



Editorial

Adherence to COVID-19 vaccines in cancer patients: *promote it and make it happen!*

**KEYWORDS**

COVID 19;
SARS-CoV-2;
Vaccine;
Cancer patients

Patients with active cancer may have a higher risk of severe complications to COVID-19 due to their disease, to cancer treatment, age and comorbidities [1]. They have been excluded from the pivotal clinical trials for COVID19 vaccines despite included in the priority category for COVID19 vulnerability [1]. Few data are available on efficacy and safety profiles of vaccines against SARS-CoV-2 in patients with cancer, resulting in imprecise predictive health models [2,3]. Recently the first analysis has been reported on the efficacy of SARS-CoV-2 vaccine in the context of a prospective study enrolling patients and health care workers who received the RNA-based SARS-CoV-2 BNT162b2 vaccine ‘BNT162b2’, with and without the second booster dose at 3 weeks [4]. At 3 weeks, 97% of health care workers had an immune response (anti-S IgG positive titers) with a single inoculum. On the other hand, only 39% of patients with solid tumours and 13% with haematological malignancies had experienced seroconversion with a single inoculum. Patients with poor seroconversion after a single inoculum were those with thoracic malignancies or receiving chemotherapy <15 days from the vaccine. Virus neutralisation assays reported inferior efficacy in cancer patients with a trend of waning for the T-cell response [4]. With the second dose, 95% of (solid) cancer patients resulted seroconverted [4]. Some modelling exercises

justified the decision to postpone the second dose in non-vulnerable populations, due to the high seroconversion rate after the first dose and the persistence of the immune protection at the time of the second dose [5]. The preliminary data of the UK prospective trial and other reports comparing cancer patients and health care workers clearly demonstrated that in patients with cancer, immunogenicity increased significantly in patients with solid cancer within 2 weeks of a vaccine boost at day 21 after the first dose [4,6]. We support prioritisation of patients with cancer for extensive SARS-CoV-2 vaccine coverage. In the current issue of *Eur J Cancer* Di Noia V. and colleagues report on adherence to SARS-CoV-2 vaccine campaign in the context of a large Italian Comprehensive Cancer Center [7]. According to the National Italian Cancer Vaccination Strategy, cancer patients were considered eligible for vaccination if they were on systemic antitumor treatment, or if received it in the last 6 months, or having an active advanced disease. The BNT162b2 vaccine was proposed to all candidates by phone contact or during a scheduled visit. Adherence to the SARS-CoV-2 vaccine and reasons of refusal were collected administering a 6-item multiple-choice questionnaire. In the current study, out of 914 patients eligible for the vaccine, 102 refused vaccination (11.2%, 95% CI 9.1–13.2). The most frequent (>10%) reasons reported were concerns about vaccine-related adverse events (48.1%), negative interaction with concurrent antitumor therapy (26.7%) and the fear of allergic reaction (10.7%). The refusal rate after 15th March [date when the Italian regulatory agency AIFA (Agenzia Italiana del Farmaco) suspended the use of AstraZeneca-AZD1222 for additional safety monitoring] was more than doubled compared to the refusal rate observed before (19.7% versus 8.6%, OR 2.60, 95% CI 1.69–3.99, $p < 0.0001$) [7]. Many countries around the world developed national vaccination strategies.

DOI of original article: <https://doi.org/10.1016/j.ejca.2021.05.006>.

According to the Italian National Vaccination Plan, health care workers, the elderly population and vulnerable patients (including cancer patients) have been prioritised. A review on the progress of national COVID-19 vaccination strategies in European Union countries includes updates on vaccine uptake overall and by target group; current vaccination phases and priority groups, including adjustments made to priority groups during the rollout; vaccination strategies and policies; and systems to monitor vaccinations and the use of vaccination certificate [8]. As of 2nd May 2021, a total of 187,490,581 COVID-19 vaccine doses have been distributed by manufacturers to European Union countries, including over 34 million in the last week. BNT162b2 represents 65.6% of all doses distributed to EU countries via the European Commission's Vaccine Strategy, followed by AZD1222 (23.8%), mRNA-1273 SARS-CoV-2 Vaccine (8.9%) and Ad26.COV2.S Vaccine (1.1%). A total of 153,770,592 vaccine doses have been administered, which represents 82% of the doses distributed to countries since the beginning of the rollout. Overall, the proportion of vaccine doses administered out of those distributed is 90.3% for BNT162b2, 67.9% for AZD1222, 69.1% for mRNA-1273, and 22.7% for Ad26.COV2.S Vaccine [8]. Since the start of COVID-19 vaccine deployment in the EU/EEA in December 2020, the cumulative vaccine uptake in the adult population (aged 18 years and older) in the EU/EEA has progressed, reaching 30% for at least one vaccine dose (range: 10.6–50.5%) and 11.6% for the full vaccination course (range: 2.5–25.8%). In people aged 80 years and above, the median vaccine uptake was 78% (range: 10.1–100%) for at least one dose and 56.1% (range: 2.4–97.8%) for the full vaccination course (24 countries reporting). Seven countries have administered the full vaccination course to more than 80% of the population aged 80 years and above [8]. In health care workers (HCW), the median vaccine uptake was 80.2% (range: 20.4–100%) for at least one dose and 53.7% (range: 17.2–100%) for the full vaccination course [8]. European Union countries have primarily prioritised elderly people (with various lower age cutoffs across countries), residents and personnel of long-term care facilities, health care workers, social care personnel and people with certain comorbidities (including cancer patients). Countries are currently continuing vaccination of these groups and progressing to vaccination of younger age groups and essential workers critical to societal infrastructure. The experience reported in this issue of the *European Journal of Cancer* by Dr Di Noia and colleagues represents the first worldwide report on the adherence of cancer patients to COVID-19 vaccination and underlines how regulatory decisions and media news spreading could influence the success of the COVID-19 vaccine campaign. Several studies evaluated SARS-CoV-2 vaccine adherence [9,13]. All studies involved health care workers. Factors associated with low vaccine uptake include younger age [10], female sex [11] and black populations [12,13]. Higher rates

