Philippine Society of Medical Oncology (PSMO) and Philippine Society for Microbiology and Infectious Diseases (PSMID) Joint Position Statement on Updated COVID-19 Guidelines for Patients with Cancer

Frederic Ivan Ting MD, Katrina Gaelic Bebero MD, Danielle Benedict Sacdalan MD, Crizel Denise Uy MD, Honey Sarita Abarquez MD, Grace Nilo MD, Buenaventura Ramos, Jr. MD, Dennis Lee Sacdalan MD, Arnold John Uson MD on behalf of the Philippine Society of Medical Oncology (PSMO)

Vegloure Maguinsay MD, Janice Caoili MD, Arthur Dessi Roman MD, Regina Berba MD, Karl Evans Henson MD, Marissa Alejandria MD, Mark Kristoffer Pasayan MD, Joseph Adrian Buensalido MD, Annabel Laranjo MD, Aileen Mae Lee MD, Kathyrn Roa MD, Dolores Rommela Ruiz MD on behalf of the Philippine Society for Microbiology and Infectious Diseases (PSMID)

The PSMO and PSMID acknowledge the importance of continuing cancer treatment during the COVID-19 pandemic. With the advent of new variants that are more transmissible,[1] these recommendations are set to augment the care of patients with solid tumors / non-hematologic cancer without compromising their safety.

Booster Dose of COVID-19 Vaccination

The PSMO and PSMID recommend that patients with cancer receive a booster dose of the COVID-19 vaccine as it has been proven to potentiate anti-COVID-19 immunity.[2] Booster dosing has addressed the concerns of waning immunity post-primary vaccination and exhibited stronger protection against SARS-CoV2 variants of concern in patients with cancer.[2-4]

Options for booster doses, as recommended by the Philippine Department of Health,[5] are as follows:

PRIMARY VACCINE	INTERVAL FOR BOOSTER	HOMOLOGOUS BOOSTER	HETEROLOGOUS BOOSTER
Astrazeneca	At least 3 months	Astrazeneca	Pfizer, Moderna
Gamaleya Sputnik	At least 3 months	Not yet for implementation	Astrazeneca, Pfizer, Moderna
Janssen	At least 2 months	Not yet for implementation	Astrazeneca, Pfizer, Moderna
Moderna	At least 3 months	Moderna	Astrazeneca, Pfizer
Pfizer	At least 3 months	Pfizer	Astrazeneca, Moderna
Sinovac	At least 3 months	Sinovac	Astrazeneca, Pfizer, Moderna

Testing for COVID-19

The PSMO and PSMID support the following testing procedures and indications for patients with cancer:[6]

- **A SARS-CoV-2 RT-PCR nasopharyngeal swab test should be done for patients with cancer presenting with COVID-19 signs and/or symptoms.** If RT-PCR is not available, commercially accessible rapid antigen tests (RAT) may be used as an alternative. RATs have lower sensitivity than RT-PCR; however, they may still be clinically useful among symptomatic patients with cancer and more so for those receiving cytotoxic chemotherapy.[7]

- **A SARS-CoV-2 RT-PCR nasopharyngeal swab test is recommended for new asymptomatic cancer patients BEFORE receiving their first cycle of immunosuppressive therapy** which includes, but is not limited to, cytotoxic chemotherapy, biologic therapy, immunotherapy, high-dose corticosteroids, extensive radiotherapy, or stem cell transplantation. The test should be done 24-48 hours prior to the procedure.[8-12] A systematic review showed that among asymptomatic individuals with possible exposure to COVID-19, the sensitivity of detecting active COVID19 infection with a 14-day symptom-based test is 92.8% and specificity is 98.3%.[13] It is important to note that the latter test was conducted in healthy individuals. A recent case-control study of 150 asymptomatic cancer patients showed that seven (4.7%) of these individuals tested positive for SARS-CoV-2 by rRT-PCR. Of these seven, five had a second comorbidity in addition to cancer. All seven patients had received chemotherapy – four on active treatment and three on follow-up. The results of this small study suggest that testing of asymptomatic cancer patients may be beneficial for vulnerable populations.[14]

