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Breast Cancer

# GEICAM Guidelines for the Management of Patients with Breast Cancer During the COVID-19 Pandemic in Spain

Miguel Martin,[a,b] Angel Guerrero-Zotano,[c] Ángel Montero,[d] Carlos Jara,[e] Elena Filipovich,[f] Federico Rojo,[b,g] Fernando Moreno,[h] Jose Ángel García-Sáenz,[b,h] Jose Enrique Alés,[f] José Ignacio Chacón,[i] Josefina Cruz,[j] Julia Gimenez,[k] Luis Cruz-Merino,[l] Manel Algara,[m] Marta Santisteban,[n] Sara López Tarruella,[a,b] on behalf of the GEICAM Spanish Breast Cancer Group Steering Committee

[a]Medical Oncology, Instituto de Investigación Sanitaria Gregorio Marañón, Departamento de Medicina, Universidad Complutense, Madrid, Spain; [b]Centro de Investigación Biomedica en Red de Oncologia, CIBERONC-ISCIII, Spain; [c]Medical Oncology, Instituto Valenciano de Oncología, Valencia, Spain; [d]Radiation Oncology, Hospital HM Sanchinarro, Madrid, Spain; [e]Medical Oncology, Universidad Rey Juan Carlos, Hospital Fundación Alcorcón, Madrid, Spain; [f]Medical Oncology, Complejo Asistencial de Ávila, Ávila, Spain; [g]Pathology, Hospital Fundación Jimenez Díaz de Madrid, Madrid, Spain; [h]Medical Oncology, Hospital Universitario Clínico San Carlos de Madrid, Madrid, Spain; [i]Medical Oncology, Hospital Virgen de la Salud de Toledo, Toledo, Spain; [j]Medical Oncology, Hospital Universitario de Canarias, Tenerife, Spain; [k]Surgery, Instituto Valenciano de Oncología, Valencia, Spain; [l]Medical Oncology, Hospital Virgen de Macarena de Sevilla, Seville, Spain; [m]Radiation Oncology, Hospital del Mar de Barcelona, Barcelona, Spain; [n]Medical Oncology, Clínica Universidad de Navarra, Navarra, Spain

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## Abstract

Breast cancer (BC) is the most common cancer in women in Spain. During the COVID-19 pandemic caused by the SARS-CoV-2 virus, patients with BC still require timely treatment and follow-up; however, hospitals are overwhelmed with infected patients and, if exposed, patients with BC are at higher risk for infection and serious complications if infected. Thus, health care providers need to evaluate each BC treatment and in-hospital visit to minimize pandemic-associated risks while maintaining adequate treatment efficacy. Here we present a set of guidelines regarding available options for BC patient management and treatment by BC subtype in the context of the COVID-19 pandemic. Owing to the lack of evidence about COVID-19 infection, these recommendations are mainly based on expert opinion, medical organizations' and societies' recommendations, and some published evidence. We consider this a useful tool to facilitate medical decision making in this health crisis situation we are facing. ***The Oncologist*** 2020;25:e1339–e1345

**Implications for Practice:** This work presents a set of guidelines regarding available options for breast cancer (BC) patient management and treatment by BC subtype in the context of the COVID-19 pandemic. Owing to the suddenness of this health crisis, specialists have to make decisions with little evidence at hand. Thus, these expert guidelines may be a useful tool to facilitate medical decision making in the context of a worldwide pandemic with no resources to spare.

## Introduction

Breast cancer (BC) is the malignancy with the highest incidence and prevalence among women in Spain [1]. Although the COVID-19 pandemic caused by the SARS-CoV-2 virus is capturing the world's attention and most of its health care resources, patients with BC still require adequate clinical management. However, patients with cancer may be more susceptible to infection with SARS-CoV-2 and, if infected, at a higher risk of serious respiratory complications due to treatment- or tumor-related immunosuppression or to disease-related malnutrition [2].

The organizational restructuring put in place to deal with the COVID-19 patient care crisis has translated into

Correspondence: Miguel Martín, M.D., Instituto de Investigación Sanitaria Gregorio Marañón, CIBERONC-ISCIII GEICAM Spanish Breast Cancer Group, Madrid, Spain. Telephone: +34670580865; e-mail: mmartin@geicam.org Received April 27, 2020; accepted for publication June 25, 2020; published Online First on July 23, 2020. http://dx.doi.org/10.1634/theoncologist.2020-0363

deeply reduced availability of operating rooms, consultations, imaging tests, and other routine activities. Furthermore, most oncology-related personnel are being referred to COVID-19 patient care or to self-isolation when infected.

