

Safety of COVID-19 Vaccine in Patients with Cancer in a High-Volume Comprehensive Cancer Center

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Abstract

Background: Few data are available on the safety of COVID-19 vaccines in cancer patients undergoing active cancer-directed treatment.

Patients and Methods: This case series analyzes outcomes in terms of adverse events in 5297 patients undergoing anti-cancer treatment who were vaccinated with anti-SARS-CoV-2 Pfizer-BioNTech vaccine at a single cancer center from March 6, 2021 to May 9, 2021. Adverse events were retrieved from the national Italian pharmacovigilance platform (<http://www.vigicovid.it>).

Results: Of the 5297 patients treated for either solid tumors (87%) or onco-hematologic malignancies (13%) who were vaccinated, 8 adverse drug reactions (ADRs) were reported. One was a severe ADR and 7 were non-severe ADRs. Non-severe ADRs resolved within 48 hours.

Conclusion: BNT162b2 Pfizer-BioNTech vaccine was safely administered in the largest cohort of cancer patients reported to date.

Key words: cancer; chemotherapy; mRNA; vaccine; COVID-19.

Introduction

Morbidity and mortality from COVID-19 in patients with cancer undergoing cancer-directed treatment are high, with approximately one-third of patients experiencing severe course of disease, approximately three quarters requiring hospitalization, with mortality rates of approximately 30%.^{1,2} Patients with hematologic cancer have been shown to have higher mortality compared with patients with solid cancer.¹⁻³

The risk of a severe form of COVID-19 is mainly related to comorbidity, with chemotherapy within the last 30 days before COVID-19 diagnosis being associated with higher risk of death.^{1,4}

COVID-19 is also associated with delay in treatment with consequent potential impact on oncologic outcomes, in light of prioritization policies with postponement of chemotherapy, radiotherapy, and/or surgery, as well as limited access to supportive care that impact quality of life.⁵

Although type and degree of immunosuppression can vary substantially among heterogeneous patient groups, there is mounting evidence that patients with cancer do not develop as much humoral immunity as non-cancer subjects and may

remain contagious and able to spread SARS CoV2 for several months.⁶ Yet, recent data suggest a role of CD8+T-cell response that might provide protection in patients with cancer even in the setting of defective humoral immunity.⁷

COVID-19 vaccines have been made available since the end of 2020. There are currently 2 mRNA vaccines (Pfizer-BioNTech and Moderna) and 2 adenovirus-based vaccines (Oxford-AstraZeneca and Johnson & Johnson) for which phase III placebo-controlled randomized clinical trials show an impressive efficacy.

Based on their high efficacy as per results of phase III trials,^{8,9} mRNA vaccines have been recommended for use in immunocompromised and frail patients by national and international guidelines.^{10,11}

Despite being highly recommended, the efficacy and safety profiles of vaccines against SARS-CoV-2 in patients with cancer are unknown since they were excluded by registration trials. Indeed, at the ESMO 2021 congress new data on efficacy of COVID-19 vaccines in patients with cancer have been presented, alongside with preliminary safety data, which hinted at a safety profile in the patient with cancer population

which could overlap to the that observed in the general population.¹¹⁻¹⁵

As per the Veneto Oncological Network (Rete Oncologica Veneta, ROV) criteria, Oncology Units in the Veneto Region are in charge for the vaccination of patients who either are being treated with chemotherapy, immunotherapy, and targeted therapy, or have completed the treatment in the past 6 months.

Results

From March 6 to May 9 2021, a total of 5297 patients treated at Veneto Institute of Oncology, IOV for either solid tumors (87%) or onco-hematologic malignancies (13%) have been vaccinated with two 30 µg doses of the BNT162b2 Pfizer-BioNTech COVID-19 vaccine (Comirnaty©) administered intramuscularly 21 days apart.

Among all patients with the above stated criteria who were therefore proposed vaccination, 207 (3.9%) refused to get vaccinated. Overall 10.820 doses of vaccines have been administered, with 226 patients (1.8%) who had received the first dose not completing the planned second dose because of either worsening of general conditions, admission to other hospital wards, occurrence of COVID-19 infection, or death. Indeed, a minority of patients (14 patients) developed COVID-19 infection right after first dose.

Overall 4324 patients (81.6%) were actively receiving oncological treatment, and 973 (18.4%) had completed it in the past 6 months. Details on treatment are presented in [Table 1](#).

No specific timing regarding the chemotherapy schedule was required, except patients were not vaccinated on the same day of chemotherapy. As a general approach, although the first vaccine dose was preferentially administered before starting cytotoxic chemotherapy whenever possible.

