EASL WHO Webinar: Covid-19 & the liver

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Q&A Session- Answers provided by EASL (Thomas Berg)

Regarding liver damages, is it recommended to treat patients with Covid-19 using hepatoprotective drugs? What about UDCA?

There are no data out showing a hepato-protective effect of UDCA in COVID 19. The best protection for the liver is probably to treat the COVID-19-associated severe systemic inflammation, if present. If the systemic inflammatory response could be well controlled, it will most likely also have positive effects on the liver.

Are patients with autoimmune liver diseases, AIH, PBC, PSC (without liver cirrhosis) more vulnerable to COVID-19 than healthy people?

As far as we know, patients with compensated autoimmune liver diseases, even when taking immunosuppressive drugs, are not at increased risk for severe COVID-19; in contrary, some studies describe a less severe course of COVID-19 in patients under certain immunosuppressive drugs, a finding that needs further confirmation.

How to manage SVR testing due to travel challenges in relation to COVID-19?

Monitoring of DAA treatment outcome is of course important but it is not really time-critical, as regardless of the outcome, it will not immediately influence the health status of the patient or change his management. Therefore, the recommendations are to wait until the travel restrictions are eased, or to involve local GPs/family doctors for viral testing.

Role of early use of Lopinavir and Ritonavir? Any special consideration in cirrhotic patients as there is significant hepatotoxicity?

Patients with advanced liver disease were excluded from these clinical trials. Ritonavir is not recommended in decompensated disease. Also, efficacy of this regimen is still unclear; results from clinical trials have to be awaited.

How has COVID-19 affected the incidence of:

1. Testing for Hep C.
2. Treatment of Hep C in naive patients (new patients)? If these incidences have dropped (relative to same time last year) what do you foresee for the impact of this change in the short vs. long term to eliminate Hep C by 2030 (WHO guidance)?

I would like to refer to the EASL WHO webinar were these issues were specifically addressed. Of course, there is a concern that the SARS-CoV-2 pandemic may negatively affect WHO elimination strategies. On the other hand, it is also possible that societies now better understand the importance of controlling viral diseases und therefore it may potentially even booster viral hepatitis elimination plans, after the national SARS-CoV-2 epidemics have stabilised.

What is the probability of a second wave in autumn? How can the high number of deaths in Spain, Italy and France be explained? How can it be explained that Italy was mainly hit in only one region?

Difficult question. I would not like to give a forecast concerning the likelihood of whether there will be a second/third wave or not. Just because of fact that we are expecting a second wave may have consequences that may lead to changes (for instance in our behaviours) that might mitigate or even prevent the occurrence of a second wave. Hence, the best what we can do so far, is to follow the dynamics of the pandemic closely and to learn from its dynamics under the different levels of restrictions and easing to draw conclusions. The only point that becomes quite clear is that the virus is best transmitted in closed spaces/rooms, if many persons are physically close together for a prolonged time. Regarding the higher infection rates seen in Spain, Italy and France, one explanation seems to be that the virus has probably spread largely unnoticed for several months before the restrictions came in place. There is also the issue of nosocomial transmission if the health care system is suddenly overloaded by COVID-19, and without having the time and chance to build up preventive measures.

Is there any clear scientific evidence showing that chronic liver disease, cirrhosis, advanced cirrhosis, or HCC are risk factors for severe course of COVID-19?

We know that infections in general are a major risk factor for a decompensation of the cirrhosis and or ACLF development; Also for SRAS-CoV-2 infection, there are data showing that the severe inflammatory response syndrome triggered by the infection is negatively affecting the course of a patient with cirrhosis, and is associated with a high risk of developing a liver decompensation or an acute of chronic liver failure with dismal prognosis.

Abnormal LFTs are reported in 10-50% of patients with COVID-19. In your experience did this ever result in liver synthetic failure - i.e. coagulopathy, encephalopathy?

There are only few descriptions of patients who develop acute liver failure due to COVID-19, and the clinical picture in those few resembles those seen in patients with severe sepsis-associated multi-organ failure. The current understanding why up to 50% of patients with COVID 19 show elevated ALT levels is that they increase as a consequence of a severe inflammatory response syndrome. There is a clear relationship between severity of COVID-19 (inflammatory markers) and frequency of ALT elevations.

How many of the changes you made in response to COVID-19 do you envisage becoming the new normal in the future post-COVID-19? and which ones?

I would like to refer to the EASL-ESCMID COVID-19 and the liver position paper where these different issues were addressed.

Are chronic liver disease patients more likely to succumb to COVID-19 than their healthy counterparts?

From all what we know this seems unlikely that patients with compensated liver disease are at higher risk for acquiring the infection; no overrepresentation of patients with liver disease was seen so far during the SARS-CoV-2 pandemic.

I would be grateful if you could share your recommendations or comments about the use of immunotherapy or biotherapy for liver diseases during the pandemics, such as tyrosine-kinase inhibitors or DAAs.

We definitively need more data to better understand the role of biologicals and the different immunosuppressive agents on the course of COVID-19. But so far, the best recommendation we can give is to treat the (autoimmune) disease in the best way and according to current guidelines, because it is likely that an uncontrolled chronic autoimmune disease could convey a higher risk when acquiring COVID-19 as compared to a well-controlled one.

The effect of COVID-19 on liver function in metabolic syndrome?

This is an unanswered question so far. It seems that a pre-existing systemic inflammatory response state, a state which is well known also to be present in patients with metabolic syndrome but also NASH (high CRP, IL6), might be a specific risk factor for a more severe course of COVID-19; more data are needed to answer this question appropriately.

How common is very high AST and ALT above 1000 IU/L with COVID-19?

This is a very rare event, less than 1%.

HCV/HBV treatment should be continued or not in COVID-19 detected?

If treatment is already started, it should definitely be continued; laboratory controls and follow-up evaluations can be done by phone, together with local GPs/family doctors.

Could you please give information concerning morphology specific structure of the liver parenchyma in patients with COVID-19?

There are very limited data on liver morphology during COVID-19. I am aware of one publication were a liver biopsy was performed in a patient with elevated ALT during COVID-19, and in this case a normal liver morphology was found.

How does COVID-19 influence liver disease progression in HCV/HIV and HBV/HIV coinfected patients? Do they need additional examination and care?

So far, there are no data showing that COVID-19 disease severity is increased in patients with HIV.

Faecal shedding of SARS-CoV-2 virus apparently happens even after patients were tested negative through nasopharyngeal swabs. What is the implication for transmission of infection to other people?

Viral RNA can be detected for extended periods in stool but so far there is no proof that this also means infectious viruses were shed by faeces.

How should patients continue treatment when it is difficult to access lab testing?

I would like to refer to the EASL-ESCMID position paper that answers all these questions.