In the context of this pandemic, it is imperative to rethink the risk/benefit ratio of each cancer treatment and each in-hospital visit aiming at minimizing pandemic-associated risks while maintaining adequate treatment efficacy. A stratification of the benefit/risk ratios for different patients with BC in different situations is difficult in the absence of more complete information about the real impact the different treatments could have on the risk of a SARS-CoV-2 infection, developing COVID-19, and having a poor outcome. Still, we believe that standard therapy should be maintained when there is curative intention or when high palliative efficacy has been shown. When faced with two options of similar efficacy, however, the one associated with a lesser risk of infection (i.e., fewer hospital visits, lower levels of myelosuppression) is preferable.

Thus, the aim of this article is to put forward a set of general and specific guidelines to be considered in the context of our national health care system in addition to individualized evaluations regarding BC treatment and patient management. These guidelines may also be applicable to similar health care systems abroad, or they may complement those developed with different health systems in mind [3].

## Materials and Methods

A multidisciplinary group of cancer experts, working under the umbrella of the GEICAM Spanish Breast Cancer Group, developed the following clinical practice- and evidence-based guidelines. Because of the sudden and unexpected pandemic situation, the evidence related to COVID-19 infection and its implications in the care of patients with breast cancer is scarce. Thus, these recommendations are mainly based on expert opinion, medical organizations' and societies' recommendations, and published evidence. First, we produced a number of general recommendations for patient management but also for hospitals and health care personnel (HCP). Second, we organized specific guidelines by stage of disease and BC subtypes. Third, we described SARS-CoV-2 testing procedures and patients to be tested. Finally, we included intensive care unit (ICU) admission criteria relevant to patients with BC.

## Results

### General Guidelines

- In all circumstances, patients and HCP should follow the instructions on SARS-CoV-2 infection prevention measures according to the European Centre for Disease Prevention and Control and the World Health Organization (WHO). In fact, stronger personal protection should be implemented for patients with cancer and cancer survivors, and a stronger surveillance should be performed when patients with cancer become infected with coronavirus.
- Suspension of any clinical sessions or meetings of more than five doctors unless absolutely necessary.
- All patients and HCP should wear masks in outpatient clinics. All medical staff should wear masks, scrubs, and gowns plus appropriate personal protective equipment when caring for infected patients.
- Telephone screening for symptoms before face-to-face visits to identify potentially infected patients before arrival to the hospital to take appropriate precautions.
- Hospitals should set up an independent screening station, where patients and companions report any symptoms and their body temperature is checked and recorded. If infection is suspected, both the patient and their companion must be kept at a safe distance from other patients or HCP. They should be managed according to the existing protocol for suspected SARS-CoV-2 cases.
- Reduction of patients' hospital visits to the minimum necessary, postponing follow-ups, reducing the number of tests, and replacing face-to-face visits with telephone consultations.
- Health care providers should discuss treatments risk/benefit ratio in the pandemic context with their patients based on their prognosis, age, comorbidities, social circumstances, and preferences. Discussion and conclusions should be recorded in writing on the medical record.
- Selection of therapeutic protocols that reduce infection risk for patients as long as patient prognoses are not significantly compromised.
- Administration of antiresorptives at longer intervals (e.g., quarterly), unless urgent therapy of hypercalcemia is deemed necessary.
- Implementation of blood draws in outpatient health centers or at patient's home, whenever possible.
- Execution of blood transfusions on a strictly necessary basis.
- Individual evaluation of each patient's treatment response, delaying therapy when safe for the patient, while keeping scheduling flexibility in case of clinical suspicion of recurrence/progression.
- Finally, regarding patients participating in clinical trials, GEICAM is setting specific guidelines per study based on the recommendations of the Spanish Health Authorities and periodic updates by the European Medicines Agency.

