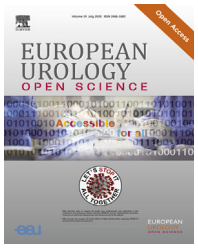
EUROPEAN UROLOGY OPEN SCIENCE 29 (2021) 77–81

available at www.sciencedirect.com
journal homepage: www.eu-openscience.europeanurology.com



European Association of Urology

Brief Correspondence

The Uro-oncology Patient and Vaccination Against SARS-CoV-2

Moises Rodriguez Socarrás [a,†], *Juan Gómez Rivas* [b,†,*], *Jeremy Yuen-Chun Teoh* [c], *Javier Puente* [d], *Marco Moschini* [e], *Jesús Moreno-Sierra* [b]

Article info

Article history:
Accepted May 19, 2021

Associate Editor:
Silvia Proietti

Keywords:
Cancer
COVID-19
Uro-oncology
Vaccine

Abstract

As of April 13, 2021, 137 million cases of COVID-19 and 2.95 million deaths have been reported worldwide. On December 21, 2020, the Pfizer-BioNTech vaccine was approved for use in the European Union, with efficacy of 95% protection against COVID-19 infection. Several other vaccines are at different stages of assessment by the European Medicines Agency. In addition to the elderly, oncology patients are a vulnerable population in which COVID-19 infection may be more severe. However, owing to the design of the initial studies, evidence on the safety and efficacy of vaccination against SARS-CoV-2 in these patients is scarce and recommendations are based on the opinion of associations, stakeholders, and experts via extrapolation of information and experience for other vaccines, especially influenza vaccines. Despite the limited evidence, the consensus is that SARS-CoV-2 vaccines are safe and vaccination of oncology patients and their close relatives is recommended, although efficacy may be lower in patients with an impaired immune response and the need for additional booster doses is not yet clear. Recommendations include avoiding the use of vaccines based on viral vectors for patients with an impaired immune response, deferring vaccination for immunosuppressed patients or administering the vaccine before immunosuppression, and avoiding chemotherapy receipt between the two doses of a vaccine or on the same day that the vaccine is administered. These recommendations can be extrapolated to urology patients and although evidence is lacking, there should not be greater interference with SARS-CoV-2 vaccines from androgen deprivation therapy or intravesical bacillus Calmette-Guérin. However, large studies to provide strong evidence for uro-oncology patients are needed.

Patient summary: We looked at the effects of COVID-19 vaccination for patients with urological cancers. The consensus is that the vaccines are safe, and vaccination of cancer patients and their close relatives is recommended.

As of April 13, 2021, 137 million cases of COVID-19 and 2.95 million deaths had been reported worldwide [1]. On December 21, 2020, the Pfizer-BioNTech vaccine was approved for use in the European Union, with efficacy of 95% against COVID-19 infection. So far, the European Commission has granted conditional marketing authorisation for three other vaccines developed by Moderna, AstraZeneca, and Janssen Pharmaceuticals following

http://dx.doi.org/10.1016/j.euros.2021.05.007

positive European Medicines Agency (EMA) assessment of their safety and efficacy. Several other vaccines are at different stages of assessment by the EMA.

SARS-CoV-2 infection appears to be more severe in vulnerable patients such as the elderly and in some groups of oncology patients. Preliminary data suggest that SARS-CoV-2 infection is associated with higher mortality among cancer patients [2], especially those receiving anticancer treatment 14 d before infection [3]. Perioperative SARS-CoV-2 infection increases postoperative mortality, so cancer surgery for patients with COVID-19 may need to be delayed [4]. The evidence is currently sparse regarding the effectiveness and safety of COVID-19 vaccination in oncology patients. This is because in the first studies performed with the vaccine, oncology patients were excluded as individuals with an impaired immune response would have confounded the efficacy rates in trials.

The recommendations from various associations [5–7] are based on the opinion of experts and stakeholders, as well as experience and information extrapolated from other vaccines, especially influenza vaccines. However, the efficacy, immune response, and protection afforded may be diminished in patients with haematological cancers, patients with neutropenia or lymphopenia, and patients who have received anti-CD20 antibodies such as rituximab [7].

