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Title: The SIOG COVID-19 Working Group Recommendations on the Rollout of COVID-19 Vaccines among Older Adults with Cancer

Authors:

Anna Rachelle Mislang
Department of Medical Oncology
Flinders Centre for Innovation in Cancer
College of Medicine and Public Health, Flinders University
Bedford Park, SA, 5042, Australia
anna.mislang@sa.gov.au

Enrique Soto-Perez-de-Celis
Department of Geriatrics
Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán
Mexico City, Mexico
enrique.sotop@incmnsz.mx

Chiara Russo
Department of Medical Oncology, Centre Léon Bérard, Regional Comprehensive Cancer Centre, Lyon, France
Chiara.RUSSO@lyon.unicancer.fr

Giuseppe Colloca
Dipartimento di Diagnostica per Immagini, Radioterapia Oncologica ed Ematologia, Fondazione Policlinico Universitario A. Gemelli IRCCS
Rome, Italy
giuseppeferdinando.colloca@policlinicogemelli.it

Grant R. Williams
Institute for Cancer Outcomes and Survivorship
University of Alabama at Birmingham School of Medicine
Birmingham, AL, USA

grwilliams@uabmc.edu

Shane O'Hanlon
University College Dublin
St Vincent's University Hospital
Dublin, Ireland
shaneohanlon@svhg.ie

Lisa Cooper
Division of Aging, Department of Medicine,
Brigham and Women's Hospital
Harvard Medical School
Boston, MA, USA
lcooper5@bwh.harvard.edu

Anita O'Donovan
Applied Radiation Therapy Trinity (ARTT), Trinity St James's Cancer Institute,
Trinity College, Dublin, Ireland
Anita.ODonovan@tcd.ie

Riccardo A. Audisio
Department of surgery
Sahlgrenska Academy - University of Gothenburg
Gothenburg, Sweden
raudisio@doctors.org.uk

Kwok-Leung Cheung
School of Medicine
University of Nottingham, Royal Derby Hospital Centre
Derby, UK
Kwok_Leung.Cheung@nottingham.ac.uk

Regina Gironés Sarrió
Department of Medical Oncology
Hospital Universitari i Politècnic La FE
Valencia, Spain
reginagiro@hotmail.com

Reinhard Stauder
Department of Internal Medicine V (Haematology and Oncology)
Innsbruck Medical University
Innsbruck, Austria
reinhard.stauder@i-med.ac.at

Michael Jaklitsch
Brigham and Women's Hospital – Dana-Farber Cancer Institute
Harvard Medical School
Boston, MA, USA
mjaklitsch@bwh.harvard.edu

Clarito Cairo
National Integrated Cancer Control Program
Department of Health
Manila, Philippines
dokclar@gmail.com

Luiz Antonio Gil Jr
Geriatric Division – São Paulo University
São Paulo, Brazil
gil.luizantonio@gmail.com

Schroder Sattar
College of Nursing – University of Saskatchewan
Regina, Canada
schroder.sattar@usask.ca

Kumud Kantilal
School of Pharmacy
University of East Anglia
Norwich, UK
k.kantilal@uea.ac.uk

Kah Poh Loh
University of Rochester Medical Center

Division of Hematology/Oncology, Department of Medicine
James P. Wilmot Cancer Institute
Rochester, NY, USA
kahpoh_loh@urmc.rochester.edu

Stuart M. Lichtman
Department of Medicine
Memorial Sloan Kettering Cancer Center
New York, NY, USA
LichtmaS@mskcc.org

Etienne Brain
Department of Medical Oncology
Institut Curie
Saint-Cloud & Paris, France
Etienne.brain@curie.fr

Hans Wildiers
Department of General Medical Oncology
University Hospitals Leuven
Leuven, Belgium
hans.wildiers@uzleuven.be

Ravindran Kanesvaran
Division of Medical Oncology
National Cancer Centre Singapore
Singapore
ravindran.kanesvaran@singhealth.com.sg

Nicolò Matteo Luca Battisti
Breast Unit – Department of Medicine Department
The Royal Marsden NHS Foundation Trust
Breast Cancer Research Division
The Institute of Cancer Research, London, UK
nicolo.battisti@rmh.nhs.uk

Corresponding author: Anna Rachelle Mislang

Email address: anna.mislang@sa.gov.au

Twitter: @AnnaMislang

Postal address: Flinders Centre for Innovation in Cancer
Level 4, 1 Flinders Drive
Bedford Park, SA 5042
Australia

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Title: The SIOG COVID-19 Working Group Recommendations on the Rollout of COVID-19 Vaccines among Older Adults with Cancer

The COVID-19 pandemic continues to negatively impact our society. Older adults are at increased risk of morbidity and mortality. People who are frail, living in residential care facility, and/or with comorbidities, including cancer are disproportionately disadvantaged. To reduce the risk of infection among older adults with cancer, several anticancer therapies have been prioritized, delayed, de-escalated, or omitted based on clinical need (1). However, public health interventions remain critical to mitigate transmission and minimize adverse outcomes. Of these, mass immunization is perhaps a more effective preventive health measure and potentially a key exit strategy from this crisis.