### Local Therapies for Early Stages

#### *Surgery*

The American College of Surgeons' guidelines [4] do not contemplate BC oncological surgery in hospitals at or near full capacity owing to infectious diseases like COVID-19. According to those guidelines, BC surgeries should be postponed until further notice. However, we believe that the decision to postpone a BC surgery should be made on a case-by-case basis. If the hospital can guarantee a clean and safe environment, surgery should not be ruled out as post-surgery ICU requirements for BC are very low.

As securing the ideal COVID-19–free environment is currently difficult [5], implementing the following strategies will reduce the risk of infection associated with the surgical procedure:

- Prior to the procedure, it should be confirmed that the patient and the surgical team have a negative SARS-CoV-2 test and are asymptomatic.
- Presurgical visit to surgery and anesthesia departments will be scheduled for the same day. Safe distance protocol must be performed.
- Surgery should be as conservative as possible and, when feasible, performed as an outpatient procedure, especially in older patients, to minimize hospital stay.
- Minimize postoperative visits by using absorbable sutures and placing drains only when essential.
- Autologous reconstruction must be deferred.

Finally, even hospitals with the capacity to continue performing BC surgery should consider delaying surgeries by administering neoadjuvant treatments, when possible. In contrast, hospitals where BC surgery is more restricted should prioritize cases less amenable to a delay, such as patients finishing neoadjuvant therapy who are not good candidates for systemic therapy continuation.

### *Radiotherapy*

During the COVID-19 crisis, some international guidelines have been published by European [6] and American [7] experts, that have been recommended by the European Society for Radiotherapy and Oncology (ESTRO) and the American Society for Radiation Oncology (ASTRO), proposing four options to protect cancer patients: delaying irradiation, foregoing it (in very selected cases), ultrashort irradiation schemes, or preoperative irradiation.

***Delayed irradiation.*** Whenever possible, a delay of irradiation for up to 12 weeks after surgery should be considered.

***Foregoing irradiation.*** Before considering this option, patients should be informed that foregoing irradiation increases the risk of local recurrence. Patients willing to assume this risk would be eligible only if they are ≥70 years of age and their disease met the following characteristics: tumor size <2 cm, grade 1, no signs of poor local prognosis (i.e., absence of angiolymphatic and perineural infiltration), clean surgical margins, no lymph node involvement, positive hormone receptors, and human epidermal growth receptor 2 (HER2) negative [8].

***Irradiation with ultrashort schemes.*** The Spanish Group of Radiation Oncology of Breast (GEORM for its Spanish acronym) advises against skipping irradiation for patients for whom it is indicated based on the RHEMA protocol. Instead, it recommends moving forward the delivery of ultrashort schemes. The RHEMA protocol is based on the results of U.K. studies FAST Trial [9], U.K. FAST-FORWARD Trial [10, 11], and HAI-5 [12].

In selected cases, according to patient and tumor criteria defined by the GEC-ESTRO and ABS-ASTRO groups (i.e., age ≥50 years, tumor size <3 cm, pN0, grade 1–2, luminal A), physicians should consider partial breast irradiation either by intraoperative radiotherapy at the time of lumpectomy/quadrantectomy or by external radiotherapy administering doses of 30 Gy in five daily fractions of 6 Gy on tumor bed with margin.

***Preoperative irradiation.*** The delay in surgical intervention may translate into a postponement of crucial local treatment for some patients. In these cases, preoperative irradiation should be considered [13], as it has been associated with a non-negligible rate of pathological complete response (pCR), which not only may allow delaying surgery but also may even improve patients' prognoses. Actually, GEORM has developed a protocol named *Preoperative Irradiation for Breast Cancer*.

Finally, for older patients [14] for whom surgery is probably not indicated, a hypofractional scheme is proposed (6.5 Gy weekly for 5 weeks up to a total dose of 32.5 Gy), with a possible boost of two fractions of 6.5 Gy. In this scenario, if lymph nodes are to be included, they will be irradiated with 5.5-Gy fractions up to a total dose of 27.5 Gy.

## Systemic Therapies for Early Stages

During the administration of chemotherapy and afterward, patients should minimize infection risks by following safety recommendations even more strictly.

To reduce the risk of SARS-CoV-2 infection, physicians may choose well-accepted shorter chemotherapy regimens with lower myelosuppression risk and administered every 3 weeks. In addition, the administration of prophylactic colony-stimulating factor (CSF) is highly recommended. However, the reduction of chemotherapy dosage to decrease myelosuppression risk is highly discouraged.