of acceptance were associated with higher income and education levels in one setting [13]. In the current Italian report, the only factor affecting lower adherence was advanced performance status [7]. We have no information on the level of education or income of patients. Interestingly, the vaccine uptake in cancer patients had a dramatic reduction following the decision of the national regulatory agency to suspend the use of AZD1222-vaccine for safety reasons. The 'infodemic' spread increased vaccine hesitancy and resistance. A recent study looked to identify and understand COVID-19 vaccine acceptance, hesitancy and resistance in the Republic of Ireland and the United Kingdom [14]. Researchers found vaccine-hesitant or resistant respondents in both populations to show lower levels of trust in scientists/health care practitioners. Additionally, vaccine-resistant individuals were found to be less likely to obtain information regarding the pandemic from traditional and authoritative sources such as newspapers and television broadcasts; show higher levels of mistrust in the information disseminated through those sources, health care practitioners and government agencies; and consume more information from social media [14]. This observation highlights the need to both ensure the accuracy of the information disseminated through less conventional media and to regain the trust of experts in a segment of the population. A call for action and an effective health marketing tailored to reach across borders diverse populations should be incorporated into national vaccination strategies. Negative attitudes towards vaccines can be a major public health concern. General mistrust in vaccines and concerns about potential side effects can represent barriers to increase cancer patients population uptake to COVID-19 vaccines. Public health messaging should be tailored to address these concerns and specifically to women, ethnic minorities and people with lower levels of education and incomes. As health care workers, we need to engage the cancer patients community to increase vaccination awareness and acceptance by including and training volunteers in the vaccination effort, using social media and media campaigns to raise awareness, monitoring and reducing the risk of misinformation. On the other hand, national public health strategies should focus on communication by delivering education to motivate cancer patients, providing easily accessible assistance and treating all cancer patients uniquely. We need to approach each patient with a clean slate. We also need to work together; efforts to improve treatment adherence and compliance are most successful when all stakeholders are involved and work together. This can include patients and their family members, primary care physicians, specialists, nurses, pharmacists, therapists and psychologists. The title of this editorial: 'Adherence to SARS-CoV-2 Vaccines in Cancer Patients, *Promote It and Make It Happen*' indicates that without concerted action initiated by the medical community, it will not happen. Communication between various stakeholders, including media outlets and

government agencies, must be orchestrated in a way that it will happen, that it will be monitored and that we can report on better adherence numbers as a result of a successful campaign in the future [15].

Funding source

None.

Conflict of interest statement

GC has received honoraria from Pfizer, Novartis, Lilly, Roche; fees for expert testimony and medical education from Pfizer; and has participated in advisory boards for Pfizer, Roche, Lilly, Novartis, Seattle Genetics, Celltrion. All the declarations are outside the submitted work. AMME has received over the last 3 years honoraria for Scientific Advisory Board and/or Independent Data Monitoring Committee membership from Biocad, BioInvent, BioNTech, BMS, CatalYM, Ellipses, Forbion, GSK, IO Biotech, ISA Pharmaceuticals, Merck/MSD, Nektar, Novartis, Pfizer, Regeneron, Roche, Sellas, SkylineDx. All the declarations are outside the submitted work.

