HEPATOLOGY SOCIETY OF THE PHILIPPINES
418 Prince David Condominium, 305 Katipunan Ave., Loyola Heights Quezon City
http://www.hsp.org.ph

*COVID Task Force Committee*: Vanessa Co-Tanco MD, Suzette Grace Kho-Herman MD, Angelo Lozada MD, Angela Salvana MD

# POSITION STATEMENT

## COVID-19 Vaccination in Adult Patients with Chronic Liver Disease

*Released April 11, 2021

**GENERAL RECOMMENDATIONS:**

- We recommend COVID-19 vaccination and prioritization for vaccination for Filipinos with chronic liver disease (CLD) .
- Chronic liver diseases include: chronic hepatitis B, chronic hepatitis C, metabolic associated fatty liver disease, alcohol related liver disease, autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, hepatobiliary cancer, cirrhosis and liver transplant patients.
- Patients with CLD who are currently taking antiviral therapy for HBV or HCV or medication for primary biliary cholangitis or autoimmune hepatitis should NOT stop their medications while receiving the COVID-19 vaccines.
- All vaccinated patients and their caregivers or close contacts should still continue to practice general preventive health measures( face masks, face shields, social distancing and hand sanitization).
- Standard monitoring for post-vaccination side effects should be exercised in individuals with chronic liver disease.
- Caregivers and household/close contacts of CLD patients should also be strongly encouraged to get vaccinated.

**These recommendations are based on reviews of the most recent published data and other relevant society recommendations. Currently, there is no data available on the efficacy and safety of the COVID-19 vaccine specifically for patients with liver disorders. The position statement presented herewith are based on literature gathered at the time of release. These recommendations may change and will be updated as more information becomes available. Clinicians must weigh the risks and benefits of COVID-19 vaccinations in their patients with liver disease on a case to case basis.*

---

## I. Introduction

A global pandemic which originated from Wuhan, China last December 2019, coronavirus disease 2019 (COVID-19) is a highly contagious illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus. Several studies have shown that individuals with chronic liver disease (CLD) especially cirrhosis, hepatobiliary malignancies, and liver transplant recipients are more susceptible to acquiring and developing severe complications from COVID-19 including higher mortality rates [1, 2, 3, 4].

Since early this year, several vaccines have already been rolled out as a preventive measure for COVID-19. This position statement aims to serve as a guide for physicians in their recommendations for vaccinating their liver patients against COVID-19.

## II. Safety and Efficacy of Vaccines

**Table 1. Profile on the safety and efficacy of vaccines currently available against SARS-CoV-2**

| Vaccine | Vaccine type | Efficacy | Serious Adverse Events | Patients with Liver Disease Included In Studies | Adverse Effects in Patients with Liver Disease | Decreased Efficacy in Patients with Liver Disease |
|---|---|---|---|---|---|---|
| **ChAdOx1 nCoV-19 (Astra Zeneca and University of Oxford)**[5] N=11,636 | Viral vector | 62.1% (95% CI 41.0–75.7) | 1 in ChAdOx group, 1 in control, 1 masked | Yes | Data not available | Data not available |
| **Coronavac (Sinovac)**[9] N= about 10,000 healthcare workers, ongoing | Inactivated virus | Two-week dosing interval: 50.65% (95% CI 35.94 – 61.98)<br><br>moderate and severe COVID 100.0% (95% CI 56.37-100)<br><br>More than 21 days dosing interval: 62.32% (95% CI 13.91-83.51) | None reported<br><br>Standardized hypersensitivity event rates to be reported | Protocol does not exclude patients with liver disease | Data not available | Data not available |
| **BNT162b2 (Pfizer-Bio NTech)**[12] N=43,448 | mRNA | 95% (95% credible interval, 90.3 to 97.6) | Four events in vaccine group | Yes | None related to liver disease | No data |
| **mRNA-1273 (Moderna)**[13] N=15,210 | mRNA | 94.1% (95% CI, 89.3 to 96.8%) | Six events in vaccine group | Yes | None related to liver disease | No data |

