



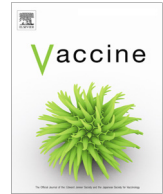
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Commentary

COVID-19 vaccination for cancer patients: Evidence, priority, and practice



Shiv Rajan ^{a,*}, Naseem Akhtar ^a, Sonali Sharma ^b, Deep Chakrabarti ^c, Vijay Kumar ^a

^a Department of Surgical Oncology, King George's Medical University, Lucknow, India

^b Department of Gynecology and Obstetrics, King George's Medical University, Lucknow, India

^c Department of Radiation Oncology, King George's Medical University, Lucknow, India

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Practising universal precautions and getting vaccinated are the only preventive strategies during this COVID-19 pandemic. The universal precautions have been there in all guidelines since the outset. The desperate pandemic situation drove the pedal of vaccine development once the viral genome was sequenced in mid-2020 and expedited their clinical trials. By the end of 2020, data for several COVID-19 vaccines started surfacing [1].

As of June 2021, a total of 18 vaccines have got Emergency Use Authorization (EUA). Only nine had available phase III data (Oxford–AstraZeneca, Pfizer–BioNTech, Moderna, SputnikV, Janssen, CoronaVac, Covaxin, Convidecia and Sinopharm) comprising approximately 0.33 million participants [2].

However, till today there is no data to prove vaccine safety and efficacy in patients with cancer. Only two vaccine trials have enrolled cancer patients but to a meagre extent. Around 1700 (4%) cancer patients were enrolled in the Pfizer vaccine trial, and approximately 200 (0.5%) patients in the Janssen vaccine trial had a diagnosis of cancer. These patients were not analyzed separately to inform immunogenicity, safety, efficacy, or duration of

protection against the virus. Therefore, the post-marketing surveillance data will provide crucial information about long-term efficacy or adverse effects. Additionally, ongoing vaccination programmes worldwide will continue to generate data and provide a real world context.

Cancer patients already remain in a varying state of immune compromise either due to cancer itself or its treatment and complications [1,2]. This has therefore led to disarray among patients who are already facing myriads of pandemic manifestations in their life [3]. Considering that the enrolment of cancer patients in these placebo-controlled randomized vaccine trials is unethical, advisories for them have been extrapolated from the general population. Consequently, several expert cancer societies have issued recommendations for vaccination in these patients [4–9]. We tried to distil the most updated knowledge and possible gaps to address the issue related to COVID vaccination in cancer patients.

1. Should cancer patients or cancer survivors get COVID-19 vaccination?

At this juncture, despite the lack of high-quality evidence but assuming benefits outweigh the risk, experts in various societies in unison recommend vaccination for patients with active cancer or its survivors [4–7].

* Corresponding author.

E-mail address: shivrajan.194@gmail.com (S. Rajan).

2. Are there cancer patients who should not be vaccinated?

Experts warn against COVID vaccination if there are contraindications to any specific vaccine component [6].

3. Should patients be prioritized according to the type of cancer treatment?

Cancer patients planned for treatment, undergoing treatment, or immediately post-treatment should have a higher priority than those receiving only hormonal therapy. There is no prioritization based on the type of treatment, i.e., surgery, radiotherapy, chemotherapy, targeted therapy, or immunotherapy [4]. Experts have proposed a four-step process for prioritization that estimates the phase of cancer, medical risk of patients, vaccine-related effects on the tumour, and informed combined decision making [5].

4. How effective and safe is the COVID-19 vaccine in cancer patients?

Every cancer patient has a different degree of immune compromise, modulated by various factors like the type of malignancy, patient fitness, pre-existing immune dysfunction, or type of anti-cancer treatment. However, the degree of immunogenicity, efficacy, and durability of protection against this virus in vaccinated cancer patients are still being investigated [5]. Nonetheless, vaccination is safe and should reduce the risk of sub-clinical or clinical COVID-19 disease [4–8].

5. What is the vaccine recommendation for patients planned or undergoing chemotherapy?

The optimal timing, type, and frequency of the vaccine in relation to chemotherapy are controversial. Few recommend vaccination whenever available [4]. While others suggest that patients who have yet to begin their first cycle of chemotherapy should receive their vaccination at least two weeks before starting chemotherapy [5,8]. Those who are already undergoing chemotherapy, leucopenia, or pancytopenia are marked during the middle of the cycles. Therefore, vaccines should be administered when this period has settled [8].

6. What is the optimal timing of vaccine in patients planned for immune checkpoint inhibitor?

There is a presumed increased risk of immunogenic adverse events with these drugs and vaccines together. There is no guiding statement for this drug category as these patients were not enrolled in the vaccine trials. Few suggest not to pause immunotherapy for vaccination [8]. Others recommend vaccination on the same day as immunotherapy to reduce added visits [4].

