Editorial

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Safety, efficacy and acceptability of SARS-CoV-2 vaccines in patients with cancer

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"Cancer patients should be reassured, and strongly encouraged and prioritized to get vaccinated as soon as possible."

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With more than 165 million cases and 3.4 million deaths currently reported across the world, the COVID-19 outbreak has been characterized by a significant burden on humankind [1]. During the current pandemic, patients with cancer have been shown to present with more severe outcomes and a four- to ten-fold increased risk of death, as compared with the general population, when diagnosed with COVID-19 [2,3]. This is especially true in patients with primary thoracic and hematological malignancies, who present with even worse outcomes, likely due to a deteriorating lung function and an intrinsic state of immunosuppression, respectively [4,5]. The poor prognosis of oncological patients facing SARS-CoV-2 is further exacerbated in those receiving systemic antineoplastic agents, including chemotherapy and targeted therapies, as evidenced by multiple cohorts [3,6,7].

SARS-CoV-2 vaccines & the related acceptability

During the past months, numerous preventive measures have been implemented internationally in order to decrease the spread of the disease. These include, but are not limited to, universal masking, social distancing and episodic lockdowns [8]. However, with an exponentially growing number of new cases reported worldwide and overwhelmed healthcare systems in many countries, all these measures have proved to be unsuccessful in controlling the COVID-19 pandemic. Hence, the acquisition of herd immunity, through widespread vaccination, represents the most plausible approach to reduce the burden of the pandemic. This preventive strategy has been actively promoted from the early onset of the COVID-19 pandemic, with many vaccines developed and tested in the clinical setting. Recently, three SARS-CoV-2 vaccines (the BNT162b2 mRNA, the mRNA-1273 and the Ad26.COV2.S vaccine) have been granted emergency use authorization from the US FDA, while a fourth one (ChAdOx1 nCoV-19 vaccine) has been approved in the UK and other European countries.

Despite critical investigation of these vaccines in Phase I/II studies for immunogenicity and safety and large Phase III trials for clinical efficacy in preventing symptomatic COVID-19 infection, a substantial proportion of the general public remains reluctant to receive them. This has been evidenced by multiple surveys which included hundreds of participants, showing very heterogeneous acceptance rates ranging from 23.6 to more than 90% [9,10]. Many factors contribute to the current hesitation seen within the general opinion in relation to SARS-CoV-2 vaccines, with misinformation playing a major role. In fact, multiple studies and reports show that social media platforms, which account for millions of users worldwide, are a frequent source of wrong information that could influence to a large degree people's attitudes toward the vaccines [11,12].

However, the acceptability of SARS-CoV-2 vaccines in patients with cancer may even be further affected. This additional hesitation is fueled by the lack of evidence regarding the administration of SARS-CoV-2 vaccines in such a vulnerable population, as the pivotal studies that lead to the approval of these vaccines did not specifically report on oncological patients or those receiving any antineoplastic therapy [13,14]. Hence, the safety and efficacy of the current vaccines remains questionable in the oncological community and patients' intention to receive them represents a matter of interest.

Safety & efficacy of SARS-CoV-2 vaccines in cancer patients

The decision to administer SARS-CoV-2 vaccines in patients with cancer is complex. In the absence of clear and straightforward studies investigating the recently developed vaccines in oncological patients, an in-depth analysis of the currently available data concerning these vaccines in healthy individuals, in addition to a thorough examination of the safety and efficacy of other known vaccines in patients with malignancies, are one way to derive potential conclusions. Additionally, the adequate assessment of the clinical benefit in comparison with the risks encountered, as an entity commonly referred to as the benefit: risk ratio, must be conducted, as it represents a powerful method to guide clinicians in their decision-making.

