

**PHILIPPINE SOCIETY OF MEDICAL ONCOLOGY (PSMO)
CONSENSUS RECOMMENDATIONS IN THE MANAGEMENT OF
HEPATOCELLULAR CARCINOMA DURING COVID-19 PANDEMIC IN THE
CORONAVIRUS DISEASE 2019 (COVID-19) ERA**

**Section of Medical Oncology
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BACKGROUND

The global pandemic, coronavirus disease 2019 (COVID 19) has resulted in over 5,723,970 confirmed cases and 357,233 deaths as of May 29, 2020¹⁶. There is no evidence of Hepatocellular cancer patients having a high risk for acquiring COVID 19. However according to the study by Warner, et. al¹⁷ cancer patients have a high risk of mortality and of severe SARS-COV-2 infection.¹³ The unexpected demand in resources, shortage of manpower, fear of the risk of infection had a huge impact in cancer care delivery.¹ As such, new guidelines are needed in order to help clinicians in the management and treatment of these subset of patients.

Hepatocellular carcinoma treatment in the time of COVID 19 should focus on the adherence to guidelines, with as little exposure as possible to both the patient and healthcare workers.¹⁸ However, deviation from the standard of care should be considered in special cases so as to bridge the patient until definitive treatment can be given.¹

Clinical Questions

I. SARS-CoV-2 testing

Q: Should asymptomatic hepatocellular cancer patients be tested for SARS-CoV-2 RNA?

A: There is no evidence that hepatocellular carcinoma increases the risk for COVID 19. However immunosuppressive therapies, defined as cytotoxic chemotherapy, solid organ or stem cell transplantation, long acting biologic therapy, cellular immunotherapy, or high-dose corticosteroids⁵ make the patient more susceptible to infections. Therefore, the Infectious Diseases Society of America (IDSA) strongly recommends SARS COV-2 RNA testing for patients who would undergo immunosuppressive therapy within 48-72 hours of the planned procedure, regardless of COVID 19 exposure.

Q: When should a retest for SARS-COV-2 be requested?

A: Patients who are ongoing treatment should undergo screening using a standardized questionnaire 48-72 hours before the next cycle. This would identify which patient has symptoms or exposure and who should be subjected to repeat testing.⁶

II. Outpatient visits

Q: Which patients should be prioritized for outpatient visits?

A: Even in areas without reported COVID 19 cases, Telehealth consultations are preferred over outpatient visits². Face to face consultations should be reserved for patients below 70 years of age¹⁵ classified as **HIGH** priority based on the European Society of Medical Oncology (ESMO) guidelines.

Those that are classified under **HIGH** priority are as follows: ⁴

- Patients with decompensated liver disease
- Patients on the waiting list for liver transplantation
- Patients with suspected HCC
- Patients with proven HCC awaiting treatment initiation or modification
- Patients showing moderate or severe side effects to treatment

Those that are classified under **MEDIUM** priority are as follows: ⁴

- Patients with HCC-suspect lesions <1 cm
- Patients showing response and tolerability to treatment
- Patients showing mild side effects to treatment
- Second opinion

Those that are classified under **LOW** priority are as follows: ⁴

- Patients in long term remission >5 years
- Patients in end-stage HCC (BCLC D, Child-Pugh C) without option for recompensation of liver function

When inevitable, proper protective equipment should be used and careful scheduling should be made so as to reduce the waiting time.⁸ Home delivery of medications, when possible, could also be done to limit visits.⁸ A nurse navigator on the other hand may be employed to help in the guidance and follow ups of the patient.

III. Imaging

Q: Should imaging be delayed?

A: If possible, surveillance imaging shouldn't be delayed as the end of the pandemic is unknown. However, a delay of 2months is acceptable.¹

Q: How should patients be prioritized for imaging?

A: Patients can be classified into 3 levels of priority, which are as follows:

Those that are classified under **HIGH** priority: ⁴

- Radiological diagnostic work-up of HCC-suspect lesions
- Radiological assessment of treatment response
- Radiological assessment of bone metastasis
- Patients with decompensation of liver function

Those that are classified under **MEDIUM** priority: ⁴

- HCC-suspect liver lesions <1 cm without progression

Those that are classified under **LOW** priority: ⁴

- HCC surveillance can be deferred based on available resources (including availability of therapeutic options in case of HCC diagnosis) at the center and the individual risk assessment. Patients with increased risk, such as patients with elevated alpha-fetoprotein levels, advanced cirrhosis, chronic hepatitis B, NASH/diabetes, etc., may be prioritized if resources are limited

Surveillance is also deferred for those who tested *positive* for COVID 19 until recovery.¹⁰

IV. Liver Biopsy

Q: Should liver biopsy be deferred?