- **For asymptomatic cancer patients who are on succeeding cycles of immunosuppressive treatment, the oncologist has the option to screen patients using repeat RT-PCR SARS-CoV-2 nasopharyngeal swab test or the 14-day COVID-19 symptom-based test.** While repeated RT-PCR testing before every cycle of chemotherapy seem ideal, these can cause additional expense and discomfort for patients. In resource-limited settings and with the limited studies available for patients with cancer, the Societies recommend that the oncologists assess the individual patient's clinical scenario and exposure risk, and apply the available evidence judiciously with consideration to patient resources and institutional logistics.

- **A saliva RT-PCR test maybe considered as an alternative to naso- / oropharyngeal RT-PCR testing in patients with contraindications against the latter method.** Several studies show that direct saliva RT-PCR test is non-inferior to nasopharyngeal swab RT-PCR in detecting SARS-CoV-2.[15-18]

- **In the absence of RT-PCR, a rapid antigen test (RAT) may be used to assess the likelihood that a patient's symptoms are due to COVID-19.** RATs possess several benefits versus laboratory-based molecular assays, such as more rapid turnaround times, lower cost, and clinical laboratory improvement amendments (CLIA) waiver for some RATs that allow use outside of a traditional laboratory setting. These advantages need to be tempered against key limitations of these tests, specifically their lower analytical sensitivity and issues related to their specificity. The possibility of false-positive results is of particular importance when the disease prevalence is low.[11,19]

  A single negative RAT in an individual with COVID-19 symptoms does not rule out a COVID-19 infection. However, if two consecutive RATs, taken at 24-to-48-hour intervals are both negative, the symptomatic individual is less likely to have COVID-19 infection. These individuals should be advised to self-isolate until they have no fever and symptoms are improving for at least 24 hours. A positive RAT would be highly indicative of a COVID-19 infection and the individual and their household members would be required to self-isolate, as per self-isolation directions for individuals with COVID-19 symptoms and their household members. [11,19]

  In alignment with the Philippine COVID-19 Living Clinical Practice Guidelines,[20] a rapid antigen test (RAT) may be used provided that ALL of the following conditions are met:

  1. Individuals are in the early phase of illness (less than or equal to 7 days from onset of symptoms);
  2. Testing kits demonstrated sensitivity of more than or equal to 80% AND have very high specificity of more than or equal to 97%

  To date, 10 commercially available COVID-19 rapid antigen kits have passed performance validation tests conducted by the Philippine Food and Drug Administration (FDA) and the Research Institute of Tropical Medicine (RITM), assuring compliance to minimum requirements for sensitivity and specificity.

All patients are highly encouraged to personally keep documentation of their COVID test results (RT-PCR or RAT), and should relay these results to their attending physicians.

Quarantine and Isolation

- **Patients with cancer with confirmed COVID-19 infection should ideally be referred to an Infectious Disease specialist and managed according to the latest Philippine COVID-19 Living Recommendations/Clinical Practice Guidelines which can be accessed at https://www.psmid.org/philippine-covid-19-living-recommendations/.**
- **Patients who test positive for COVID-19 should be advised to undergo isolation. Cancer treatment should be delayed for a minimum of 10 days from symptom onset (if mildly or moderately symptomatic) or from date of first positive SARS-CoV-2 RT-PCR (if asymptomatic). For severely symptomatic or severely immunocompromised patients, a minimum of 21 days of isolation is recommended.** Prolonged viral shedding could occur in individuals with cancer, and some studies show that severely immunocompromised patients can shed viable virus for as long as 20 days.[8,10,21-24]

Resumption of Cancer Treatment

Before cancer treatment is resumed, we recommend that the following conditions are present in the patient: 1) COVID-19 symptoms should be resolved or markedly improved, and 2) the patient has been afebrile without antipyretics for at least 24 hours (unless fever of malignancy is suspected). Generally, durations of delaying administration of chemotherapy are guided by the approximate durations of infectious viral shedding, the severity of COVID-19 symptoms, type of cancer and treatment, and the risk of disease progression because of delaying cancer therapy.

