

# EARLY SARS-COV-2-RELATED MORTALITY OF LIVER CANCER PATIENTS: CANCER STAGE MATTERS

2<sup>o</sup> part of the CERO-19 project - First interim analysis  
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## INTRODUCTION

The SARS-CoV-2 infection in cirrhotic patients has been associated with liver function deterioration and the 30 day-COVID-19-associated-mortality rate of 25% (Iavarone et al JHEP, 2021).

However, there are no mortality data in a large cohort of liver cancer patients with SARS-CoV-2 infection.

## AIM

To evaluate the 30 day-mortality of liver cancer patients with SARS-CoV-2 infection.

## METHOD

CERO-19 is a retrospective, observational, multicenter and international project.

This is the first interim analysis of the individual data from liver cancer patients diagnosed with SARS-CoV-2 infection during the period from February to December 2020.

Variables related to type of liver cancer, BCLC or TNM-8th stage at SARS-CoV-2 for HCC and ICC diagnosis, respectively. Variables related to patient outcome were also registered.

30-day SARS-CoV-2-related mortality rate and sub-distribution hazard ratios (HR) were estimated considering non-related-SARS-CoV-2 deaths as competing risks.

## RESULTS

Interim analysis that evaluated 242 patients infected with SARS-CoV-2 from 38 centers (Europe, America, Asia, and Africa).

### HCC Baseline Characteristics

| HCC  |                  | n = 213        |
|--|------------------|----------------|
| Age at SARS-CoV-2 diagnosis, median [IQR]            |                  | 67 [ 60 - 73 ] |
| Gender, n(%)   | Female           | 60 ( 28.2 )    |
|  | Male             | 153 ( 71.8 )   |
| Aetiology, n(%)                                      | HCV              | 79 ( 37.1 )    |
|  | Alcohol          | 42 ( 19.7 )    |
|  | NAFLD            | 34 ( 16 )      |
|  | Combination      | 24 ( 11.3 )    |
|  | HBV              | 19 ( 8.9 )     |
|  | No liver disease | 7 ( 3.3 )      |
|  | Others           | 6 ( 2.8 )      |
|  | HCV + HBV        | 2 ( 0.9 )      |
| HCC diagnosis, n (%)                                 | de-novo HCC      | 54 ( 25.4 )*   |
|  | History of HCC   | 159 ( 74.6 )   |
| BCLC stage at the time of SARS-CoV-2 diagnosis, n(%) | 0                | 12 ( 5.6 )     |
|  | A                | 65 ( 30.5 )    |
|  | B                | 51 ( 23.9 )    |
|  | C                | 57 ( 26.8 )    |
|  | D                | 28 ( 13.1 )    |

\*60% were BCLC ≥ B stage

### iCCA Baseline Characteristics

| iCCA  |                  | n = 29         |
|---|------------------|----------------|
| Age at SARS-CoV-2 diagnosis, median [IQR]   |                  | 64 [ 57 - 71 ] |
| Gender, n(%)  | Female           | 12 ( 41.4 )    |
|   | Male             | 17 ( 58.6 )    |
| Aetiology, n(%)   | No liver disease | 17 ( 58.6 )    |
|   | HCV              | 4 ( 13.8 )     |
|   | NAFLD            | 4 ( 13.8 )     |
|   | Alcohol          | 3 ( 10.3 )     |
|   | PSC              | 1 ( 3.4 )      |
| iCCA diagnosis, n (%)   | de-novo iCCA     | 6 ( 20.7 )*    |
|   | History of iCCA  | 23 ( 79.3 )    |
| iCC stage according to TNM 8 <sup>o</sup> edition at the time of SARS-CoV-2 diagnosis, n(%) | IA               | 4 ( 13.8 )     |
|   | IB               | 2 ( 6.9 )      |
|   | IIIA             | 1 ( 3.5 )      |
|   | IIIB             | 7 ( 24.1 )     |
|   | IV               | 13 ( 44.8 )    |

\*5 were stage IV

### Whole cohort (HCC and iCCA)

- 29% of the patients received systemic treatment.
- 67 (27.7%) patients died:
  - 42 SARS-CoV-2-related (71.4% were cirrhotic).
  - 25 non-SARS-CoV-2-related (92% were cirrhotic).
- The small sample size of iCCA limited the 30-day mortality rate analysis in this group.

### HCC cohort

#### HCC SARS-CoV-2 30-day-related mortality rate

|                  | % (95% CI)         |
|------------------|--------------------|
| All HCC**        | 19.5 (13.8 – 25.2) |
| ■ History of HCC | 23.2 (16.2 – 30.2) |
| ■ de-novo HCC    | 8.3 (0.5 – 16.1)   |

\*\*30 patients died:  
26 patients with history of HCC and  
4 patients with de-novo HCC.

#### Liver cancer 30-day-mortality rate

|                          | % (95% CI)         |
|--------------------------|--------------------|
| Whole cohort*            | 21.2 (15.7 – 26.7) |
| ■ SARS-CoV-2-related     | 17.4 (12.7 – 22.8) |
| ■ Non-SARS-CoV-2-related | 3.8 (1.8 – 7.1)    |

\*46 patients died: 38 SARS-CoV-2 related and 8 non-SARS-CoV-2 related.

#### 30-day mortality due to SARS-CoV-2 infection to BCLC stage in HCC patients

| BCLC stage at SARS-CoV-2 diagnosis | Events (30-day SARS-CoV-2 related death) | Competing Events (30-day non-SARS-CoV-2 related death) | Patients at risk | 30-day mortality rate for SARS-CoV-2, % (95%CI) | p-value <sup>§</sup> | p-value excluding BCLC-D <sup>§</sup> | HR (95%CI)          | p-value |
|------------------------------------|--|--|------------------|---|----------------------|---------------------------------------|---------------------|---------|
| 0 or A                             | 4  | 1  | 77               | 6.1 (1.9 - 13.7)                                | 0.007                | 0.048                                 | ref.                |         |
| B                                  | 7  | 1  | 51               | 14.6 (6.3 - 26.1)                               |                      |                                       | 2.59 (0.76 - 8.81)  | 0.13    |
| C                                  | 11                                       | 0  | 57               | 21.2 (11.2 - 33.3)                              |                      |                                       | 3.86 (1.25 - 11.93) | 0.02    |
| D                                  | 8  | 5  | 28               | 33.1 (15.2 - 52.3)                              |                      |                                       | -                   |         |
| Total                              | 30                                       | 7  | 213              |   |                      |                                       |                     |         |

<sup>§</sup>Grey's Test

## CONCLUSIONS

The 30-day SARS-CoV-2-related mortality in HCC seems similar to the mortality reported in cirrhotic patients without HCC.

However, the 30-day SARS-CoV-2-related mortality rate varies according to the BCLC stage, even when BCLC D patients are excluded.

The small sample size of iCCA limited the interpretation of the 30-day SARS-CoV-2-related mortality in this population.

## CONTACT INFORMATION

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**Abbreviations:** HCC: Hepatocellular carcinoma; iCCA: intrahepatic cholangiocarcinoma; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; IQR: Interquartile range; CI: Confidence interval; HCV: Hepatitis C virus; NAFLD: Non-alcoholic fatty liver disease; HBV: Hepatitis B virus; PSC: Primary sclerosing cholangitis; BCLC: Barcelona Clinic Liver Cancer; TNM: Classification of Malignant Tumors (Tumor, Nodule, Metastasis).

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