A: The European Association for the Study of the Liver (EASL) recommends the performance of biopsies on those with transaminases more than 5x elevated without an unknown etiology and liver masses suspicious of malignancy. However, for those patients who tested positive for COVID 19, treatment of COVID 19 should be prioritized. Proceeding with biopsy in patients with COVID 19 could increase the transmission of the virus and the inflammation may obscure the diagnosis.¹⁰

V. Surgery

Q: Should liver transplantation or surgical intervention be delayed?

A: ESMO indicates that there is no change in the criteria for liver transplantation. However, it should be reserved for those who are at high risk of progression of disease¹ and those whose chance of success is more than 50%³. This is due to the lack of transplantation units, inpatient post-operative care beds, donors, and increased risk for SARS-COV2. On the other hand, bridging therapy with systemic treatment, locoregional treatment, or active monitoring should be offered.²

ESMO guidelines divided the cases into two levels of surgical priorities, high and medium

Those that are classified under **HIGH** priority are as follows: ⁴

- Liver transplantation (listing prioritized for patients with poor short-term prognosis including those with acute/acute-on-chronic liver failure (ALF/ACLF), high model for end-stage liver disease (MELD) score (including exceptional MELDs) and HCC at the upper limits of the Milan criteria)
- Surgical intentions with curative intent for patients with large or multifocal but still curatively resectable HCC lesions

Those that are classified under **MEDIUM** priority are as follows: ⁴

- Listing for transplantation of patients with compensated liver disease and within the lower limits of Milan criteria
- Curative surgical resection of small single HCC lesions

Patients who underwent liver transplantation should also be vaccinated against streptococcus pneumoniae and influenza.¹⁰

VI. Locoregional treatments

Q: Should locoregional treatments (LRT) replace surgery?

A: The American Association of Liver Diseases (AALD) recommends proceeding with treatment rather than delaying so as not to lose a curative window. LRTs are preferred over surgery because they reduce the duration of hospitalization. Surgery is thus reserved for those who fail to respond after LRT.²

Q: How do we prioritize patients for LRTs?

A: Below are the levels of priority according to the ESMO Guidelines⁴

Those that are classified under **HIGH** priority are as follows: ⁴

- Radiological treatments (e.g. TACE, SIRT/TARE) as bridging therapy for patients in stage BCLC A awaiting liver transplantation
- Patients receiving radiological treatments with expected survival benefit in a palliative setting (stages BCLC B or C)

Those that are classified under **MEDIUM** priority are as follows: ⁴

- Radiological treatment as bridging for liver transplantation in very early stage (BCLC 0)
- Curative ablation of small single HCC lesions (≤ 2 cm)

Those that are classified under **LOW** priority are as follows: ⁴

- Delay all treatments with modest benefit expected

VII. Systemic Treatment

Q: Which patients should be prioritized for systemic treatment?

A: ESMO has given a HIGH priority to those receiving first and following line of systemic treatments.⁴ To avoid frequent visits, NICE guidelines¹¹ on the other hand recommends the following:

- Switching intravenous treatments to subcutaneous or oral alternatives where this would be beneficial

- Using shorter treatment regimens
- Decreasing the frequency of immunotherapy regimens, for example moving to 4-weekly or 6-weekly
- Providing repeat prescriptions of oral medicines or other at-home treatments without patients needing to attend hospital
- Using home delivery of oral medicines where possible (but check the resilience of home care providers)
- Using treatment breaks for long-term treatments (possibly for longer than 6 weeks)

Q: If the patient tests positive for COVID 19, should treatment be stopped?

A: American Society of Clinical Oncology (ASCO) recommends withholding of immunosuppressive treatment for at least 14 days from the onset of symptoms.⁶ Studies on the immunosuppressive effect of checkpoint inhibitors are inconclusive¹¹. These may be continued depending on the discretion of the physician.

Q: When should treatment be restarted?

Immunosuppressive treatment can be resumed when the patient becomes symptom-free for at least 72 hours with 2 negative SARS-CoV2 tests at least 24 hours apart.⁶

VIII. Multidisciplinary Team Meeting

Q: How should Multidisciplinary Team meetings be conducted?

A: Weekly² multidisciplinary team meetings should be considered. During these meetings, images can be reviewed¹⁵ virtually and any deviation in the standard of care could be discussed¹. The healthcare team should discuss the plan of care and finalize the treatment schedule as well as screening procedures before asking the patient to come in.

IX. Clinical Trials

Q: What about the patients enrolled in clinical trials, should treatment be stopped?

A: International Liver Cancer Association (ILCA) recommends that trial-related treatments and scheduling be discussed with the sponsor. They can also be shifted to oral TKIs to reduce hospital visits and exposure. Medications can be shipped through mail and assessment of response (i.e. Imaging, blood tests) can be done at a nearby center.¹

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