The recommendations [11, 25, 26] for resumption of treatment in patients with cancer who tested positive for SARS-CoV-2 are as follows (Figure 1):

- **Asymptomatic patients**: Chemotherapy is generally delayed for a **minimum of 10 days** after the date of their first positive RT-PCR test for SARS-CoV-2 RNA for as long as they remain asymptomatic.
- **Mild/moderately symptomatic non-hematologic cancer patients**: Chemotherapy is generally delayed until resolution or marked improvement of all COVID-19 related symptoms and a **minimum of 10 days** after symptom onset.
- **Severely symptomatic patients / severely immunocompromised** (including those receiving intensive cytotoxic chemotherapy, patients with prolonged neutropenia, among others): Chemotherapy is generally delayed until resolution or marked improvement of all symptoms and a **minimum of 21 days** after symptom onset.
- **Repeat RT-PCR testing for SARS-CoV-2 RNA is not strongly advocated unless patients continue to have symptoms past day 21**. The significance of a persistently positive RT-PCR result is best discussed in consultation with an infectious disease specialist. If available, a cycle-threshold measurement could be cautiously interpreted by the infectious disease consultant and the medical oncologist within the context of patient symptoms and level of immunosuppression to aid clinical decision-making regarding the timing of chemotherapy
- **In all cases, however, if chemotherapy or other cancer treatment is urgently required due to uncontrolled cancer, it should be administered without delay after a thorough evaluation and discussion of the oncologist and infectious disease consultant with the patient to minimize the risk of COVID-19 progression.[10] If chemotherapy is recommended while the patient is still within the isolation period, oncologists should work with infectious diseases specialists and/or the hospital infection control staff to ensure that isolation precautions are maintained throughout the patient's stay in the chemotherapy unit or inpatient room.**

Recommendations for resumption of treatment in patients with non-hematologic cancer who tested positive for SARS-CoV-2	
Asymptomatic, mild, moderate symptoms	**Minimum of 10 days**
Severely symptomatic/severely immunocompromised*	**Minimum of 21 days**
In all cases, however, if chemotherapy or other cancer treatment is urgently required due to uncontrolled cancer, it should be administered without delay after a thorough evaluation and discussion of the oncologist and infectious disease consultant with the patient.	

**Includes patients receiving intensive cytotoxic chemotherapy, patients with prolonged neutropenia, among others.*

Disclaimer

Data presented here are based on the best current evidence as of this writing. However, information about COVID-19 is rapidly evolving, and new evidence may have emerged by the time this article is published. Information contained in this article does not substitute for the independent professional judgment of the medical oncologist or other physicians in the context of treating an individual patient. This document is for informational purposes only and does not constitute medical or legal advice.

Prepared by the **Clinical Consensus Committee** of the **Philippine Society of Medical Oncology (PSMO):**

Technical Working Group	**Technical Advisory Group**
• Dr. Frederic Ivan L. Ting (Chair) • Dr. Katrina Gaelic Bebero • Dr. Danielle Benedict Sacdalan • Dr. Crizel Denise Uy	• Dr. Honey Sarita Abarquez • Dr. Grace Nilo • Dr. Buenaventura Ramos Jr. • Dr. Dennis Lee Sacdalan • Dr. Arnold John Uson

