HBV Treatment as Prevention – Scientific Support

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Studies in the European HBV cohorts have shown that long term suppression of HBV replication may reduce HCC risk over time.

Unlike HCV, HCC also develops in non-cirrhotic HBV patients making surveillance strategies more complex.

Most of the existing data supporting HBV treatment as prevention are reported in HIV cohorts which have a higher mortality than mono-infected cases.

Plot of cumulative meta-analysis for the effect of hepatitis B virus infection on overall mortality among HIV+ patients.

Keep in mind that HIV infection accelerates progression of HBV related liver diseases & mortality is higher among HIV/HBV coinfection individuals.

Prospective analysis of 4 European HIV cohorts showed that TDF treatment has a large impact on reducing HCC incidence over time.

The two arms had similar median age and sex. The TDF arm had more cirrhotic patients.

Over 3,393 py, HCC incidence was 5.90 per 1,000 py among cirrhotic case on TDF and 1.17 per 1,000 py in non-cirrhotic cases on TDF.

The study found that screening (using a cutoff of 2 cases per 1,000py) may not be necessary if non-cirrhotic patients start treatment before age 45.

Adjusted incidence of hepatocellular carcinoma among HIV/HBV coinfected individuals at initiation of TDF-containing ART (n = 2,537). Dotted line represents the recommended screening threshold; shaded area represents the 95% CI.

Once the patients are cirrhotic, they need to be screened for HCC even if on treatment.

After the initiation of TDF, the incidence of HCC remained stable over time, suggesting that an assessment of HCC risk at TDF start would be adequate to inform long term individual HCC screening strategies.

A matched cohort study in Hong Kong (n= 692 HBV/HIV+, n= 2,380 HBV+) found HIV/HBV co-infected patients had lower risk of HCC compared with antiviral therapy treated HBV mono-infected patients.

- **Inclusion criteria:**
  - All patients with HBV/HIV co-infection
  - All HBV mono-infected patients treated with antiviral therapy
  - All patients identified from an electronic database involving all public hospitals in Hong Kong from 2000 to 2017

- **Exclusion criteria:**
  - Hepatitis C virus (HCV) infection
  - HCC diagnosed within six months
  - Follow up less than 6 months

- **Primary outcome was HCC**

- **A propensity score (PS) for each patient was defined as the conditional probability of having HIV infection given the baseline characteristics (including age, sex, cirrhosis, bilirubin, alanine transaminase/ALT, platelet, albumin, and prothrombin time).**

- **HBV/HIV coinfection and HBV mono-infected patients were matched in a 1:5 ratio by PS matching.**

- **85% were male, mean (± SD) age was 42±12 years, and 4.5% had cirrhosis at baseline.**

- **Weighted Fine Gray model showed that HIV infection was associated with a lower risk of HCC (sub-distribution hazard ratio 0.39, 95% confidence interval 0.16 0.94, p=0.036)**

**Conclusion:** This observation can be explained by a lower threshold, in terms of severity of liver disease, to start antiviral treatment in HBV/HIV coinfected compared to HBV mono-infected patients.

An economic analysis from France showed that a test and treat all HBV patients was the most cost-effective strategy in France.

Treating all patients (S4) was the most expensive but also the most effective strategy (with a lifetime mean gain of 0.04, 0.21, 0.21 QALYs compared with S3, S1 and S1 respectively) and was cost effective compared to S3 (ICER = 26,569 Euros /QALY)
Our study in Saudi Arabia also showed that testing & treating all HBV patients becomes highly cost effective after 2036

The study also highlighted that 90% diagnosis and 80% treatment of eligible patients (WHO targets) does not achieve the WHO mortality targets (65% reduction in mortality) → we need to switch to test & treat

Similar economic analyses were conducted for Brazil, Philippines, Uganda, Uzbekistan with the same conclusions.

Appendix
We know that antiviral treatment will result in fibrosis regression among HBV patients

- A Zambia cohort of 463 HIV patients (61 HIV/HBV) on TDF containing ART – observed a reduction in liver stiffness measurement after one year.

- A Nigeria cohort of 106 HIV+ and 71 HIV/HBV saw a reduction in liver stiffness measurement after 3 years


A retrospective cohort study in Brazil compared HCV or HBV (n=405) and HIV/HBV+ or HIV/HCV+ (n=399) between 2007-2014

- Coinfected patients were younger (36.7 ± 10 vs 46.3 ± 12.5, p < 0.001)
- Liver cirrhosis was observed in 31.3% of HIV-negative patients and in 16.5% of coinfectected (p < 0.001)
- The incidence density of HCC in coinfectected and mono-infected patients was 0.25 and 0.72 cases per 100 patient-years (95%CI: 0.12-0.46 vs 0.47-1.05) (long-rank p = 0.002)
- When adjusting for age or when only cirrhotic are analyzed, the absence of HIV lost statistical significance for the development of HCC

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<tr>
<th>HIV</th>
<th>n</th>
<th>HCC</th>
<th>%</th>
<th>Patient-years</th>
<th>Rate x 100 patient-years</th>
<th>RR</th>
<th>95%CI</th>
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<td>+</td>
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<td>10</td>
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<td>-</td>
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<td>Model 3: adjusted for age and DM</td>
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<td>Model 4: adjusted for age, DM and alcohol</td>
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