The general consensus is that the vaccine against COVID-19 is considered safe in oncology patients and they and their close relatives should be vaccinated [5–7], although some considerations are required regarding the stage of the disease, chemotherapy and immunotherapy receipt, and immunosuppression status, as described below for uro-oncology patients.

As of April 2021, there were 12 vaccines in use and another 77 under study in phase 1 (n = 24), phase 1/2 (n = 26), phase 2 (n = 7), phase 3 (n = 16), and phase 4 (n = 4) trials, as well as 277 being evaluated in preclinical studies [8]. Vaccines are based on RNA (n = 38), DNA (n = 26), nonreplicating viral vectors (n = 37), replicating viral vectors (n = 24), inactivated virus (n = 20), live attenuated virus (n = 4), protein subunits (n = 99), virus-like particles (n = 22), and other/unknown mechanisms (n = 39).

Table 1 summarises the characteristics of five of the available vaccines against COVID-19. Figure 1 presents vaccination rates by country to date, for individuals with at least one dose received, adjusted by income (gross domestic product per capita in US dollars).

Regarding safety and efficacy in oncology patients, the consensus is that COVID-19 vaccination is safe, but with some special considerations. However, the main concern is that efficacy may be diminished in patients with weakened immune systems, and it is not yet clear whether these patients need additional booster doses of the vaccine [7,9]. Some cancer treatments, such as chemotherapy, radiation, stem cell or bone marrow transplantation, and immunotherapy, can affect the immune system, which could make any vaccine less effective [6,7]. To address this gap, the VOICE study (vaccination against COVID in cancer; NCT04715438) is currently investigating this issue and hopefully will answer some questions [10].

The initial studies testing COVID-19 vaccines did not include patients being treated with immunosuppressive drugs or chemotherapy or individuals with an impaired immune response for other reasons. Therefore, the efficacy and duration of immunity in patients with

Table 1 – Characteristics and status of the main vaccines available against COVID-19

	BioNTech/Pfizer BNT162b2	Gamaleya Gam-COVID-Vac/Sputnik V	Janssen Ad26.COV2.S	Moderna mRNA-1273	Oxford/AstraZeneca ChAdOx1-S
Developer(s)	BioNTech, Pfizer, Fosun Pharma	Gamaleya Research Institute	Janssen Pharmaceuticals	Moderna, NIAID	University of Oxford, AstraZeneca
Platform	RNA	Nonreplicating viral vector	Nonreplicating viral vector	RNA	Nonreplicating viral vector
Dosing	2 doses, intramuscular	2 doses, intramuscular	1 or 2 doses (to be determined), intramuscular	2 doses, intramuscular	2 doses, intramuscular
Efficacy data	Efficacy against COVID-19 95% according to primary efficacy analysis of 170 confirmed cases	Efficacy against COVID-19 92% according to primary efficacy analysis of 78 confirmed cases	Efficacy against moderate to severe COVID-19 66% according to a press release on Jan 29, 2021; estimates based on 468 confirmed cases	Efficacy against COVID-19 94% according to primary efficacy analysis of 196 confirmed cases	Efficacy against COVID-19 62–90% according to interim data from 131 cases
Storage requirements	Ultracold (−60 °C to −80 °C)	Lyophilised formulation requiring refrigeration (2–8 °C) or frozen formulation (maximum −18 °C)	Refrigeration (2–8 °C)	Refrigeration (2–8 °C) for up to 30 d or frozen (−15 °C to −25 °C) for long-term storage	Refrigeration (2–8 °C)
Manufacturing projections	Up to 2 billion doses in 2021 (February 2, 2021)	No information on institute website; up to 1 billion doses in 2021 according to media reports (November 24, 2020)	1 billion doses per year as of 2021 (January 5, 2021)	Up to 1 billion doses in 2021 (February 25, 2021)	3 billion doses in 2021 (December 30, 2020)
Approval status	Full or emergency use in numerous countries; granted emergency use approval by the World Health Organization on December 31, 2020	Early or emergency use in numerous countries, including Russia, Belarus, Argentina, Serbia, and Algeria	Early or emergency use in South Africa, Bahrain, and USA	Full or emergency use in numerous countries, including USA, Canada, EU, UK, and Israel	Emergency use in numerous countries, including UK, EU, India, Argentina, Dominican Republic, and El Salvador