- ChAdOx1(AstraZeneca and Univ of Oxford) data from the UK and Brazil were pooled for interim analysis
    - Primary efficacy endpoint was symptomatic disease among seronegative participants with a positive nucleic acid amplification test more than 14 days after the second vaccine dose
    - 62.1% efficacy for the primary endpoint was seen (Group given standard doses (N=4,440)[5]

- Hepatitis B and hepatitis C serologies were obtained from the UK group, but data are not yet available[6]
- Overweight subjects and those with significant alcohol consumption, diabetes and cardiovascular disease were included in the UK trial[6]. A good number of these participants, although not explicitly characterized in the publication, were assumed to have liver disease
- There were no reports of liver-related adverse events[5]

- Coronavac (Sinovac) published data pertain to Phase 1/2 trials published in The Lancet[7, 8]. Unpublished data from Brazil on healthcare workers provided to the Hong Kong Advisory Group on COVID-19 Vaccines formed the basis for approval for use in Hong Kong and the Philippines [9]
  - Primary efficacy endpoint was symptomatic COVID-19 at least two weeks after receiving two doses of the vaccine
  - 50.65% efficacy was seen with the original two-week dosing interval, which improved to 62.32% with a longer interval between doses[9]
  - No liver-related adverse events were reported

- The ongoing BNT162b2 (Pfizer-BioNTech) phase 3 multicenter trials primary efficacy endpoint is COVID-19 symptoms with onset at least 7 days after the second dose in participants who had been without serologic or virologic evidence of SARS-CoV-2 infection. BNT162b2 was 95% effective in preventing Covid-19 (95% credible interval, 90.3 to 97.6). Vaccine efficacy of 90 to 100% was observed across subgroups including those with coexisting conditions.
  - Patients with hepatitis B and hepatitis C were included. One hundred twenty five participants in the vaccine arm (0.7%) had mild liver disease, and one subject had moderate or severe liver disease.
  - Four related serious adverse events were reported among BNT162b2 recipients, specifically shoulder injury related to vaccine administration, right axillary lymphadenopathy, paroxysmal ventricular arrhythmia, and right leg paresthesia.
  - No liver-related adverse events were reported[12]

- Moderna's Coronavirus Efficacy (COVE) mRNA-1273 phase 3 trial conducted in the United States had a primary efficacy endpoint of preventing a first occurrence of symptomatic Covid-19 with onset at least 14 days after the second injection among seronegative participants. Vaccine efficacy was 94.1% (95% CI, 89.3 to 96.8%; P<0.001) for the prevention of symptomatic SARS-CoV-2 infection. Vaccine efficacy for severe COVID was 100%.
  - One hundred (0.7%) of vaccine recipients had liver disease.
  - Six (<0.1%) serious vaccine-related adverse events were seen in the vaccine group. No liver-related adverse events were recorded.

- The Hepatology Society of the Philippines does not have any brand preference from any of the vaccines currently available. All the vaccines (shown in Table 1) were studied through clinical trials, and were all noted to confer protection against COVID-19 infection including lower risk of morbidity and mortality. Patients with chronic liver disease can receive any of the vaccines whichever is available to them as long as it is FDA approved, the patient has no specific vaccine contraindications, and after a comprehensive evaluation and discussion with their attending physicians.

## III. Specific Recommendations for COVID-19 Vaccination in Chronic liver disease patients

### Chronic Hepatitis B & C

- COVID-19 vaccination is recommended for chronic hepatitis B and C patients, whether on or off antiviral treatment.
  - These patients should be prioritized for vaccination.

    - Viral hepatitis patients on antiviral therapy for hepatitis B or C should NOT withhold their medications while receiving the COVID-19 vaccines.[2]
- Simultaneous administration of Hepatitis A and B vaccines with COVID-19 vaccine is not advisable
    - Co-administration may decrease the efficacy of either vaccine. It is recommended that they be administered at least 2-3 weeks apart.