References

- [1] The Lancet Oncology. COVID-19 and cancer: 1 year on. *Lancet Oncol* 2021 Apr;22(4):411. [https://doi.org/10.1016/S1470-2045\(21\)00148-0](https://doi.org/10.1016/S1470-2045(21)00148-0). PMID: 33794199; PMCID: PMC8007133.
- [2] Corti C, Curigliano G. SARS-CoV-2 vaccines and cancer patients. *Ann Oncol* 2021 Apr;32(4):569–71. <https://doi.org/10.1016/j.annonc.2020.12.019>. Epub 2021 Jan 12. PMID: 33450404; PMCID: PMC7831848.
- [3] Gnanvi JE, Salako KV, Kotanmi GB, Glèlè Kakaï R. On the reliability of predictions on Covid-19 dynamics: a systematic and critical review of modelling techniques. *Infect Dis Model* 2021;6: 258–72. <https://doi.org/10.1016/j.idm.2020.12.008>. Epub 2021 Jan 12. PMID: 33458453; PMCID: PMC7802527.
- [4] Monin L, Laing AG, Muñoz-Ruiz M, McKenzie DR, Del Molino Del Barrio I, Alaguthurai T, et al. Safety and immunogenicity of one versus two doses of the COVID-19 vaccine BNT162b2 for patients with cancer: interim analysis of a prospective observational study. *Lancet Oncol* 2021 Apr 27;S1470–2045(21):213–8.
- [5] Marra A, Generali D, Zagami P, Cervoni V, Gandini S, Venturini S, et al. Seroconversion in patients with cancer and oncology health care workers infected by SARS-CoV-2. *Ann Oncol* 2021 Jan;32(1):113–9.
- [6] Saad-Roy CM, Morris SE, Metcalf CJE, Mina MJ, Baker RE, Farrar J, et al. Epidemiological and evolutionary considerations of SARS-CoV-2 vaccine dosing regimes. *Science* 2021 Apr 23; 372(6540):363–70.
- [7] Di Noia V, Renna D, Barberi V, Dicitiva M, Riva F, Costantini G, et al. The first report on Covid-19 vaccine refusal by cancer patients in Italy: early data from a single-institute survey. *Eur J Canc* 2021;153:260–4.
- [8] Overview of the implementation of COVID-19 vaccination strategies and vaccine deployment plans in the EU/EEA. European Centre for Disease Prevention and Control. <https://www.ecdc.europa.eu/en/publications-data/overview-implementation-covid-19-vaccination-strategies-and-vaccine-deployment>.
- [9] Pamplona G, Sullivan T, Kotanko P. COVID-19 vaccination acceptance and hesitancy in dialysis staff: first results from New York City. *Kidney Int Rep* 2021 Apr;6(4):1192–3.
- [10] Schrading WA, Trent SA, Paxton JH, Rodriguez RM, Swanson MB, Mohr NM, et al. Project COVERED emergency department network. Vaccination rates and acceptance of SARS-CoV-2 vaccination among US emergency department health care personnel. *Acad Emerg Med* 2021 Apr;28(4):455–8.
- [11] Barry M, Temsah M-H, Aljamaan F, Saddik B, Al-Eyadhy A, Alenezi S, et al. COVID-19 vaccine uptake among healthcare workers in the fourth country to authorize BNT162b2 during the first month of rollout. medRxiv 2021. <https://doi.org/10.1101/2021.01.29.21250749>.
- [12] Martin CA, Marshall C, Patel P, Goss C, Jenkins DR, Ellwood C, et al. Association of demographic and occupational factors with SARS-CoV-2 vaccine uptake in a multi-ethnic UK healthcare workforce: a rapid real-world analysis. medRxiv 2021. <https://doi.org/10.1101/2021.02.11.21251548>.
- [13] Kim D. Associations of race/ethnicity and other demographic and socioeconomic factors with vaccination during the COVID-19 pandemic in the United States. medRxiv 2021. <https://doi.org/10.1101/2021.02.16.21251769>.
- [14] Murphy J, Vallières F, Bentall RP, Shevlin M, McBride O, Hartman TK, et al. Psychological characteristics associated with COVID-19 vaccine hesitancy and resistance in Ireland and the United Kingdom. *Nat Commun* 2021 Jan 4;12(1):29.
- [15] Corti C, Crimini E, Tarantino P, Pravettoni G, Eggermont AMM, Delalage S, et al. SARS-CoV-2 vaccines for cancer patients: a call to action. *Eur J Canc* 2021 May;148:316–27.

Giuseppe Curigliano

European Institute of Oncology, IRCCS, Milan, Italy

Department of Oncology and Hematology, University of Milan, Milan, Italy

Alexander M.M. Eggermont*

Princess Máxima Center, Utrecht, Netherlands

University Medical Center Utrecht, Utrecht, Netherlands

*Corresponding author: University Medical Center Utrecht, Utrecht, Netherlands.

E-mail address:

alexander.eggermont@prinsesmaximacentrum.nl

17 May 2021