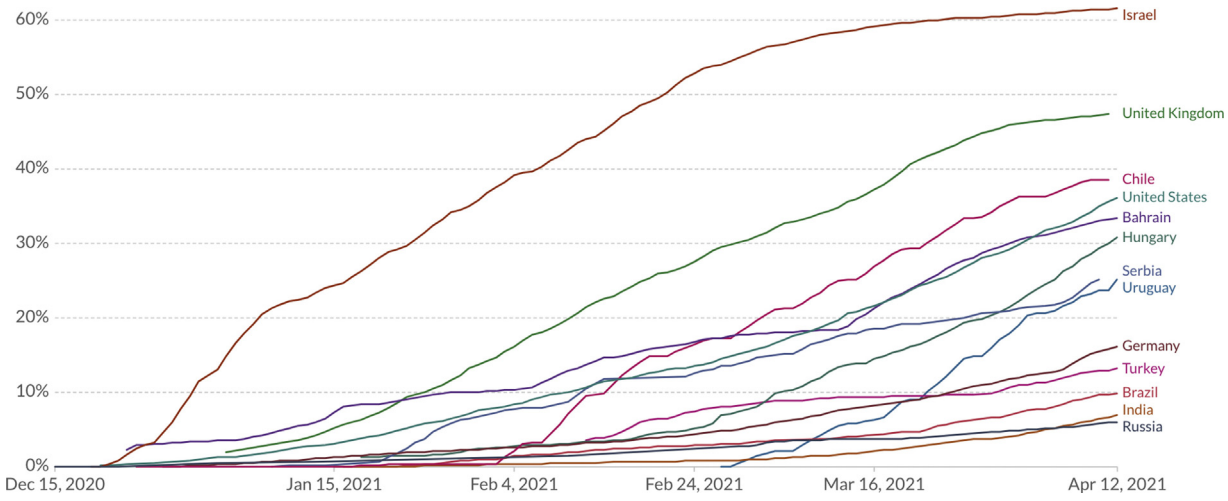


Fig. 1 – Total population that has received at least one vaccine dose for selected countries. This may not equal the number of fully vaccinated if the vaccine requires two doses. Source: https://ourworldindata.org/covid-vaccinations.

cancer are still unknown and unexplored. A study on the short-term safety of mRNA vaccines among cancer patients being treated with immune checkpoint inhibitors (ICI) revealed that the adverse events appeared to be similar to healthy controls and the authors conclude that vaccine should be given [11]. Considering the risk-benefit balance and knowing that SARS-CoV-2 infection in oncology patients can be more severe, the recommendation is that these patients and their relatives should be vaccinated.

One question that arises is whether cancer patients should receive a specific vaccine against COVID-19. There are no studies that directly compare different types of vaccine in oncology patients. Therefore, it is not yet clear whether any of the vaccines are safer or more effective than the others. It is also not known whether any of the vaccines will be more (or less) effective against some of the new variants of SARS-CoV-2 [5].

Efficacy data for older people suggest that higher immunity is induced by the mRNA vaccines produced by Pfizer-BioNTech and Moderna in comparison to the Oxford-AstraZeneca vaccine [7]. While there are no specific data for cancer patients to date, it bears mentioning that nonreplicating viral vectors are not contraindicated in immunocompromised patients. Vaccines based on inactivated whole virus or on part of the virus, most often combined with an adjuvant to enhance the immune response, are currently under development (Sinopharm, China). While these vaccines do not seem to be particularly immunogenic, they may be of use for cancer patients [12]. Some of the most advanced vaccine candidates are mRNAs encapsulated in lipid carriers, and small liposomes are expected to accumulate in tumour tissues through the enhanced permeation and retention effect. However, it remains unknown to what extent solid tumours could take up a significant proportion of the vaccine dose [13].

Recommendations and considerations for oncology patients are as follows [5–7,9]:

- Considering the safety and risk-benefit balance, the general recommendation is that cancer patients should be vaccinated even if the immunity achieved is lower than in the general population, as even this may reduce the risk of severe COVID-19 caused by SARS-CoV-2 infection.
- Health care workers and family members and close relatives of cancer patients should be vaccinated.
- Vaccines based on live attenuated and replicating viruses should not be used, in patients with impaired immune response.
- Future studies should investigate the most effective vaccine in the oncology population, if possible, which could have implications for selection of the type of vaccine used in cancer patients.
- The decision to receive a COVID-19 vaccine should be stratified by age, type of cancer, and stage of disease.
- Whenever possible, the vaccine should be administered before initiation of chemotherapy. For patients who have already started chemotherapy, the existing data do not support a specific timing for vaccine administration with respect to chemotherapy infusions [14].
- A pharmacovigilance plan is mandatory for the vaccination programme. Continued research in the context of clinical trials and registries, as well as in-trial and post-trial follow-up, is advised in order to generate more data on vaccine efficacy and safety in both the general population and special populations, including patients with cancer or a history of cancer [15].