### *Neoadjuvant Therapy*

***Triple-negative BC.*** Chemotherapy is crucial for these patients and should be administered according to standard practice despite the pandemic. Neoadjuvant chemotherapy is the usual initial treatment in patients with tumor size ≥1.5–2 cm and/or with positive lymph-nodes (although it can be given to any patient regardless of tumor size).

Patients ≥70 years of age, a population more vulnerable to SARS-CoV-2 infection and at higher risk for serious complications, should discuss the risk/benefit ratio of neoadjuvant chemotherapy administration with their doctor. Initial surgery (if available) could be an option while the situation improves to be able to start the risk-adjusted chemotherapy needed after surgery, which should not be delayed any longer than 4–5 weeks.

Patients <70 years of age refusing neoadjuvant chemotherapy for fear of SARS-CoV-2 infection may undergo initial surgery under the aforementioned conditions.

***HER2-Positive BC.*** Chemotherapy, in combination with anti-HER2 monoclonal antibodies, is also crucial for patients with this BC subtype and should be administered according to standard practice.

Neoadjuvant therapy is normally applied to the same clinical situations described for patients with triple-negative BC.

***Hormone Receptor-Positive and HER2-Negative BC.*** The majority of these tumors have low risk of recurrence, making surgery the initial therapy of choice. However, neoadjuvant endocrine therapy (ET) to delay surgery may be a good option for women who do not wish to undergo

surgery in the current situation or if operating rooms are not readily available. This is particularly true for women ≥70 years of age and for patients with high hormone receptor expression and low Ki67 tumors.

The expected benefit of adding chemotherapy (neo/-adjuvant) to ET in these patients varies by well-established clinicopathological factors. Patients with histological grade 3 and elevated Ki67 tumors or significant axillary involvement generally benefit more from chemotherapy than others. Genomic platforms (Oncotype, Mammaprint, Prosigna, Endopredict) and online tools such as PREDICT [15] may help with the decision.

Patients with high-risk tumors may benefit from neoadjuvant chemotherapy (vs. adjuvant) by increasing the likelihood of having conservative surgery and establishing their prognosis. These benefits should be weighed together with the potential increased risk of SARS-CoV-2 infection and the availability of surgery. The doctor and the patient should then decide whether initial surgery is the best option (although postsurgery chemotherapy should be administered anyway).

### *Adjuvant Therapy*

***General Guidelines.*** Health status of patients ≥70 years of age must be carefully evaluated to estimate life expectancy and the risk/benefit ratio of chemotherapy. Physicians may find online tools such as ePrognosis [16] and genomic platforms very useful in such cases.

- The initiation of systemic adjuvant myelosuppressive therapies may be delayed until the COVID-19 crisis improves. However, the decision must be taken based on patients' individual risk and tumor subtype.

***Triple-Negative BC.*** Chemotherapy is crucial for these patients and should be administered according to standard practice despite the pandemic. Treatment should start ≤2 months after surgery as delays are associated with an increased risk of recurrence and death [17]. For older patients, regimens with low hematological toxicity and low hospital attendance should be favored. For younger patients, the regimen should be selected individually.

For patients at high risk of recurrence or in the absence of pCR after neoadjuvant chemotherapy, we suggest the extension of adjuvant treatment with capecitabine for 6–8 months. However, to minimize hospital visits, we recommend controlling toxicity by telephone and performing safety laboratory tests in outpatient health centers or at the patient's home.

***HER2-Positive BC.*** Chemotherapy is essential for these patients and should be administered according to standard practice.

The exclusive use of adjuvant therapy based on anti-HER2 and ET for HER2-positive/hormone receptor-positive tumors is not recommended, as there are no data supporting this.

To reduce patient exposure to SARS-CoV-2 infection, physicians may use the following strategies:

- Use of subcutaneous trastuzumab to reduce the length of hospital stay.
- Patients with good prognosis (i.e., stages I–II or with pCR after neoadjuvant chemotherapy) may receive a total of 6 months of treatment with trastuzumab (neoadjuvant plus adjuvant). This is especially advised for women >70 years of age and/or with comorbidities, that is, a high-risk group for severe COVID-19 disease if infected. Although Goldvaser's meta-analysis [18] endorses 1 year of therapy, data from the PERSEPHONE study showed no worse patient outcomes with 6 months versus 12 months of adjuvant trastuzumab treatment in HER2-positive early breast cancer [19].
- Adjuvant anti-HER2 therapy may be delayed for up to 2–3 months in patients receiving neoadjuvant chemotherapy in combination with anti-HER2 antibodies.
- Adjuvant administration of trastuzumab-DM1 (T-DM1) is adequate for patients without pCR after neoadjuvant chemotherapy. Its initiation may be delayed up to 3 months after surgery [20].

