, time first dose of vaccine to be at least 2 weeks prior to initiation of therapy, if that does not delay commencing therapy, to maximise time for seroconversion.
- If possible, for patients already on chemotherapy, time first dose of vaccine in between chemotherapy cycles, away from nadir.
- If possible, for patients completing chemotherapy, time first dose of vaccine to be given after therapy complete and nadir resolved

If the above is not possible then avoid giving the COVID-19 vaccine on the same day as chemotherapy, based on extrapolated information on efficacy rather than safety (3)

### Considerations for Cancer related surgery

Vaccinations have been used in many patients and has been shown to be low risk. There is no specific policy for the timing for vaccine efficacy for patients undergoing surgery though vaccine side effects could be confused from postoperative complications. Some patients may have fever and chills especially after the second dose. (4)

Major surgery should be separate from vaccination by a week.

Emergency surgery should not be delayed.

There are no head-to-head trials comparing the different vaccines so patients should be encouraged to accept what they are offered in their countries.

Given the risks of contracting COVID-19 at the time of surgery, ideally all patients should be offered vaccination prior to surgery,

### References

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2.Kamboj M, Hohl T, Vardhana S, et al. MSK COVID-19 VACCINE INTERIM GUIDELINES FOR CANCER PATIENTS. <https://www.asco.org/sites/new-www.asco.org/files/content-files/covid-19/2021-MSK-COVID19-VACCINE-GUIDELINES.pdf>

3. UK Chemotherapy Board. Clinician Frequently Asked Questions (FAQs) and guidance on COVID-19 vaccine for patients receiving Systemic Anti-Cancer Therapy.

<https://www.ukchemotherapyboard.org/publications/2021>

4. Joint RCOG/BGCS Guidance for Care of Patients with Gynaecological Cancer during the COVID-19 Pandemic

Version 4.0: Published 19 April 2021 <https://www.rcog.org.uk/globalassets/documents/guidelines/2021-04-19-bgcs-guidance.pdf>