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Updated SIOG COVID-19 Working Group Recommendations on COVID-19 Vaccination among Older Adults with Cancer

Two years after the declaration of the COVID-19 pandemic by the World Health Organization (WHO), its effects continue to have a negative social and health impact. Despite the implementation of global vaccination campaigns which have successfully reduced hospitalizations and mortality rates in many regions of the world, there are still many unresolved issues and challenges to tackle before the pandemic is over. While 65% of the world's population has received at least one dose of the COVID-19 vaccine, vaccination coverage is still very low in many regions of the world, particularly in low- and middle-income countries (LMIC).[1]

Older adults, particularly those who are unvaccinated and those with comorbidities such as cancer, continue to be at significant risk of increased morbidity and mortality when contracting COVID-19.[2] While early in the pandemic significant changes in the administration of anticancer therapies (including omitting and delaying therapy) were undertaken, in many parts of the world cancer care delivery has returned to the same level as before COVID-19 [3]. The emergence of the omicron variants of SARS-CoV-2, which shows substantial resistance to vaccine-induced serum neutralizing activity, highlights the relevance of ongoing public health interventions, continued mass immunization, and booster campaigns targeting the most vulnerable members of society, including older adults with cancer.[4]

In 2021, the International Society of Geriatric Oncology (SIOG) published an initial set of recommendations regarding COVID-19 vaccinations among older adults with cancer.[5] However, recent changes in the epidemiology of the disease and in data regarding COVID-19 vaccines require updated recommendations.

Considerations on the role of COVID-19 vaccines in older patients with cancer

As of April 2022, data for 34 COVID-19 vaccines have been successfully submitted for authorization by the WHO, 14 have been approved, and over 150 are currently under clinical development.[6] As vaccinations and vaccine boosters are becoming increasingly available in most regions of the world, those at higher risk of adverse outcomes including hospitalization and/or death should continue to be prioritized. Older people have been grossly underrepresented in randomized clinical trials (RCT) of the COVID-19 vaccine [7]. In the same way, patients with cancer, comorbidities, or those receiving immunosuppressive therapy have been excluded. The only published RCT including patients with cancer was the BNT162b2 Pfizer/BioNTech mRNA vaccine trial, which recently reported a subgroup analysis of the 3,813 patients with a history of cancer (median age 64 years, range 16-91 years), showing an efficacy of 92-94%, with only four cases reported among the 1802 participants who received the vaccine compared with 71 among those who received placebo.[8] This causes clinicians to make recommendations based on the risk-benefit ratio, on extrapolation of RCT data, on subgroup analyses, or on observational studies, particularly in the context of the emergence of novel variants.

The efficacy of vaccines relies on an intact host response, which could be disrupted in people with myelosuppression due to cancer or its treatment, and in older adults (secondary to an age-related dysregulation and immune dysfunction commonly called immunosenescence) leading to potentially lower immunogenicity of vaccines in these population subgroups[9]. A reduced magnitude and duration of immune responses among older adults after receiving mRNA and inactivated virus vaccines has also been reported, with reduced IgG levels, a lower proportion of specific memory B-cells, and a reduction in IL-2-producing T-cells.[10] Humoral responses and T cell activation have been found to be significantly lower among older adults, and to have a sharper decline over time, highlighting the relevance of providing booster doses for this population.[10-12]

Likewise, patients with cancer seem more likely to develop a reduced immune response to COVID-19 vaccination. Vaccination effectiveness for preventing severe COVID-19 infections, although high, is lower among patients with cancer than among the general population, and even lower for those receiving active treatments and of advanced chronological age.[13,14] Real-world evidence shows that both patients aged ≥65 years and those with cancer have a higher risk of developing COVID-19 infections, and of adverse outcomes, despite vaccination.[15] Specifically, patients aged ≥65 with a diagnosis of cancer have an increased risk of adverse COVID-19-related outcomes (OR 1.42, p = 0.01) than their younger counterparts.[15] Data from the United Kingdom shows that patients on moderate-to-high intensity chemotherapy are at increased risk of dying from COVID-19 despite being vaccinated (two doses).[16] The exact timing of the vaccination during active chemo/immunotherapy does not seem to influence the efficacy of the vaccination significantly, except for patients undergoing stem cell-transplantation or receiving anti-CD20 therapies.[17] Importantly, booster doses of COVID-19 vaccine seem to be effective at increasing antibody titres, as well as improving immune response to variants of concern among patients with cancer, and thus this should be a priority population in booster campaigns.[18,19]

The SIOG COVID-19 Working Group advocates for continued prioritization of older adults with cancer in vaccination campaigns and boosters to protect this vulnerable group from the adverse outcomes of COVID-19, even in the absence of robust data, following the recommendations included in **Table 1**.[5]

Therefore, SIOG continues to stress the prioritization of initial vaccination and vaccine boosters among patients at higher risk of morbidity and mortality from COVID-19, specifically older adults with cancer, when implementing global and local vaccination plans.