***Hormone Receptor-Positive and HER2-Negative BC.*** There are tools to facilitate treatment decisions for these patients. PREDICT [15] helps estimate the risk of recurrence and the benefit of adjuvant chemotherapy. Also, the preoperative endocrine prognostic index score guides the prescription of adjuvant chemotherapy to patients with tumors treated with neoadjuvant ET [21].

Other suggestions to reduce patients' risk include the following:

- Minimize the use of chemotherapy in stage II tumors, including those with low lymph node involvement, by using genomic platforms if the immunohistochemical profile supports it.
- Based on individual risk/benefit evaluation, the initiation of adjuvant chemotherapy may be delayed up to 3 months after surgery without sacrificing efficacy [13].

## Management of Metastatic Disease

The treatment of metastatic BC is palliative with the objective to improve survival while maintaining quality of life.

### *Triple-Negative BC*

For these patients, we recommend the following [22–24]:

- Adjust chemotherapy schemes switching from weekly to every-3-weeks regimens.
- Prioritize oral chemotherapy regimens as an alternative to the parenteral route, when possible.
- Evaluate the option of chemotherapy regimens associated with lower myelosuppression while favoring monotherapy over combination regimens.
- Consider prophylaxis with CSF to minimize neutropenia.
- Reduce the use of corticosteroids according to the characteristics of the scheme used.

Concerning biological therapies for advanced triple-negative metastatic disease:

- Poly (ADP-ribose) polymerase inhibitors should be considered while taking into account the risk of myelosuppression and the potential for drug–drug interactions through CYP3A (olaparib) and P-gp (talazoparib) according to their label. Additionally, pneumonitis,

although rare (<1% with olaparib), is a highly relevant adverse event in the context of COVID-19.
- Antiangiogenic therapy may provide added efficacy while increasing thrombotic/hemorrhagic risk.
- Immunotherapy in the context of clinical trials should be considered on a case-by-case basis. Anti–programmed death protein 1/programmed death-ligand 1 monoclonal antibodies induce a wide set of immune-related toxicities but with low risk of infections and myelotoxicity. Furthermore, in the Impassion130 trial, grade 3/4 neutropenia was 8.2%, irrespective of the treatment received (with/without atezolizumab); thus, it could be inferred that immunochemotherapy does not confer a higher risk of hematological complications with respect to standard chemotherapy [25, 26].

### *HER2-Positive BC*

***HER2-Positive and Hormone Receptor-Positive BC.*** In patients with controlled disease undergoing chemotherapy plus anti-HER2 agents, chemotherapy may be discontinued and replaced with oral ET, while maintaining the anti-HER2 blockage [27].

When considering first-line treatment (also applicable for subsequent cycles):

- In patients <70 years of age, to minimize both hospital visits and risk of toxicity, paclitaxel every 3 weeks with dual anti-HER2 blockage may be an option. If docetaxel is used, we recommend the administration of CSF starting on the first cycle [28].
- In patients ≥70 years of age, low myelosuppressive chemotherapy regimens, such as capecitabine or vinorelbine plus anti-HER2 antibodies, may be an option. Also, dual anti-HER2 blockage associated with ET may be an alternative in patients with low tumor burden [29].

