Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Perspectives

Updated International Society of Geriatric Oncology COVID-19 working group recommendations on COVID-19 vaccination among older adults with cancer

Enrique Soto-Perez-de-Celis a,*, Anna Rachelle Mislang b, Celia Gabriela Hernández-Favela c, Chiara Russo d, Giuseppe Colloca c, Grant R. Williams e, Shane O’Hanlon f, Lisa Cooper g, Anita O’Donovan h, Riccardo A. Audisio i, Kwok-Leung Cheung j, Regina Gironés-Sarrió k, Reinhard Stauder l, Michael Jaklitsch m, Claudio Cairo n, Luis Antonio Gil Jr o, Mahmood Alam p, Schroder Sattar q, Kumud Kantilal r, Kah Poh Loh s, Stuart M. Lichtman t, Etienne Brain u, Hans Wildiers v, Ravindran Kanesvaran w, Nicolò Matteo Luca Battisti x

a Department of Geriatrics, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico
b Department of Medical Oncology, Flinders Centre for Innovation in Cancer, College of Medicine and Public Health, Flinders University, Bedford Park, SA 5042, Australia
c Department of Medical Oncology, Centre Leon Bérard, Regional Comprehensive Cancer Centre, Lyon, France
d Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
e Institute for Cancer Outcomes and Survivorship, University of Alabama at Birmingham School of Medicine, Birmingham, AL, USA
f University College Dublin, St Vincent’s University Hospital, Dublin, Ireland
ghi Department of Geriatric Medicine, Robin Medical Center, Sackler Faculty of Medicine, Division of Aging, Department of Medicine, Tel Aviv University, Israel
j Department of Internal Medicine V (Haematology and Oncology), Innsbruck Medical University, Innsbruck, Austria
k Department of Internal Medicine, Division of Hematology and Oncology, University Hospitals Leuven, Leuven, Belgium
l Department of Surgery, Sahlgrenska Academy - University of Gothenburg, Gothenburg, Sweden
m School of Medicine, University of Nottingham, Royal Derby Hospital Centre, Derby, UK
n Department of Medical Oncology, Hospital Universitari i Politècnic La Fe, Valencia, Spain
o Department of Internal Medicine V (Haematology and Oncology), Innsbruck Medical University, Innsbruck, Austria
p Brigham and Women’s Hospital – Dana-Farber Cancer Institute, Harvard Medical School, Boston, MA, USA
q National Integrated Cancer Control Program, Department of Health, Manila, Philippines
r Geriatric Division, São Paulo University, São Paulo, Brazil
s Head of Medical, Pfizer Oncology, Developed Asia and Japan, Sydney, Australia
t College of Nursing, University of Saskatchewan, Saskatoon, Canada
u School of Pharmacy, University of East Anglia, Norwich, UK
v University of Rochester Medical Center, Division of Hematology/Oncology, Department of Medicine, James P. Wilmot Cancer Institute, Rochester, NY, USA
w Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY, USA
x Department of Medical Oncology, Institut Curie, Saint-Cloud & Paris, France
y Department of General Medical Oncology, University Hospitals Leuven, Leuven, Belgium
z Division of Medical Oncology, National Cancer Centre, Singapore
aa Breast Unit – Department of Medicine Department, The Royal Marsden NHS Foundation Trust, Breast Cancer Research Division, The Institute of Cancer Research, London, UK