**Metabolic Associated Fatty Liver Disease (MAFLD), Alcohol related Liver Disease (ALD), Autoimmune Hepatitis (AIH), Autoimmune Biliary Disease (PBC / PSC)**

- COVID-19 vaccination is recommended for patients with stable chronic liver disease such as MAFLD, ALD, AIH, PBC/ PSC.
    - These patients should be prioritized for vaccination.[2]
    - Medical therapy for primary biliary cholangitis or autoimmune hepatitis should NOT be withheld while receiving the COVID-19 vaccines[2]

**Hepatobiliary cancer**

- COVID-19 vaccination is recommended for patients with active and past history of hepatobiliary cancer[1, 2]
    - These patients should be prioritized for vaccination.
    - ChAdOx1(AstraZeneca and Univ of Oxford) interim data excluded patients with malignancy. This was not clearly characterized in the Coronavac (Sinovac) interim data; therefore this recommendation is based on theoretical consideration.
- Patients with hepatobiliary cancer planned for major surgery should separate date of surgery from vaccination by at least a few days (~3days) and until patients medical status is stable.[10]
    - The primary reason for avoiding vaccination in the perioperative period is so that symptoms (i.e. fever) can be correctly attributed to surgery versus vaccination.[10]
- Patients with hepatobiliary cancer undergoing locoregional therapy, radiation or systemic therapy (cytotoxic chemotherapy, targeted therapy, immunotherapy, tyrosine kinase inhibitors) should consider COVID-19 vaccination whenever the vaccine is available and without interruption to their treatment.[10]
    - There is currently no data on timing of vaccine administration
- Patients with recent infections or fever should NOT receive the COVID-19 vaccine until they are medically stable.[10]
- Immunosuppressed patients will likely have blunted immune responses when compared to the general population and thus should continue to practice general preventive health measures post-vaccination. Caregivers and household/close contacts should also be strongly encouraged to get vaccinated when the vaccine is available.[10]

**Cirrhosis**

- COVID-19 vaccination is recommended for all stable compensated cirrhotic patients.
    - Vaccination should be performed as early as possible in the course of the disease, when immune response is still preserved[11]. These patients should therefore be prioritized for vaccination.
    - Medical therapy for cirrhosis should NOT be withheld while receiving the COVID-19 vaccines.
- Decompensated cirrhotic patients are advised to be referred for specialist evaluation prior to vaccination.
- Deferral of COVID-19 vaccination should be considered for those with acute events (i.e. bleeding varices, hepatorenal syndrome, hepatic encephalopathy) and acute infections (i.e. spontaneous bacterial peritonitis) until resolution of these event and re-establishment of baseline liver function.
- Cirrhotic patients will likely have blunted immune responses when compared to the general population and thus should continue to practice general preventive

health measures post-vaccination. Caregivers and household/close contacts should also be strongly encouraged to get vaccinated when the vaccine is available.[10]

### Liver Transplant

- COVID-19 vaccination is recommended for liver transplant candidates prior to transplantation and liver transplant recipients after transplantation.[1, 2]
    - These patients should be prioritized for COVID-19 vaccination whenever authorized vaccines are available
- The ideal time to administer the COVID-19 vaccine in liver transplant recipients is within 3-6 months post transplantation.
    - This is the timeframe when immunosuppression is expected to be lowered and stable, in addition it is at this time that other prophylactic medications are expected to be tapered.
    - A reduction in immunosuppression doses to increase vaccine efficacy is NOT recommended due to the risk of acute cellular rejection.[2]
    - However, this can be expedited to as early as 6 weeks post transplant if risk of community transmission is deemed high.[2]
- Deferral of COVID-19 vaccination in liver transplant recipients can be considered with active acute cellular rejection or those on high daily doses of corticosteroids, until the episode of rejection has resolved and baseline immunosuppression is re-established. [2]
- Given the life-saving nature of the procedure, liver transplantation should not be delayed in a patient who received COVID-19 vaccination.[2]
- If the patient is due for a second dose of vaccine in the immediate post-transplant period, this may be delayed after 6 weeks to elicit a better immune response.[2]
- Potential liver donors and recipients of liver donation should be prioritized for COVID-19 vaccination and preferably receive the second dose of COVID-19 vaccination at least two weeks before transplantation when feasible based on vaccine availability.[2]
- A lack of COVID-19 vaccination should not delay lifesaving liver transplantation[2]
- Immunosuppressed patients will likely have blunted immune responses when compared to the general population and thus should continue to practice general preventive health measures post-vaccination. Caregivers and household/close contacts should also be strongly encouraged to get vaccinated when the vaccine is available[10]