### *HER2-Positive and Hormone Receptor–Negative BC*

- In patients <70 years of age (with expected overall survival >5 years), with BC symptoms, for whom treatment cannot be delayed, there are two good chemotherapy options in combination with dual anti-HER2 blockage: taxanes every 3 weeks, or oral therapy with vinorelbine or capecitabine. Myelosuppressive regimens may be supported with CSF to reduce risks.
- In patients ≥70 years of age, low myelosuppressive chemotherapy regimens plus dual anti-HER2 blockage may be an option as above.
- In patients with controlled disease undergoing chemotherapy plus anti-HER2 agents, but at high risk for COVID-19 (≥70 years of age and/or relevant comorbidity), chemotherapy may be discontinued while maintaining the anti-HER2 therapy.
- For patients on second/third lines of therapy, oral regimens (e.g., lapatinib-capecitabine scheme) should be considered to reduce the risk of infection. Administration of T-DM1 to comorbidity-free patients should not be ruled out if taking the aforementioned precautions in outpatient hospitals.
- In successive lines of therapy, physicians should consider delaying doses to minimize the risk during the current pandemic, according to risk/benefit ratio and/or patient comorbidity.

### *Hormone Receptor-Positive and HER2-Negative BC*

For patients without visceral crisis, we recommend the use of ET as the first treatment option. In postmenopausal patients, an aromatase inhibitor or fulvestrant may be used (depending on prior therapies and sensitivity to ET). In premenopausal patients, ovarian suppression should additionally be induced, either by surgical oophorectomy or with luteinizing hormone-releasing hormone agonists administered monthly (preferred option during the current state of emergency) [30].

In case of visceral crisis, chemotherapy stands as the treatment of choice. However, this strategy is under review since the incorporation of CDK 4/6 inhibitors (CDK4/6-i). During the current health care emergency, treating visceral crisis with CDK4/6-i agents in combination with ET can exceptionally be considered in situations in which it is safe to assume that the disease may be very sensitive to ET.

CDK4/6-i treatment is associated with grade ≥ 3 neutropenia in >60% of patients and grade ≥ 3 lymphopenia in about 6% of patients. Neutropenia might increase the risk of bacterial infection, which may complicate a viral infection. Meanwhile, lymphopenia might be associated with a less favorable course in SARS-CoV-2–infected patients. However, in this new pandemic context, we lack enough evidence to advise against CDK4/6-i treatment for these patients, and the risk/benefit ratio of administering this therapy should be individually weighed. Until the current situation resolves, temporary suppression of the CDK 4/6-i may be considered in the presence of lymphopenia, while maintaining ET.

A subsequent ET line should be considered beyond endocrine plus CDK4/6-i progression. The combination of everolimus with ET should be cautiously assessed as this drug may cause complications, such as pneumonitis or immunosuppression, which may be associated with a worse course of a SARS-CoV-2 infection.

Taxanes and anthracyclines are the drugs with the highest response rates if chemotherapy is considered, but both have a high risk of myelosuppression. Chemotherapies with lower myelosuppressive effect, such as capecitabine or oral vinorelbine, should be considered as an alternative. If anthracyclines, taxanes, or eribulin are used, prophylactic CSF should be administered.

## Testing Patients for SARS-CoV-2

Patients with cancer on active or recently finished (≤3 months) myelosuppressive therapy are more susceptible to infections as compared with individuals without cancer. Once diagnosed with COVID-19, they are at a higher risk of severe events (i.e., need for invasive ventilation or death) and quick deterioration [2]. In a scenario in which four out of five infected patients might be asymptomatic [31], our recommendation is that all patients in need of any major surgery or invasive medical procedure with involvement of the respiratory tract (e.g., bronchoscopy) or sedation (e.g., gastrointestinal surgery, endoscopy) and starting or resuming myelosuppressive therapy should be first

tested for SARS-CoV-2 regardless of their symptoms or contact history with infected individuals. In case of a shortage of tests available, high-risk patients (e.g., older age, obesity, diabetes, chronic obstructive pulmonary disease, hepatopathy, nephropathy, cardiopathy, heavy smokers) should be prioritized for testing.

Patients positive for SARS-CoV-2 should have their myelosuppressive treatment delayed until they test negative. If testing is not available, the patient should be symptom free for at least 2 weeks before weighing with the physician the risk/benefit ratio of resuming treatment.

Patients presenting symptoms suggestive of infection such as fever, dry cough, dyspnea, anosmia, ageusia, myalgia, and gastrointestinal symptoms (nausea, vomiting, or diarrhea) should also postpone treatment even if they test negative for the virus.

### *Tests Based on Detection of Viral RNA*

These tests confirm an active infection with SARS-CoV-2 allowing detection of patients with clinical or asymptomatic presence of the virus and preventing transmission. This information benefits both patients and others as the isolation of infected patients reduces the spread of the virus and protects public health.

