



# CLINICAL RECOMMENDATIONS FOR THE MANAGEMENT OF CANCER PATIENTS DURING THE COVID-19 PANDEMIC

## RECOMENDACIONES CLÍNICAS PARA EL MANEJO DE PACIENTES ONCOLÓGICOS EN EL MARCO DE LA PANDEMIA COVID-19

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### ABSTRACT

The disease by the new coronavirus strain (COVID-19) has been classified as a pandemic by the WHO. In Peru, a state of national emergency and compulsory social isolation had been declared since 15 March. Global health systems have been greatly impacted by COVID-19, which forced health systems, societies and medical associations to design prioritized intervention strategies to provide continuity of patient care in infected areas and COVID-19-free areas. A cancer patient is classified as vulnerable and represents a risk factor for complications due to COVID-19, such as admission to the intensive care unit, intubation, and early death due to infection due to COVID-19. This is how the Asociación de Médicos Ex Residentes de Oncología Médica (AMEROM), has endeavored to give recommendations adaptable to our health system, to continue with the prioritized care of cancer patients. Through the modified methodology of expert consensus, based on the literature, recommendations have been generated at different stages of the pandemic, reaching a final consensus of clinical recommendations for the management of cancer patients in the framework of the COVID-19 pandemic in Peru, to provide useful information to health professionals. This article indicates the processes by which agreements were reached to make recommendations and generate the order of priority adopted by AMEROM.

**Key words:** COVID-19; SARS-CoV-2; Neoplasms (source: MeSH NLM).

### RESUMEN

La enfermedad por la nueva cepa de coronavirus (COVID-19) ha sido catalogada como una pandemia por la OMS. En el Perú, se decretó estado de emergencia nacional y aislamiento social obligatorio desde el 15 de marzo. Los sistemas de salud a nivel mundial han sufrido un gran impacto debido a la COVID-19, la cual obligó a los sistemas de salud, sociedades y asociaciones médicas a diseñar estrategias de intervención priorizada para dar continuidad a la atención de los pacientes en áreas COVID-19 y áreas libres de COVID-19. El paciente con cáncer es catalogado como vulnerable y representa un factor de riesgo para complicaciones por COVID-19, como ingreso a unidad de cuidados intensivos, intubación y muerte temprana por infección por COVID-19. Es así como la Asociación de Médicos Ex Residentes de Oncología Médica (AMEROM), se ha esforzado en dar recomendaciones adaptables a nuestro sistema de salud, con la finalidad continuar con la atención priorizada de los pacientes con cáncer. Mediante la metodología modificada de consenso de expertos, bajo el sustento bibliográfico, se han generado recomendaciones en diferentes etapas de la pandemia, llegando a un consenso final de recomendaciones clínicas para el manejo de pacientes oncológicos en el marco de la pandemia COVID-19 en Perú, con el fin de brindar información útil a los profesionales de la salud. El presente artículo indica los procesos con los que se llegaron a los acuerdos para dictar las recomendaciones y generar el orden de prioridad adoptado por AMEROM.

**Palabras clave:** COVID-19; SARS-CoV-2; Neoplasias (fuente: DeCS BIREME).

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## GENERAL

Coronavirus disease 2019 (COVID-19) was first detected in Wuhan, China in December 2019<sup>(1)</sup>. The General Director of the World Health Organization (WHO), on 30 January 2020, declared the outbreak as a public health emergency<sup>(2)</sup>. The first case of COVID-19 was filed in Peru on March 6, 2020. Five days later the WHO declared it a pandemic, and on March 15, it was a state of National Emergency and compulsory social isolation was declared in Peru<sup>(3)</sup>.

Cancer is an associated risk factor for severe outcomes in patients with a COVID-19 infection<sup>(4)</sup>. Cancer patients are in the vulnerable population as they have a 0.79% probability of being diagnosed with COVID-19, as opposed to the general population, whose probability is 0.37% (OR 2.31, 95% CI 1.89-3.02). In the study described by Liang et al., there was a higher admission to the intensive care unit, invasive ventilation, and death compared to non-oncological patients (39% vs. 8% p=0.003)<sup>(4)</sup>. These findings were also corroborated in an Italian study evaluating lethality among 355 patients, of whom 20.3% had an active neoplasm<sup>(5)</sup>.

The Asociación de Médicos Ex Residentes de Oncología Médica (AMEROM), made a consensus of recommendations for the management of cancer patients, in order to provide information to health professionals who care for cancer patients, to prioritize and give continuity to the care of these patients. In this way, their exposure to health services and the exposure of health personnel would decrease.

## POPULATION AND OBJECTIVES

- The target population is all patients with a confirmed or suspected diagnosis of this malignant disease and require clinical intervention for diagnosis, treatment, and recovery.
- Generate a practical prioritization order for the clinical intervention of cancer patients during the COVID-19 pandemic.
- Provide recommendations for the clinical intervention of cancer patients during the COVID-19 pandemic.