* Corresponding author at: Enrique Soto-Perez-de-Celis, Department of Geriatrics, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Vasco de Quiroga 15, Sección XVI, Tlalpan, CDMX, 14080. 525535333981, Mexico City, Mexico.
E-mail addresses: enrique.sotop@incnmsz.mx (E. Soto-Perez-de-Celis), anna.mislang@sa.gov.au (A.R. Mislang), Chiara.RUSSO@lyon.unicancer.fr (C. Russo), giuseppepederindano.colloca@policlinicogemelli.it (G. Colloca), grwilliams@uabmc.edu (G.R. Williams), shaneohanlon@svhg.ie (S. O’Hanlon), Anita.ODonovan@ tcd.ie (A. O’Donovan), raudioio@doctors.org.uk (R.A. Audisio), Kwok.Leung.Cheung@nottingham.ac.uk (K.L. Cheung), reinhard.stauder@i-med.ac.at (R. Stauder), mjaklitsch@bwh.harvard.edu (M. Jaklitsch), mahmood.alam2@pfizer.com (M. Alam), schroder.sattar@usask.ca (S. Sattar), k.kantilal@uea.ac.uk (K. Kantilal), kahpoh.loh@urmc.rochester.edu (K.P. Loh), etienne.brain@curie.fr (E. Brain), hans.wildiers@uzleuven.be (H. Wildiers), ravindran.kanesvaran@ singhealth.com.sg (R. Kanesvaran), nicolo.battisti@rmh.nhs.uk (N.M.L. Battisti).

https://doi.org/10.1016/j.jgo.2022.07.005
Received 12 May 2022; Received in revised form 10 July 2022; Accepted 12 July 2022
Available online 15 July 2022
1879-4068/© 2022 Elsevier Ltd. All rights reserved.
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 show 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.

| Table 1 | Updated SIOG COVID-19 Working Group recommendations for COVID-19 vaccinations among older patients with cancer. |
|---------|----------------------------------------------------------------------------------------------------------|
| **Recommendation**                                                                                   | **Rationale** |
| A. For immediate action                                                                               | 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]. 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]. 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]. 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. 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]. Higher incidence and mortality from COVID-19 in racial/ethnic minorities likely related to underlying disparities in social determinants of health [27]. COVID-19 vaccine hesitancy is a global phenomenon which is highly variable across countries, and which is related to lower education and awareness, as well as inefficient government efforts [28]. Tackling this hesitancy is necessary to increase vaccination rates. 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]. 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 prioritizing the administration of booster doses in vulnerable populations [2]. |
| B. 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. | |
| C. Ensure equitable and timely access to primary vaccination for older people within community, local, or national level. | |
| D. 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. | |
| E. 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. | |
| F. 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. | |
| G. 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. | |
| H. 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. | |

Abbreviations: SIOG, International Society of Geriatric Oncology; LMIC, low- and middle-income counties; WHO, World Health Organization.
1. 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 3813 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. Vaccine 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 (odds ratio [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 to receive vaccines 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.

Disclosures

AM: Honoraria Janssen, MSD, Novartis.
KPL: National Cancer Institute in the United States (R00CA37744), Wilmot Cancer Institute Research Fellowship Award. Receipt of consultation fees: Pfizer and Seattle Genetics; Receipt of honoraria: Pfizer.
KLC: Consultancy: Roche.
SML: National Cancer Institute Cancer Center Support Grant (P30CA008748).
EB: Receipt of travel supports: Pfizer, Sandoz. Receipt of honoraria: Eli Lilly, Pfizer, Seagen. Receipt of consultation fees: Daiichi, Pfizer, Sandoz.
RK: Speaker/Advisory Board / Honoraria: AstraZeneca, Pfizer, MSD, BMS, Astellas, J&J, Eisai, Ipsen, Amgen, Merck.
NMLB: Advisory board: Pfizer, Abbott, Sanofi; speaker fees: Abbvie, Pfizer, Roche, Sanofi; travel grants: Genomic Health, Pfizer, Lilly.
MA: Honoraria from Pfizer.

Author Contributions

All authors contributed to the manuscript.