Patients remained under observation for 15 or 30 minutes after vaccination according to medical history. Overall, out of 8 adverse drug reactions (ADRs) reported through the national pharmacovigilance website (www.vigicovid.it), 1 was a severe ADR and 7 were non-severe ADRs. The severe ADR was a central retinal artery thrombosis in a patient undergoing treatment with gefitinib for EGFR-mutated non-small cell lung cancer, causing blindness in the affected eye. Patient was given anti-platelet agent acetyl-salicylic acid and is being followed up with condition not resolved to date. All the reported non-severe ADRs (“fainting, hypertensive episode, hypotension”; “skeletal pain, muscle pain, fever, rhinitis”; “back pain, fatigue, fever; reddening at injection site, hot flashes”; “tongue pruritus”; “paresthesia, pruritus,

skin rash”; “headache, myalgia, fever, rigidity”, respectively) resolved in 48 hours. Patients were observed for severe adverse reaction up to 1 month after second dose, with all the reported ADRs developing within 14 days from the vaccine administration.

Only 4 patients showed symptoms consistent with hypersensitivity reactions, which were not serious and resolved in <1 hour; no patients required hospitalization for hypersensitivity reactions, and they resolved with medical management with anti-histamine drugs in 3 cases, and with observation in the other case.

Discussion

Our data show that COVID-19 vaccination with BNT162b2 Pfizer-BioNTech vaccine was highly safe in one of the largest reported series of patients with cancer treated with chemotherapy, immunotherapy, or targeted therapy reported to date.

The rate of vaccine refusal in our cohort of cancer patients undergoing cancer-directed treatment was lower than expected. Indeed, colleagues of the Regina Elena Cancer Institute- Rome reported a 11% refusal rate in their cohort of 914 patients, with refusal being mostly due to fear of adverse events.¹⁶

These findings are consistent with the reassuring safety signals regarding the BNT162b2 mRNA COVID-19 vaccine reported in smaller cohorts of patients with cancer.^{11-15,17} In our case series the only severe adverse event recorded was a central retinal artery occlusion, which notwithstanding the unsure causality relationship, negatively compares with findings from general population in which COVID mRNA vaccination was shown to be protective against cerebrovascular events.¹⁸

As for the scheduling, an every-3 week dosing schedule was feasible, with only 1.8% of patients not completing the full schedule with the second dose. Indeed, recent data from the UK showed poor efficacy of a single dose of the BNT162b2 vaccine in patients with cancer, whereas immunogenicity increased significantly in patients with solid cancer within 2 weeks of a vaccine boost at day 21 after the first dose.¹⁷ Recent data also point at the usefulness of an additional dose of mRNA vaccine.¹⁹

Conclusion

These data confirm the safety of the BNT162b2 Pfizer-BioNTech vaccine in the largest cohort of cancer patients reported to date. As for the effectiveness, longer follow-up is needed in order to provide data on the rate of COVID19 infections among fully vaccinated cancer patients.

Conflict of Interest

Antonella Brunello: Eli Lilly, Eisai, GlaxoSmithKline (C/A), PharmaMar (Speakers’ fees and travel expenses, outside the submitted work); **Valentina Guarneri:** Roche, Novartis, Eli Lilly, MSD, GlaxoSmithKline, Gilead (personal fees outside the submitted work); **Sara Lonardi:** Amgen, Merck Serono, Roche, Lilly, AstraZeneca, Bristol-Myers Squibb, Bayer (RF), Amgen, Merck Serono, Roche, Lilly, AstraZeneca, Bristol-Myers Squibb, Daiichi-Sankyo, Servier, MSD, Pierre-Fabre, GlaxoSmithKline (personal fees outside the submitted work); **Vittorina Zagonel:** Bristol-Myers Squibb, Merck, Astellas Pharma, Servier, AstraZeneca, Lilly (personal fees outside the

Table 1. Oncological treatment details for patients on-treatment at the time of COVID-19 vaccination (N = 4324).

	N	%
Cytotoxic chemotherapy	1669	38.6
Immunotherapy	341	7.9
Targeted therapy	934	21.6
Endocrine therapy	615	14.2
Chemotherapy + immunotherapy	85	2.0
Targeted therapy + endocrine therapy	364	8.4
Immunotherapy + targeted therapy	68	1.6
Chemotherapy + targeted therapy	248	5.7

submitted work). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (ET) Expert testimony; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

Author Contributions

Conception/design, provision of study material or patients, collection and/or assembly of data, data analysis and interpretation, manuscript writing, final approval of manuscript: All authors

Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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