The safety of all recently approved COVID-19 vaccines has been proved in the corresponding studies. Rates of grade 3/4 adverse events have been consistently always low, ranging between 0.7 and 9% [14,15]. Moreover, no single death linked to any of these vaccines was ever reported. While these findings are related to the general population, there are no plausible hypotheses or scientific proofs that would suggest a different profile of side effects in cancer patients. Even when considering the immune suppression that can be encountered in patients with hematological malignancies or those receiving aggressive antineoplastic regimens, more frequent and/or severe adverse events are not expected. In fact, two of the vaccines currently approved are mRNA vaccines [16,17], while the others are replication-incompetent vectors of the adenovirus family [18,19] and none of these represents an attenuated form of SARS-CoV-2. Thus, from a biological perspective, the reactivation of the virus in immunocompromised individuals is not possible. When considering different studies assessing other well-known vaccines in patients with cancer, including those with leukemia, no major side effects were reported, further substantiating the safe administration of SARS-CoV-2 vaccines in this particular population [20,21].

With efficacy rates ranging between 70 and 95%, all vaccines presently evaluated or authorized have shown great effectiveness in preventing symptomatic COVID-19 infection [13,14,19]. With such high numbers and a neutralizing activity even against novel variants of the virus for many of these vaccines, the capacity to end the pandemic appears quite concrete. In a recent study evaluating the immunogenicity of the BNT162b2 mRNA vaccine in patients with cancer, a lower efficacy was seen in patients with solid and hematologic malignancies as compared with healthy subjects, particularly following the first dose [22]. This delineates the potential lower susceptibility of cancer patients to mount an effective immune response, and remains to be further investigated in many currently ongoing trials evaluating SARS-CoV-2 vaccines in the oncological population. It is possible to assume that these novel vaccines will be characterized by a decreased immunogenicity profile in cancer patients. However, this should be explored in relation to many confounding factors, including specific cancer types (e.g., B-cell and other hematologic malignancies), cancer stage (i.e., localized vs advanced) and disease activity (e.g., active disease, in remission). Additionally, the various classes of antineoplastic agents (e.g., B-cell depleting agents, immune checkpoint inhibitors) and other aggressive therapeutic modalities (e.g., CAR T cells, allogeneic stem cell transplantation) currently used in clinical practice should be interrogated, as they could affect significantly the ability of oncological patients to respond adequately to SARS-CoV-2 vaccines. All of these factors highlight the complexity and the steep learning curve in understanding thoroughly this process, as well as the challenges faced in answering questions related to the many possible scenarios. The efficacy of other types of vaccines in patients with cancer has been previously evaluated, with conflicting results: while some studies investigating influenza vaccines have previously shown substantial efficacy in cancer patients [23,24], others have shown decreased or nondurable immune responses [25,26]. This further highlights the heterogeneity and complexity of immune responses in this specific population.

Even when supposing a lower clinical benefit of SARS-CoV-2 vaccines as compared with that seen in the general population, their administration is still strongly encouraged in cancer patients. In fact, a moderate reduction of 50–60% of symptomatic disease rate, as compared with around 90% in healthy patients, could still help reduce to a significant extent the burden of the pandemic in this fragile population; thereby, avoiding thousands of deaths. Moreover, the risks associated with the side effects of the vaccines and the probability of contracting COVID-19 during the vaccination encounter are extremely small compared with the chance of contracting SARS-CoV-2 from other sources, especially as the virus is spreading at fast rates and that more transmissible variants are emerging [27]. The need to vaccinate cancer patients against SARS-CoV-2 is further supported by international societies, such as the American Society of Clinical Oncology (ASCO) and the European Society for Medical Oncology (ESMO), which strongly emphasize in their statements the importance of vaccination in this vulnerable group [28,29].

Conclusion & future perspective

In conclusion, studies evaluating the immunogenicity and the safety of SARS-CoV-2 vaccines in patients with cancer are undergoing and are strongly awaited. However, the vaccination of this vulnerable category of individuals should definitely not be postponed, as this would further increase the massive death toll already attained. Cancer patients should be reassured, and strongly encouraged and prioritized to get vaccinated as soon as possible. They should also keep on following strictly public health measures related to the prevention of SARS-CoV-2 transmission, until vaccination rates in the general population reach acceptable levels. Additionally, clear explanations regarding the mechanism of action, the safety and the efficacy of the vaccines must be provided, helping to counteract misleading information and increase acceptability.

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