7. What is the optimal timing of vaccine in patients planned for surgery?

Surgical treatment should not alter the candidacy for vaccination. Though vaccination and surgery often accompany a fever, vaccination and major surgery should be separated by a few days or weeks. For patients undergoing splenectomy, this interval should be at least two weeks [4,8,9].

8. What is the optimal timing of vaccine in patients planned for radiotherapy?

No specific timing constraint exists, and vaccination should be offered to patients undergoing radiotherapy whenever available [4,8].

9. Should cancer patients be routinely tested for antibodies titer post-vaccination?

There is no known correlation between antibody titers and the period or level of protection from COVID-19 infection [1]. Therefore, routine assessment of antibody titer is not recommended. Additionally, evaluation of T-cell responses should not be done routinely [4].

10. Are cancer patients protected from COVID infection after complete vaccination?

Current vaccines are potentially effective in preventing COVID infection and associated mortality. Nevertheless, a fully vaccinated individual can get infected if exposed to the virus. These are known as breakthrough cases. The reason behind it is that the mucosal protection (IgA) is weak with the available vaccines [10]. Hence, it is recommended that even after being fully vaccinated, physical distancing and hand hygiene measures are followed religiously [4–8].

11. Should people caring for cancer patients be prioritized for vaccination?

Healthcare workers taking care of cancer patients should be prioritized for vaccinations to minimize sources of transmission [5]. Additionally, those directly around cancer patients (e.g., household members or caregivers) should also be considered for early vaccination [4].

12. Do the COVID-19 vaccines have any interaction with antineoplastic therapies?

There is no data on the interaction of the vaccines with antineoplastic therapies. There is a real need to generate substantial evidence in these directions from post-trial surveillance or by monitoring various cancer registries [5].

13. Should cancer patients get revaccinated if the vaccine was administered during a period of immunosuppression?

There is no relevant data for this at present from any studies, and therefore no recommendations have been made [8].

14. Will booster doses of vaccines be needed in the future?

There is no current evidence or recommendation for the need for booster doses for the COVID-19 vaccine beyond the manufacturer-recommended dosing schedule for any patients [8]. Theoretically, there could be a need for a booster in the future if the pandemic persists, but it has to be supplemented by phase IV data before any such recommendation.

15. Should patients who have recovered from COVID-19 infection be vaccinated?

Patients with prior COVID-19 infection should also be vaccinated. Though there is no recommended minimum interval between infection and vaccination [8].

16. Should vaccines be given to patients with positive COVID-19 antibodies?

The vaccine is considered safe in patients with positive COVID-19 antibodies. There is not enough data to correlate antibodies with long-term immunity, and routine serological tests should not guide vaccination timing [5,8].

17. Is any premedication required in cancer patients before the vaccination to reduce side effects?

There is no recommendation in this regard over the general population. For patients with a history of allergy, premedication may mask early life-threatening symptoms of hypersensitivity and is therefore not recommended [8].

18. Where do cancer patients stand in the worldwide COVID-19 vaccination strategy?

Only 11.6% of the world population is fully vaccinated at present. Despite the fact, the vaccination is 30 times faster in High-income countries (HIC; 10% of the global population), vaccine deployment is sluggish in some HICs (Canada, Japan, Taiwan, South Korea, New Zealand, Australia) where < 5% population is immunized [11]. Low-middle Income countries (LMICs) are considerably lagging because of vaccine hoarding, unequal demand, delivery obstacles, financial hurdles, and lack of a national vaccination plan [12].

Countries across the globe have prioritized elderly and health care workers in their national vaccination plans. However, the inclusion of cancer patients has been inconsistent. Only 14 countries are routinely vaccinating cancer patients (USA, UK, Chile, Canada, Turkey, Lebanon, Jordan, India, Argentina, France, Australia, Belgium, Luxembourg, and Sweden) [5,11].

19. Will there be a new hope with the nasal COVID vaccines?

The currently available vaccines provide systemic immunity (IgG) but do not provide adequate immunity (IgA or T cell) at nasal or pharyngeal mucosa. This means a person can lodge the virus and transmit it back to others. The upcoming nasal vaccines (BBV154, AdCOVID) claim to provide both mucosal and systemic immunity and therefore augment the virus transmission chain break [2].

20. Conclusion

Cancer patients are at a high risk of COVID-19 and should be prioritized for vaccination. At this juncture, expert's recommendations regarding appropriate timing should be followed for surgery, radiotherapy, chemotherapy, or immunotherapy. Given the insufficient data on cancer patients from the vaccination trials, growing numbers of vaccines, different scheduling, genetically and geographically diverse patient population, and multiple cancer types, there is a demand for urgent analysis of the vaccine in cancer patients across the globe on a unified platform to guide ongoing policies and plans ahead.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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