To make known the actions taken by oncologists that are members of AMEROM of different Social Safety Health Networks regarding the care of cancer patients during the COVID-19 pandemic.

## METHODS

The members of the board of directors of AMEROM have evaluated the scientific evidence available

on the internet on the care of cancer patients during the COVID-19 pandemic; review of technical and regulatory documents at the national level, recommendations of specialized institutions in the care of cancer patients and finally through the consensus of experts in the area of Oncología Médica de la Seguridad Social del Perú<sup>(6)</sup>.

## RESULTS

The recommendations are based on a consensus of experts in the field of medical oncology, using the modified nominal group methodology, which has been developed through virtual meetings, with exposure of ideas, electronic voting, and generation of ideas based on the revised literature.

Clinical oncologists who developed initial measures in the early stages of the pandemic were consulted in order to gather their experience in developing practical methods of cancer patient care under COVID-19<sup>(6)</sup>.

These recommendations are not intended to be a management guide, but to give an idea to publicize the order of priority for cancer patient care during the development of the COVID-19 pandemic, which may change according to the development of scientific evidence available in the current context.

The consensus of recommendations was worked in three phases.

- 1) Local prioritization, where each Health Network indicated its priorities, prior to the publication of other prioritization systems.
- 2) Local consensus meeting with experts from different health networks that treat cancer patients in the Social Security of Peru where they set out the order of priorities for the institutional management consensus.
- 3) Meeting with experts from different health networks that serve cancer patients in the Social Security of Peru and AMEROM Board of Directors, to evaluate the order of local prioritization in contrast to the normative documents and guidelines of recommendation published.

## GENERAL CLINICAL RECOMMENDATIONS

### Recommendations for the care and monitoring of patients

- General recommendations
  - Promote the appropriate use of personal



protective equipment according to the areas of care, respect for social distancing and minimization of the time of contact with the patient.

- Implementation of symptom-directed triage by COVID-19 upon admission to the institution, administrative care areas, chemotherapy areas, biological therapy and medical offices.
- To the extent possible, divide into physician groups for levels of care: office, telemedicine, and hospitalization.
- During the highest stage of infection, we suggest conducting studies to rule out COVID-19 infection, in order to assess the patient early, protect users of common areas and the staff that care for patients.
- It will be recommended to patients who do not come accompanied by minors, older adults or people with risk factors for complications from COVID-19.
- The patient waiting room must maintain the respective social distancing of patients, as well as personal protection measures for patients and companions.

### The areas intended for patient care

- Communication channels with patients
  - Communication through a telephone exchange for the care of cancer patients.
  - Use of social networks to optimize communication.
- External consultation areas
  - Care for cancer patients is in designated places where patients with COVID-19 infection are not actively attended, called "COVID-19 free areas".
  - To allocate exclusive areas for the ambulatory care of cancer patients.
  - Implement clear signs of "COVID-19 free areas".
- Hospitalization areas
  - If possible, have "COVID-19 free areas" in areas intended for hospitalization of oncological and oncohematological patients<sup>(13,14,2,12)</sup>.
  - Target specific areas for the movement of patients<sup>(13)</sup>.
  - Implement clear signs of "COVID-19 free areas".
- Areas of support for diagnosis
  - Minimize the requisition of laboratory studies and images during the pandemic.
  - Implement clear signs of "COVID-19 free areas" within the diagnostic support areas.

- Coordinate patient care at exclusive hours for cancer and cancer patients.

### Prioritized consultation visits

- Immediate attention consultation and prioritized external appointments.
  - They are intended to serve the patient who has emergency needs or prioritized care and avoid visiting the emergency room.
  - Provide prioritized new patient care for the service.
  - Evaluation of patients requiring ambulatory or hospitalized intravenous therapy.

### Telemedicine

- In places that have implemented telemedicine service<sup>(15)</sup>.
  - Perform triage of medical records at three levels:
    - I. Patients with active intravenous therapies or patients requiring hospitalization.
    - II. Patients with active oral treatment.
    - III. Control and follow-up patients.
  - Schedule appointments in an immediate care office or an external patient office for active intravenous therapies or hospitalization.
  - Programming for telemedicine to patients requiring oral therapy and close follow-up.
  - Medication dispensing centralized (Hospital) or in pharmacies near the patient's place of residence.
  - Priority evaluation of the patient referred for the first time to the oncology services, in order to carry out initial approach planning.
  - Indicate warning signs of cancer disease and general care and warning signs of COVID-19 infection.
  - If a patient who requires prioritized care is identified, this should be referred to prioritized care or immediate care.
- In places where there is no implemented telemedicine service<sup>(13)</sup>.
  - Organize by telework with the support of the electronic medical record system, telephone calls or video calls for patient care.
  - Follow Telemedicine Recommendations.