References

[1] Our World in Data. Coronavirus (COVID-19) Vaccinations. Disponible en línea en, https://ourworldindata.org/covid-vaccinations?country—MEX. Accesed March 11, 2022.
[2] Elkrief A, Hennecy C, Kuderer NM, Robinstein SM, Wulf-Burchfeld E, Rosovsky RP, et al. Geriatric risk factors for serious COVID-19 outcomes among older adults with cancer: a cohort study from the COVID-19 and cancer consortium. Lancet Healthy Longev 2022;te2143–52. https://doi.org/10.1016/s2666-7568(22)00089-5.
[3] Battisti NMI, Mislang AR, Cooper L, O’Donovan A, Audittio RA, Cheung KL, et al. Adapting care for older cancer patients during the COVID-19 pandemic: Recommendations from the International Society of Geriatric Oncology (SIGO) COVID-19 Working Group. J Geriatric Oncol 2020;11:1190–8. https://doi.org/10.1016/j.jgo.2020.07.008.
[4] Vanshylla K, Tober-Lau P, Gruell H, Munn F, Egelhoff P, et al. Durabiliy of omicron-neutralising serum activity after mRNA booster immunisation in older adults. Lancet Infect Dis 2022;22:445–6. https://doi.org/10.1016/s1473-3099(22)00135-9.
[5] Mislang AR, Soto-Perez-de-Celis E, Russo C, Colloca G, Williams GR, O’Hanlon S, et al. The SIOG COVID-19 working group recommendations on the rollout of COVID-19 vaccines among older adults with cancer. J Geriatr Oncol 2021;12: 848–50. https://doi.org/10.1016/j.jgo.2021.03.003.
[6] World Health Organization. COVID-19 vaccine tracker and landscape. https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines. Accesed April 15, 2022.
[7] Helfand BK, Webb M, Gartnergais SL, Fuller L, Kwon CS, Inouye SK. The exclusion of older persons from vaccine and treatment trials for coronavirus disease 2019–2020: a scoping review of the evidence. JAMA Intern Med 2020;180(11):1546–9. https://doi.org/10.1001/jama.2020.5084.
[8] Thomas SJ, Perez JL, Lockhart SP, Hariharan S, Kitchin N, Bailey R, et al. Efficacy of COVID-19 vaccines among older adults with cancer. J Geriatr Oncol 2021;12: 848–50. https://doi.org/10.1016/j.jgo.2021.03.003.
[9] World Health Organization. COVID-19 vaccine tracker and landscape. https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines. Accesed April 15, 2022.
[10] Crooke SN, Ovsyannikova IG, Poland GA, Kennedy RB. Immunosenescence and human vaccine immune responses. Immune Age 2019;16:25. https://doi.org/10.1016/j.image.2019.06.007.
[11] Collier DA, Ferreira IATM, Kotagiri P, Datir PR, Lim EY, Touizer E, et al. Age-related immune response heterogeneity to SARS-CoV-2 vaccine BNT162b2. Nature. 2021;596:417–22. https://doi.org/10.1038/s41586-021-03759-0.
[12] Broekman MA, Mwimanzu F, Lapointe HB, Sang Y, Agafitei O, Cheung PK, et al. Reduced magnitude and durability of humoral immune responses to COVID-19 mRNA vaccines among older adults. J Infect Dis 2021;225:1129–40. https://doi.org/10.1093/infdis/jiaa592.
[13] Bag Soytas R, Cengiz M, Islamoglu MS, Borku Uysal B, Yavuzer S, Yavuzer H. Antibody responses to COVID-19 vaccines in older adults. J Med Virol 2022;94:50. https://doi.org/10.1002/jmv.25904.
[14] Wu JT-Y, La J, Branch-Ellman W, Huhmann LB, Han SS, Parmigiani G, et al. Association of COVID-19 vaccination with SARS-CoV-2 infection in patients with
cancer: A US nationwide veterans affairs study. JAMA Oncol 2022;8:281–6. https://doi.org/10.1001/jamaoncol.2021.5771.

[15] Song Q, Baten B, Shao YR, Hsu FC, Liu F, Madhira V, et al. Risk and outcome of breakthrough COVID-19 infections in vaccinated patients with cancer: real-world evidence from the national COVID cohort collaborative. J Clin Oncol 2022 Mar 14: JCO2102419. https://doi.org/10.1200/JCO.21.02419.

[16] Hippisley-Cox J, Coupland CA, Mehta N, Keogh RH, Diaz-Ortiz K, Khunti K, et al. Risk prediction of COVID-19 related death and hospital admission in adults after covid-19 vaccination: National prospective cohort study. BMJ. 2021;374:n2244. https://doi.org/10.1136/bmj.n2244.