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References

1. Katella, Kathy. Omicron, Delta, Alpha, and More: What To Know About the Coronavirus Variants, Yale Medicine (Dec 2021). https://www.yalemedicine.org/news/covid-19-variants-of-concern-omicron
2. Shapiro LC, Thakkar A, Campbell ST, et al. Efficacy of booster doses in augmenting waning immune responses to COVID-19 vaccine in patients with cancer. *Cancer Cell*. 2022;40(1):3-5. doi: 10.1016/j.ccell.2021.11.006
3. Zeng C, Evans JP, Chakravarthy K, Qu P, Reisinger S, Song N, et al. COVID-19 mRNA booster vaccines elicit strong protection against SARS-CoV-2 omicron variant in patients with cancer. Cancer Cell. 2021 Dec 30 (doi: 10.1016/j.ccell.2021.12.014)
4. Greenberger LM, Saltzman LA, Senefeld JW, Johnson PW, DeGennaro LJ, Nichols GL. Anti-spike antibody response to SARS-CoV-2 booster vaccination in patients with B cell-derived hematologic malignancies. Cancer Cell. 2021 Oct 11; 39(10): 1297-1299
5. Philippine Department of Health Memorandum 2021-0492-B. Interim Guidelines on the Administration and Management of COVID-19 Vaccine Booster/Additional Doses to Priority Group A2: Senior Citizens ages 60 years old and above and Priority Group A3: Adults with Comorbidities. December 2021.
6. Ting FI, Mendoza MJ, Sacdalan DB, Abarquez HS. Updated general recommendations in cancer management during the COVID-19 pandemic in the Philippines. *Ecancermedicalscience*. 2020; 14:1128. Published 2020 Oct 20. doi:10.3332/ecancer.2020.1128
7. Geisen N, Sprute R, Rutrich M, et al. 2021 update of the AGIHO guideline on evidence-based management of COVID-19 in patients with cancer regarding diagnostics, viral shedding, vaccination, and therapy. European Journal of Cancer 2021 Feb 10; 147 (2021) 154e160
8. ASCO Special Report: A Guide to Cancer Care Delivery During the COVID-19 Pandemic (American Society of Clinical Oncology) Updated: July 2021. https://www.asco.org/sites/new-www.asco.org/files/content-files/2020-ASCO-Guide-Cancer-COVID19.pdf
9. Curigliano G, Banerjee S, Cervantes A, et al. Managing cancer patients during the COVID-19 pandemic: an ESMO Interdisciplinary Expert Consensus. Ann Oncol. 2020 doi: 10.1016/j.annonc.2020.07.010.
10. COVID-19 Treatment Guidelines Panel. Coronavirus Disease 2019 (COVID-19) Treatment Guidelines. National Institutes of