Polymerase chain reaction (PCR) tests detect SARS-CoV-2 directly by identifying viral RNA by amplification based on PCR. The sample is immersed in a virus-inactivating solution; the RNA is subsequently purified and amplified by means of PCR with reverse transcription.

Sample types: nasopharyngeal or oropharyngeal swab, the former being the most sensitive. If both are obtained, they can be combined in a single reaction. Other useful samples are bronchoalveolar lavages in patients with pneumonia, sputum, and nasal and oral mucosa samples.

Limiting factors:

- The amount of virus present in a patient at any specific time.
- Detection of RNA does not necessarily mean that the virus is transmissible.
- Preservation of highly fragile RNA in the sample.

### Tests to Determine the Host's Response to the Virus

These tests are based on IgM and IgG antibodies produced in suspected cases starting around 2 weeks after SARS-CoV-2 infection. These antibodies are detected in peripheral blood by commercial immunoassays (rapid lateral flow immunoassays, automated chemiluminescence immunoassays, enzyme-linked immunosorbent assay, and other formats). IgM can be detected in patients 10 to 30 days after infection, whereas IgG can be detected 20 days onward. The IgM response occurs earlier than that of IgG, only to decrease and disappear. IgG can persist after infection for a long time and may play a protective role.

Limiting factors:

- The host develops antibodies against SARS-CoV-2 between 7 and 11 days after exposure to the virus.
- We still do not know whether, and for how long, the presence of antibodies protects against future SARS-CoV-2 infections.

Precautions: samples must be sent appropriately identified, in a safe bag, following the WHO recommendations (refer to Laboratory biosafety guidance related to the novel coronavirus [2019-nCoV]. Interim guidance 12 February 2020) [32].

### ICU Admission Criteria for Patients with Cancer

SARS-CoV-2–infected patients with cancer are especially vulnerable to inadequate management of COVID-19 because this condition is still associated with inexorable incurability or near death, even among certain HCP. However, many patients with cancer can benefit from intensive care when the evolution of pneumonia or any other complication so advises. Decisions regarding care should be made based on each patient's prognosis. Overall, decisions regarding admission to ICU will greatly benefit from a consultation with the patient's oncologist, who has the most complete information of the specific disease's natural history, including its prognosis and the patient's life expectancy. For instance, the following patients with BC would benefit from ICU admission:

- Previously diagnosed patients, already operated, disease free, and currently being followed up.
- Patients currently on treatment with (neo) adjuvant therapies with curative intention.
- Patients whose single metastasis has been surgically removed, who are being followed up or in treatment with "adjuvant" therapy with a good prognosis for survival.
- Patients with metastatic disease on treatment with targeted therapies in response, with an expected median survival ≥5 years.
- Patients in any other circumstances, in response, with an expected prolonged survival, evaluated together with oncology.

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## Author Contributions

**Manuscript writing:** Miguel Martin, Angel Guerrero-Zotano, Ángel Montero, Carlos Jara, Elena Filipovich, Federico Rojo, Fernando Moreno, Jose Ángel García Sáenz, Jose Enrique Alés, José Ignacio Chacón, Josefina Cruz, Julia Gimenez, Luis Cruz-Merino, Manel Algara, Marta Santisteban, Sara López Tarruella

**Final approval of manuscript:** Miguel Martin, Angel Guerrero-Zotano, Ángel Montero, Carlos Jara, Elena Filipovich, Federico Rojo, Fernando Moreno, Jose Ángel García Sáenz, Jose Enrique Alés, José Ignacio Chacón, Josefina Cruz, Julia Gimenez, Luis Cruz-Merino, Manel Algara, Marta Santisteban, Sara López Tarruella

## Disclosures

**Miguel Martín:** Roche, PUMA, Novartis (RF), AstraZeneca, Amgen, Taiho Oncology, Roche/Genentech, Novartis, PharmaMar, Eli Lilly, PUMA, Daiichi Sankyo, Pfizer (C/A), AstraZeneca, Amgen, Roche/Genentech, Novartis, Pfizer (H); **Fernando Moreno:** Pfizer, Merck Sharp & Dohme, Novartis, Roche/Genentech, AstraZeneca (C/A), Pfizer, Roche (H), Roche/Genentech, Novartis, Pfizer (travel

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