## Conclusion

Although vaccine effectiveness may be lower in patients with chronic liver disease compared to the general population, vaccination is still highly recommended because it can lower morbidity and mortality against COVID-19 infection. All vaccinated patients, including their close contacts are still encouraged to practice the general preventive health measures such as use of face masks and face shields, social distancing, and hand hygiene even after vaccination.

**References**


1. *Cornberg, Markus, et al. "EASL position paper on the use of COVID-19 vaccines in patients with chronic liver diseases, hepatobiliary cancer and liver transplant recipients." Journal of Hepatology, vol. 74, 2021, pp. 944 - 951*
2. *Fix, Oren K., et al. "AASLD Expert Panel Consensus Statement: Vaccines to Prevent COVID- 19 Infection in Patients with Liver Disease." AASLD COVID-19 Vaccine Working Group, 12 February 2021, https://aasldpubs.onlinelibrary.wiley.com/doi/10.1002/hep.31751. Accessed 7 April 2021*
3. *Marjot, Thomas, et al. "Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: An international registry study." Journal of Hepatology, vol. 74, no. 3, 2021, pp. 567-577*
4. *Ji D, Zhang D, Yang T, Mu J, Zhao P, Xu J, Li C, Cheng G, Wang Y, Chen Z, Qin E, Lau G. Effect of COVID-19 on patients with compensated chronic liver diseases. Hepatol Int. 2020 Sep;14(5):701-710. doi: 10.1007/s12072-020-10058-6. Epub 2020 Jul 30. PMID: 32734407; PMCID: PMC7391917*
5. *Voysey M et al. Oxford COVID Vaccine Trial Group. 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. Lancet. 2021 Jan 9;397(10269):99-111*
6. *Ramaswamy MN et al. Oxford COVID Vaccine Trial Group. 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. Lancet. 2021 Dec 19;396(10267):1979-1993*
7. *Zhang Y et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine in healthy adults aged 18-59 years: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis. 2021 Feb;21(2):181-192*
8. *Wu Z et al. Safety, tolerability, and immunogenicity of an inactivated SARS-CoV-2 vaccine (CoronaVac) in healthy adults aged 60 years and older: a randomised, double-blind, placebo-controlled, phase 1/2 clinical trial. Lancet Infect Dis. 2021 Feb 3:S1473-3099(20)30987-7*
9. *Hong Kong Advisory Group on COVID-19 Vaccines. Report on Evaluation of Safety, Efficacy and Quality of CoronaVac COVID-19 Vaccine (Vero Cell) Inactivated. 22 Feb 2021*
10. *NCCN. "Recommendations of the NCCN COVID-19 Vaccination Advisory Committee." NCCN: Cancer and COVID-19 Vaccination, 10 March 2021, https://www.nccn.org/covid-19/pdf/COVID-19_Vaccination_Guidance_V2.0.pdf. Accessed 7 April 2021*
11. *Van Thiel, D. H. "Vaccination of patients with liver disease: Who, when, and how." Liver Transpl Surg., no. 4, 1998, pp. 185-187*
12. *Polack FP et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med. 2020 Dec 31;383(27):2603-2615*
13. *Baden LR et al. COVE Study Group. Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine. N Engl J Med. 2021 Feb 4;384(5):403-416.*