Health. Available at https://www.covid19treatmentguidelines.nih.gov/. Accessed 22 January 2022.
11. Ontario Ministry of Health. COVID-19 Integrated Testing & Case, Contact and Outbreak Management Interim Guidance: Omicron Surge. Version 2.0 – January 13, 2022. https://www.health.gov.on.ca/en/pro/programs/publichealth/coronavirus/docs/contact_mngmt/management_cases_contacts_omicron.pdf. Accessed 22 January 2022.
12. Madariaga A, McMullen M, Sheikh S, Kumar R, Liu FF, Zimmermann C, Husain S, Zadeh G, Oza AM. COVID-19 testing in patients with cancer: does one size fit all?. Clinical Cancer Research. 2020 Sep 15;26(18):4737-42.
13. Dans L, Dans A, Cabaluna IA, et al. Is the 14-day COVID-19 symptom-based test an accurate screening test to clear persons to return to work? Rapid Evidence Reviews on COVID-19 Management (UP Institute of Clinical Epidemiology and Asia-Pacific Center for Evidence-Based HealthCare) 2020. 11 June 2020
14. Motlagh A, Elmi F, Yamrali M, Ranjbar M, Azmin M, Moshiri F, Hamelmann C, Slama S, Tavakoli N, Hammerich A, Pourghazian N. Routine COVID-19 testing may not be necessary for most cancer patients. Scientific Reports. 2021 Dec 2;11(1):1-8.
15. Tee, M. L., Ubial, P. J. R., Ranoa, D. R. E., Tee, C. A., Abrilla, A. A., Trinidad, L. J. P. L., Chiong, C. M., Berba, R. P., Carrillo, R. J. D., Lim, M. C. F., & Dalmacio, L. M. M. (2021). Direct Saliva versus Conventional Nasopharyngeal Swab qRT-PCR to Diagnose SARS – CoV2: Validity Study. *Asian Journal of Research in Infectious Diseases*, *6*(2), 37-46. https://doi.org/10.9734/ajrid/2021/v6i230193
16. Huber M, Schreiber PW, Scheier T, Audigé A, Buonomano R, Rudiger A, Braun DL, Eich G, Keller DI, Hasse B, Böni J, Berger C, Günthard HF, Manrique A, Trkola A. High Efficacy of Saliva in Detecting SARS-CoV-2 by RT-PCR in Adults and Children. *Microorganisms*. 2021; 9(3):642. https://doi.org/10.3390/microorganisms9030642
17. Carrillo, R., Sarmiento, A., Ang, M.C., Diwa, M.H., Dungog, C.C., Tan, D., Lacuata, J.A., Salud, J., Lopa, R.A., Velasco, J.S., Berba, R., & Chiong, C.M. (2021). Validation of Snort-spit Saliva in Detecting COVID-19 Using RT-PCR and Rapid Antigen Detection Test.
18. Philippine Society for Microbiology and Infectious Diseases (PSMID) Saliva RT-PCR for COVID-19 detection Evidence Summary
19. Stokes NL, Reed KA, Berbari EF, Vetter S, Binnicker MJ. Evaluation of the BinaxNOW COVID-19 Rapid Antigen Test in an Asymptomatic Patient Population Undergoing Preprocedural Screening. Journal of Clinical Microbiology. 2021 Sep 15;59(12):e01650-21.
20. Adajar GA, Perez MA, Miranda MC, Bayona HH, Alejandria M, Dans L. Among patients suspected to have COVID-19, how accurate are self-administered rapid antigen tests alone compared to RT-PCT for the diagnosis of COVID-19?. Philippine COVID-19 Living Clinical Practice Guidelines.
21. Jessica Tarabay, MPH, MHR, CIC, Ahmed Babiker, MBBS, Max W Adelman, MD, MSc, Victoria D Stittleburg, BSc, Jay Varkey, MD, Stephanie M Pouch, MD, MS, FAST, Jesse Waggoner, MD, Anne Piantadosi, MD, PHD, 278. Immunocompromised Patients with Prolonged Viral Shedding of SARS-COV-2, *Open Forum Infectious Diseases*, Volume 8, Issue Supplement_1, November 2021, Pages S244–S245, https://doi.org/10.1093/ofid/ofab466.480
22. Leung WF, Chorlton S, Tyson J, et al. COVID-19 in an immunocompromised host: persistent shedding of viable SARS-CoV-2 and emergence of multiple mutations: a case report. *Int J Infect Dis*. 2022;114:178-182. doi:10.1016/j.ijid.2021.10.045
23. NCCN Best Practices Guidance: Management of COVID-19 Infection in Patients with Cancer. March 2021. https://www.nccn.org/docs/default-source/covid-19/2021-covid-infectious-disease-management.pdf?sfvrsn=63f70c30_7
24. CDC. Duration of Isolation and Precautions for Adults with COVID-19. https://www.cdc.gov/coronavirus/2019-ncov/hcp/durationisolation.html?CDC_AA_refVal=https%3A%2F%2Fwww.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fcommunity%2Fstrategy-discontinue-isolation.html. Accessed January 22, 2021. Accessed January 20, 2022.
25. Nakajima Y, Ogai A, Furukawa K, et al. Prolonged viral shedding of SARS-CoV-2 in an immunocompromised patient. *J Infect Chemother*. 2021;27(2):387-389. doi:10.1016/j.jiac.2020.12.001
26. Niyonkuru M, Pedersen RM, Assing K, et al. Prolonged viral shedding of SARS-CoV-2 in two immunocompromised patients, a case report. *BMC Infect Dis*. 2021;21(1):743. Published 2021 Aug 3. doi:10.1186/s12879-021-06429-5