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

To date, data on eight COVID-19 vaccines have been successfully submitted for authorization by the World Health Organization (2), five vaccines have reported results on efficacy and/or safety (Table 1), and over 50 are at various stages of development. As vaccines are made available to the general population, their rollout should be prioritized for those at higher risk of adverse outcomes including hospitalization and/or death. Older individuals are traditionally excluded from or underrepresented in clinical trials, and the same holds true for COVID-19 vaccine studies (3). Similarly, patients with cancer, comorbidities, or immunosuppression have been excluded. Therefore, clinicians are expected to make recommendations based on the risk-benefit ratio and extrapolation of trial data to the real world until more information becomes available.

The efficacy of vaccines relies on an intact host response, which could be disrupted in people with myelosuppression due to cancer or its treatment. Age-related dysregulation and immune dysfunction, called immunosenescence, could potentially result in lower immunogenicity of vaccines in older adults (4). Physical exercise may augment vaccine-specific antibody responses; however, activities are limited by the imposed counter-pandemic measures. An adjuvanted vaccine may be used to overcome immunosenescence, as shown in the AZD1222 trial (5).

Variability in the relationship between neutralizing- and binding-antibody titres in older adults was seen in the Ad26.COV2.S trial (6). Nevertheless, vaccine efficacy appears to be consistent in older subgroups with a trend for lower reactogenicity (Table 1). Notably, these findings are all based on short-term analyses, where the long-term efficacy is still unclear. Also, these studies did not include frailty measures nor large

groups of older individuals, which limit the characterization of those recruited. Longer follow-up from vaccine trials will provide insight into the impact of vaccination on COVID-19 transmissibility, asymptomatic infections, or emerging mutant strains. The role of anticancer treatments, age, frailty and functional status on vaccine efficacy also needs to be investigated. Despite these caveats, the International Society of Geriatric Oncology (SIOG) COVID-19 Working Group advocates for a call to action to prioritize older adults with cancer in the vaccine rollout to protect this vulnerable group from the adverse outcomes of COVID-19, even in the absence of robust data.

The SIOG COVID-19 Working Group supports the following recommendations on the rollout of the COVID-19 vaccines for all older patients with cancer:

Recommendation	Rationale
A. For immediate action	
Prioritize the rollout of vaccines to 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 observed in patients with older age, comorbidities, active or progressive cancer (7).
Implement the use of regulated vaccines at the earliest opportunity, especially in areas with high community transmission • For older patients receiving active anticancer therapy - if possible, schedule vaccination at the time of bone marrow function recovery and a few days before the next cycle to maximize its efficacy and minimize the impact of potential side effects on ongoing anticancer treatments.	No specific data available on COVID-19 vaccine. Data extrapolated from experiences with influenza vaccine (8). Recommendations from the UK Chemotherapy Board and Public Health England “Green Book” on Immunization Against Infectious Disease. The efficacy and timing on patients on immunosuppressive therapy still needs to be established.
Persevere with community-based intervention strategies, such as physical distancing, hand hygiene, mask wearing,	Limited evidence exists on the impact of vaccines on COVID-19 transmission.

and use of personal protective equipment to mitigate transmission, even for patients and healthcare professionals that have already been vaccinated	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 (9).
Facilitate the availability of vaccines for older adults with cancer living in low and middle-income countries by means of negotiation of fair prices and by equitable distribution of the vaccine supply through international collaborations and partnerships. Ensure equitable and timely access to vaccines in older people within community, local, or national level.	In line with WHO recommendations for Let's #ACTogether for #VaccinEquity and the United Nations COVAX program.
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 (10).
Create and disseminate educational messaging and risk communication campaigns aimed at convincing older adults with cancer and their caregivers of the value and safety of vaccination Foster collaboration with advocacy groups to dispel simplistic and populist statements suggesting that "access to vaccines should be prioritized based on the capacity to contribute to economy", as these stigmatize ageing people as a	Avoid "fake news", misinformation, and minimise confusion from several media platforms by disseminating accurate information that is readily available/accessible to a wider audience. Advocacy, community engagement, and cross-sectoral collaborations are key strategies to COVID-19 response (11).

burden, thereby compromising ethics and health equity	
B. For subsequent action	
Investigate the vaccines' long-term safety, seroconversion, and seroprotection rates in older adults with cancer	Populations included in phase III randomized controlled trials were mostly younger individuals without comorbidities. "Real-world" evidence can further support the effectiveness COVID-19 vaccines among other populations such as older adults and patients with cancer.
Prioritize investigations on the impact of aging, reduction in physical activities, function, frailty, and anticancer treatments on vaccine efficacy and adverse effects	

Therefore, SIOG joins the call of other international organizations for prioritizing 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. Summary of the published results on COVID-19 Vaccines and efficacy in older people (in alphabetical order)