### Medical Board and Multidisciplinary Evaluation

- Any initial decision of a patient should be made to the extent possible by a multidisciplinary team.
- Promote academic meetings, medical boards



and multidisciplinary meetings through virtual platforms of multi-person communication, trying to keep the basic characteristics of face-to-face meetings.

- Recommendations for decision-making intervention.

**Order of prioritization**

- First adoption of recommendations: each service presented its order of priorities based on priority scale, such as high, medium high, medium, medium low and low. This prioritization was carried out in consensus of local experts<sup>(13)</sup>.
- Second adoption of recommendations: the members carried out an analysis of the publication of order of priorities dictated by the Ministry of Health, which is based on the six-level prioritization

scale of the United Kingdom National Health Service (NHS)<sup>(12)</sup>.

- Third and last adoption of recommendations: after evaluating the scales and simulating applicability in relation to practicality of use, an update of the bibliographic search was carried out where the Ontario Health Cancer Care prioritization scale turned out to be practical in terms of applicability in our health system. Likewise, the evaluation of the benefit was carried out according to the indications of the Ontario ABC scale and according to the Clinical Benefit Scale of the European Society of Medical Oncology (ESMO). AMEROM members performed the following scale, which is adaptable to our system during the COVID-19 pandemic in relation to the Peruvian health system<sup>(5,8,9,11,15)</sup>.

SPECIAL SECTION

Priority Level	Description	Example
High	Patients whose condition immediately jeopardizes their life, are clinically unstable or on the clinical scale of benefit, qualify as high priority (significant overall survival gain or improvement substantial in quality of life).	<ul style="list-style-type: none"> <li>• Rapidly progressive tumors and risk of early death.</li> <li>• Oncological Emergencies.</li> <li>• Therapies with healing intentions.</li> <li>• Acute decompensations.</li> </ul>
Average	Non-critical patients where delaying their therapy for more than 6 weeks could potentially impact the result or magnitude of benefit.	<ul style="list-style-type: none"> <li>• Stable tumors requiring adjuvant or neoadjuvant therapy.</li> <li>• Assessment of toxicities related to cancer treatment.</li> <li>• Palliative care with survival benefit.</li> </ul>
Low	Patients in stable condition in which the delay of their attention during the pandemic or the intervention is not a priority depending on the magnitude of the benefit (no gain in survival, no change or reduction in quality of life).	<ul style="list-style-type: none"> <li>• Second or third line therapies.</li> <li>• Routine visits.</li> <li>• Palliative therapy with improvement in morbidity.</li> </ul>

Adapted from Ontario Health Cancer Care Ontario and ESMO.

## General recommendations for intervention

- Visits reduced in time and frequency in infusion rooms for chemotherapy and biological therapy.
  - Monitoring by telemedicine or similar to patients with intermediate and high toxicity therapies on a weekly basis.
  - Consider indicating oral treatment in stable patients for two to three cycles, in order to minimize the patient's exposure to health services.
  - Consider deferring systemic (non-oral) therapy in order to reduce exposure during the peak stage of the COVID-19-infection curve in the community during the pandemic stage. This recommendation is indicated, since the patient with cancer and systemic therapy is more vulnerable (ICU use and death), so it is reasonable to consider dose reductions, change to shortened treatment schedules, deferral of therapies or definitive suspension.
  - Elective laboratory studies and images should be deferred for a maximum time, depending on the type of malignancy.
  - If an urgent laboratory study is required, in order to define the systemic treatment of a patient, it is suggested to request the strictly necessary studies.
  - Patients who may be delayed in therapy while respecting treatment windows are those with medium priority.
  - Evaluate symptom control therapies in patients with advanced stages of disease, such as those with low priority.
  - Preferably, low priority patients should be seen remotely or through the caregiver.
  - Assess the use of prophylactically with colony-stimulating factor using chemotherapy regimens that have unusual indications.
- Offer neoadjuvant therapy in order to delay surgery. If radiotherapy is necessary, it can be applied before adjuvant, especially in tumors with positive hormonal receptors (HR), without affecting the evolution<sup>(17)</sup>.
  - HR positive patients, intermediate grade EC I or II, usually do not benefit from preoperative chemotherapy but from antihormonal management<sup>(16,17)</sup>.
  - Patients with triple negative tumors should receive standard chemotherapies. Consider the use of sequential therapies in monodrug, in order to minimize events of hematological toxicity<sup>(16,18,19)</sup>.
  - Adjuvant Trastuzumab can be considered shortened to 6 months instead of 12 months without affecting the evolution of the patients<sup>(17-19)</sup>.
  - In advanced disease, consider the use of single-drug therapies and window deferrals (every 4 weeks, for example)<sup>(18)</sup>.
  - HER2 breast cancer patients with more than 2 years of treatment duration and minimal tumor burden with trastuzumab-based regimens may discontinue maintenance therapy<sup>(17-19)</sup>.