Reasonable criteria for postponing COVID-19 vaccination are as follows [7,9]:

(1) Patients who have received anti-CD20 antibodies in the past 6 mo or recent therapy with immunotherapy and immunosuppressants;
(2) Patients after stem cell transplantation with a high degree of T-cell suppression who generally respond poorly to vaccines; and

(3) Patients receiving high doses of corticosteroids (1 mg/kg prednisolone or equivalent >60 mg/d) owing to lower efficacy.

A scheduled surgery is not a reason to defer vaccination. Although there is no evidence, we consider that urological surgery can be safely performed after a reasonable period of time, such as 10 d after vaccination.

Regarding considerations for uro-oncology patients, radiotherapy and androgen deprivation therapy in prostate cancer patients should not interfere with the vaccine response. The opinion is that the COVID-19 vaccine can be safely administered in patients receiving intravesical bacillus Calmette-Guérin [6,7]. Retrospective data sets suggest good tolerability and safety for influenza vaccination among patients with cancer receiving immune checkpoint inhibitors, as well as patients on cytotoxic therapy or targeted agents [16–20]. According to bladder cancer stakeholders, patients undergoing active systemic chemotherapy or radiotherapy, those receiving treatment with pembrolizumab, atezolizumab, or avelumab, and those for whom cancer surgery is scheduled in the near future should be prioritised for vaccination [6].

The aim of the COVID-19 vaccination programme is to first vaccinate the population at greatest risk of harm from COVID-19 infection. A valid question is how long the response lasts in oncology patients and whether they need more booster doses. It would be desirable to be able to quantify the immune response and protection against COVID-19 on an individualized basis.

In conclusion, although the evidence is sparse, vaccination against COVID-19 is recommended for oncology patients and their close relatives. It is expected that the immunological effect may be lower in patients with an altered immune response, but the need for extra booster doses is unclear. Longer studies providing strong evidence in oncology patient populations are needed.

Author contributions: Juan Gómez Rivas had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Rodriguez Socarrás, Gómez Rivas.
Acquisition of data: Rodriguez Socarrás, Gómez Rivas, Teoh, Puente.
Analysis and interpretation of data: Rodriguez Socarrás, Gómez Rivas, Teoh, Puente, Moschini.
Drafting of the manuscript: Rodriguez Socarrás, Gómez Rivas, Teoh, Puente.
Critical revision of the manuscript for important intellectual content: Rodriguez Socarrás, Gómez Rivas, Teoh, Puente, Moschini, Moreno-Sierra.
Statistical analysis: None.
Obtaining funding: None.
Administrative, technical, or material support: Rodriguez Socarrás, Gómez Rivas.
Supervision: Rodriguez Socarrás, Gómez Rivas, Teoh, Puente, Moschini, Moreno-Sierra.
Other: None.

Financial disclosures: Juan Gómez Rivas certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

***Funding/Support and role of the sponsor*:** None.

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[a]*Instituto de Cirugía Urológica Avanzada, Madrid, Spain*
[b]*Department of Urology, Hospital Clínico San Carlos, Madrid, Spain*
[c]*Department of Surgery, S.H. Ho Urology Centre, Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong*
[d]*Department of Oncology, Hospital Clínico San Carlos, Madrid, Spain*
[e]*Department of Urology, San Raffaele University and IRCCS San Raffaele Hospital and Scientific Institute, Milan, Italy*

*Corresponding author. Department of Urology, Hospital Clínico San Carlos, Calle del Prof Martín Lagos, S/N, 28040 Madrid, Spain. Tel.: +34 9 91 330 37 65.
E-mail address: juangomezr@gmail.com (J. Gómez Rivas).
†These authors contributed equally and are joint first authors.