Table 1. Updated SIOG COVID-19 Working Group recommendations for COVID-19 vaccinations among older patients with cancer:

Recommendation	Rationale
A. For immediate action	
Prioritize initial vaccination courses and vaccine boosters for individuals at disproportionate risk of death and other complications from COVID-19, including older patients with active or progressive cancer, or anticancer therapy at high risk for immunosuppression.	Higher 30-day all-cause mortality from COVID-19 observed in patients with older age, comorbidities, active or progressive cancer [20]. Immune response to COVID-19 vaccines declines faster among older individuals and thus specific measures to boost vaccine responses in this population are warranted.[10,11] Administering at least one booster dose seems to be effective in increasing immune response among patients with cancer. Data regarding subsequent booster doses is currently missing or very limited.[18,19,21]
Implement the use of regulated vaccines and vaccine boosters in areas with high community transmission and with a high prevalence of variants of concern as soon as possible and without interrupting active treatment.	Except for patients receiving anti CD-20 antibodies or undergoing stem cell transplantation (for whom a delay of at least three months after treatment may be appropriate),[22] patients receiving anticancer therapies such as chemotherapy, targeted, endocrine therapy, or immunotherapy seem to be able to mount appropriate immune responses, particularly after boosters.[17]

Persevere with community-based intervention strategies, such as physical distancing, hand hygiene, mask wearing, and use of personal protective equipment to mitigate transmission, even for patients and healthcare professionals that have already been vaccinated.	Emerging COVID-19 variants, particularly omicron variants, are highly transmissible even among vaccinated individuals, and specifically among patients with cancer.[23, 24] The timing and level of measures to contain the virus, such as travel restrictions, facilities shutdowns, and social distancing have impacted the incidence and mortality from COVID-19 [25].
Facilitate the availability of vaccines and boosters for older adults with cancer living in LMIC by means of negotiation of fair prices and by equitable distribution of the vaccine supply through international collaborations and partnerships.	COVID-19 vaccines have been disproportionately utilized in high-income regions of the world.[1] Increasing access in LMIC is in line with WHO recommendations for Let's #ACTogether for #VaccinEquity and the United Nations COVAX program.
Ensure equitable and timely access to primary vaccination for older people within community, local, or national level.	Achieving high and equitable global coverage with a COVID-19 primary vaccination series remains the highest priority and is fundamental to reducing COVID-19–related morbidity and mortality.[26]
Prioritize older patients with cancer from socially and medically disadvantaged populations, including those with poor access to healthcare or from underrepresented racial/ethnic groups, in vaccination campaigns.	Higher incidence and mortality from COVID-19 in racial/ethnic minorities likely related to underlying disparities in social determinants of health [27].

Governments, international organizations, and medical associations, including SIOG, should create and disseminate educational messaging and risk communication campaigns aimed at combating misinformation and convincing the public, older adults with cancer, and their caregivers of the value and safety of vaccination.	COVID-19 vaccine hesitancy is a global phenomenon which is highly variable across countries, and which is related with lower education and awareness, as well as inefficient government efforts.[28] Tackling this hesitancy is necessary to increase vaccination rates.
Ensure the availability of antiviral medications and monoclonal antibodies for non-hospitalized vaccinated older adults aged ≥65 with hematologic malignancies, for older adults with cancer aged ≥65 who have not been previously vaccinated, and for those aged ≥75 years regardless of vaccination status.	Antiviral medications and monoclonal antibodies may decrease disease progression and hospitalization among ambulatory patients with COVID-19. Prioritization of their use is recommended by the National Institutes of Health.[29]
We encourage our members to continue investigating the vaccines' long-term safety and efficacy in older adults with cancer (including booster shots), particularly in the emerging variants of concern.	Populations included in phase III RCT were mostly younger individuals without comorbidities. "Real-world" evidence can further support the effectiveness COVID-19 vaccines among populations such as older adults with cancer, particularly with the emergence of novel, more transmissible, variants. "Real-world" evidence can also inform the incidence of COVID-19 infections after primary vaccination and support
We encourage our members to prioritize investigations on the impact of previous COVID-19 infections, aging, physical activity, function, frailty, and various anticancer treatments on vaccine efficacy and adverse effects. Experts in geriatrics	

should be embedded in the planning of future studies regarding COVID-19 and cancer.	prioritizing the administration of booster doses in vulnerable populations.[2]

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