## Prostate cancer

- In early detection, patients with elevated PSA and / or abnormal rectal examination, additional tests (laboratory, imaging, and prostate biopsy) should be deferred until COVID-19 conditions are safe<sup>(20)</sup>.
- Routine care can be delayed, in most cases minimal damage is expected with delays of care of 3 to 6 months, especially when compared to the risk of mortality from COVID-19<sup>(21)</sup>.
- In favorable, low or very low intermediate risk disease; you should not undergo further staging, active surveillance, monitoring or confirmatory testing, or treatment until it is safe<sup>(21)</sup>.
- In asymptomatic, high and very high unfavorable intermediate risk disease, further staging and radical treatment may be postponed until considered safe<sup>(3)</sup>.
- In symptomatic disease, conservative measures should be prioritized (medical therapy, ADT, catheterization). If necessary, consider surgery or radiation therapy<sup>(22)</sup>.
- In metastatic disease, consider non-myelosuppressive regimens, when alternatives exist. If cytotoxic is used, use of growth factor injections should be considered<sup>(23)</sup>.
- The dispensing of ADT medications for 3, 4 or 6 months should be preferred, according to criteria, for application outside the hospital<sup>(23)</sup>.

## SPECIFIC CLINICAL RECOMMENDATIONS FOR THE MOST FREQUENT MALIGNANCIES

It was requested that after the simulation with the order of prioritization and recommendations, important recommendations be made for each malignancy. These have been elaborated, in order to provide specific recommendations, since they are based on the best available evidence and on consensus of recommendation of the members. The five most frequent neoplasms were chosen.

### Breast cancer

- For new patients, you must have a multidisciplinary opinion<sup>(16)</sup>.



- Consider delaying repeat imaging, if PSA is decreasing and symptoms are absent until the risk of COVID-19 is resolved<sup>(23)</sup>.

### Cervical cancer

- Patients with high-grade cervical screening tests defer diagnostic evaluation to three months<sup>(24)</sup>.
- In the context of a macroscopic visible tumor, consideration of neoadjuvant chemotherapy<sup>(25)</sup>.
- Stage IB3, IIB-IVA chemotherapy in association with radiotherapy<sup>(24)</sup>.
- First line Stage IVB, or first local recurrence after 12 months from QT + primary RT, consider first-line QT<sup>(25)</sup>.
- Locally advanced disease: consider hypofractionation (increase the dose per day and reduce the number of fractions) to reduce the number of times the patient has to go to the consultation and hospital treatments<sup>(26)</sup>.

### Lung cancer

- In patients with locally advanced disease, chemotherapy plus definitive radiotherapy should be considered, evaluating sequential therapy<sup>(27)</sup>.
- In patients with surgical possibility, where their centers have limitations of operative shifts, it is recommended to offer induction or neoadjuvant chemotherapy<sup>(27,28)</sup>.
- Adjuvant chemotherapy can delay its initiation until 4 months after resection. Consider not initiating adjuvant in patients older than 75 years and with ECOG 3 or more<sup>(11,28-30)</sup>.
- It is recommended to choose chemotherapy regimens with low risk of myelosuppression, of short times and with less frequency of visits to the facility. Preferably schemes with 4 cycles of duration.
- Prophylactic stimulating factors are recommended<sup>(28-30)</sup>.
- In the metastatic scenario, always consider conducting the study for mutations in tissue or plasma. If a driver mutation is present, the respective treatment must be started and its prescription is recommended every 2 months according to tolerance<sup>(28)</sup>.

- It is recommended not to start third-line treatment or more, since the benefit of these treatments is low, and to offer palliative support best care therapy<sup>(27,29)</sup>.

### Lymphoma

- It is recommended to delay the onset of rituximab during the rise of the pandemic curve (phase 2 and 3) and then incorporate it sequentially<sup>(10)</sup>.
- Autologous transplantation of precursors is only recommended in patients with lymphomas at high risk of relapse that ends rescue schemes with good response. Consider adding a chemotherapy cycle before the autologous transplant<sup>(10,31,32)</sup>.
- The DA-EPOCH-R regimen is recommended in patients with primary mediastinal B-cell lymphoma and lymphomas associated with HIV. Patients with double / triple hits could receive R-CHOP and then autologous consolidation transplant<sup>(10,32)</sup>.
- It is recommended that patients with aggressive B lymphoma and high risk of CNS relapse should receive high-dose intravenous methotrexate treatment, at least 2 courses, after the six cycles of chemotherapy<sup>(10,32)</sup>.
- For localized NK/T-cell lymphoma, it is suggested to use sequential regimes but not concomitants<sup>(32)</sup>.

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