Vaccine	N	Design	Type	Main Inclusion Criteria	Main Exclusion Criteria	Dose interval	Efficacy	Older Adults inclusion and vaccine safety
AstraZeneca AZD1222 (5, 12)	11,636	Single blind	Chimpanzee adenovirus vectored vaccine	Age ≥18 years	Severe or uncontrolled medical comorbidities Participants aged ≥65 years with a Dalhousie Clinical Frailty Score of ≥4	LD ($2{\cdot}2 \times 10^{10}$ virus particles) or SD ($3{\cdot}5–6{\cdot}5 \times 10^{10}$ virus particles) x2 28 days apart	70.4%	≥70 years (9.5%) In phase II component <70 (n=79) vs. ≥70 (n=49) years: Similar antibody response across all age groups Fewer reactogenicity events *Localized AEs:* 82% vs. 61% *Systemic AEs: 82% vs. 65%*

Gam-COVID-Vac (Sputnik V) (13)	19,866	Double blind	recombinant replication-deficient adenovirus	Age ≥ 18 years	Immunosuppression	$1x10^{11}$ viral particles x 2, 21 days apart	91.6% >60: 91.8%	>60 years (10.8%)
Janssen Ad26.COV2.S (6)	805	Single blind	Modified adenovirus	Healthy adults of 2 age cohorts 1a: 18-55 years 3: ≥65 years	-	LD: ($5×10^{10}$ viral particles) or HD*:* ($1×10^{11}$ viral particles) in single vs. 2 doses, 56 days apart	>90%	≥65 years (50%) **Cohort 1a vs. 3** Lower Immune response LD: 100% vs. 91% HD: 100% vs. 94% Lower incidence of AEs *Localized AEs* LD: 64% vs.41% HD: 65% vs.84% *Systemic AEs* LD: 78% vs. 42% HD: 46% vs. 55%

Moderna mRNA-1273 (14)	30,420	Double blind	mRNA	Age ≥ 18 years At high risk of COVID-19 infection by location or comorbidities	Immunosuppression	100mcg x2 28 days apart	94.1% <*64:* 95.6% ≥*65:* 86.4%	>65 years (25%) Less common AEs in ≥65 (89%) vs. 18-64 (93%) years
Pfizer BioNTech BNT162b2 (15)	43,548	Double blind	mRNA	Age ≥16 Healthy or stable chronic medical conditions	Immunosuppression	30 mcg x2 21 days apart	95%	>65 years (21%) Lower reactogenicity events in >55 years (2.8%) vs. 16-55 years (4.6%)

LD: low dose; HD: high dose; SD: standard dose; AE: adverse events

References

1. Battisti NML, Mislang AR, Cooper L, O'Donovan A, Audisio RA, Cheung KL, et al. Adapting care for older cancer patients during the COVID-19 pandemic: Recommendations from the International Society of Geriatric Oncology (SIOG) COVID-19 Working Group. Journal of geriatric oncology. 2020;11(8):1190-8.
2. Organization WH. Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process 2021 [Available from: https://extranet.who.int/pqweb/sites/default/files/documents/Status_COVID_VAX_25Jan2021.pdf.
3. Helfand BKI, Webb M, Gartaganis SL, Fuller L, Kwon CS, Inouye SK. The Exclusion of Older Persons From Vaccine and Treatment Trials for Coronavirus Disease 2019-Missing the Target. JAMA Intern Med. 2020.
4. Crooke SN, Ovsyannikova IG, Poland GA, Kennedy RB. Immunosenescence and human vaccine immune responses. Immun Ageing. 2019;16:25.
5. Ramasamy MN, Minassian AM, Ewer KJ, Flaxman AL, Folegatti PM, Owens DR, et al. Safety and immunogenicity of ChAdOx1 nCoV-19 vaccine administered in a prime-boost regimen in young and old adults (COV002): a single-blind, randomised, controlled, phase 2/3 trial. The Lancet. 2020;396(10267):1979-93.
6. Sadoff J, Le Gars M, Shukarev G, Heerwegh D, Truyers C, de Groot AM, et al. Interim Results of a Phase 1-2a Trial of Ad26.COV2.S Covid-19 Vaccine. N Engl J Med. 2021.
7. Kuderer NM, Choueiri TK, Shah DP, Shyr Y, Rubinstein SM, Rivera DR, et al. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. The Lancet. 2020;395(10241):1907-18.
8. Vollaard A, Schreuder I, Slok-Raijmakers L, Opstelten W, Rimmelzwaan G, Gelderblom H. Influenza vaccination in adult patients with solid tumours treated with chemotherapy. European journal of cancer. 2017;76:134-43.
9. Thu TPB, 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.
10. 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(33):1122-6.
11. Schiavo R. Advocacy, community engagement and cross-sectoral collaborations as key strategies during COVID-19 response and beyond. Journal of Communication in Healthcare. 2020;13(1):1-5.
12. Voysey M, Clemens SAC, Madhi SA, Weckx LY, Folegatti PM, Aley PK, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. The Lancet. 2021;397(10269):99-111.
13. Logunov DY, Dolzhikova IV, Shcheblyakov DV, Tukhvatulin AI, Zubkova OV, Dzharullaeva AS, et al. Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia. The Lancet. 2021.
14. Baden LR, El Sahly HM, Essink B, Kotloff K, Frey S, Novak R, et al. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2020.
15. Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020;383(27):2603-15.