[17] Thakkar A, Gonzalez-Lugo JD, Goradia N, Gali R, Shapiro LC, Pradhan K, et al. Seroconversion rates following COVID-19 vaccination among patients with cancer. Cancer Cell 2021;39:1081–1090.e2. https://doi.org/10.1016/j.ccell.2021.06.002.

[18] Narazhni V, Sk. Denis KJ, Lam EC, Ofoman O, Garcia-Beltran WF, Mairena CR, et al. Neutralization breadth of SARS-CoV-2 viral variants following primary series and booster SARS-CoV-2 vaccines in patients with cancer. Cancer Cell 2022;40:103–108.e2. https://doi.org/10.1016/j.ccell.2021.12.002.

[19] Fendler A, Shepherd STC, Au L, Wilkinson KA, Wu M, Byrne F, et al. Adaptive immunity and neutralizing antibodies against SARS-CoV-2 variants of concern following vaccination in patients with cancer: the CAPTURE study. Nat Cancer 2021;2:1135–20. https://doi.org/10.1038/s43018-021-00274-w.

[20] Kuderer NM, Choueiri TK, Shah DP, Sosman JA, Hellmann MD, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet 2020;395:1907–18. https://doi.org/10.1016/s0140-6736(20)31187-9.

[21] Bar-On YM, Goldberg Y, Mandel M, Bodenheimer O, Amir O, Freedman L, et al. Protection by a Fourth Dose of BNT162b2 against Omicron in Israel. N Engl J Med. 2022. https://doi.org/10.1056/NEJMoa2201570.

[22] National Comprehensive Cancer Network. Recommendations of the NCCN COVID-19 vaccination advisory committee version 2.0 03/10/2021. https://www.nccn.org/covid-19/pdf/COVID-19_Vaccination_Guidance_V2.0.pdf. Accessed March 23, 2022.

[23] Araf Y, Akter F, Tang YD, Fatemi R, Parvez SA, Zheng C, et al. Omicron variant of SARS-CoV-2: Genomics, transmissibility, and responses to current COVID-19 vaccines. J Med Virol 2022;94:1825–32. https://doi.org/10.1002/jmv.27588.

[24] Pinato DJ, Aguilar-Company J, Ferrante D, Hanbury G, Bower M, Salazar R, et al. Outcomes of the SARS-CoV-2 omicron (B.1.1.529) variant outbreak among vaccinated and unvaccinated patients with cancer in Europe: results from the retrospective, multicentre, OnCovid registry study. Lancet Oncol 2022 Jun 2. https://doi.org/10.1016/S1470-2045(22)00273-X.

[25] Thu TP8, Ngoc PNH, Hai NM, Tuan LA. Effect of the social distancing measures on the spread of COVID-19 in 10 highly infected countries. Sci Total Environ. 2020;742:140430. https://doi.org/10.1016/j.scitotenv.2020.140430.

[26] Mbaeyi S, Oliver SE, Collins JP, Godfrey M, Goswami ND, Hadler SC, et al. The advisory committee on immunization practices’ interim recommendations for additional primary and booster doses of COVID-19 vaccines - United States, 2021. MMWR Morb Mortal Wkly Rep 2021;70:1545–52. https://doi.org/10.15585/mmwr.mm7044e2.

[27] Moore JT, Ricaldi JN, Rose CE, Fuld J, Parise M, Kang GJ, et al. Disparities in incidence of COVID-19 among underrepresented racial/ethnic groups in counties identified as hotspots during June 5–18, 2020–22 States, February–June 2020. MMWR Morb Mortal Wkly Rep 2020;69:1122–6. https://doi.org/10.15585/mmwr.mm6933e1.

[28] Shakell CS, Mejeeb AA, Mirza MS, Chaudhry B, Khan SJ. Global COVID-19 vaccine acceptance: A systematic review of associated social and behavioral factors. Vaccines. 2022;10:119.

[29] COVID-19 Treatment Guidelines Panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. National Institutes of Health. https://www.covid19treatmentguidelines.nih.gov/. Accessed April 15 2022.