History of HBV drug trials and current treatment
Prospect for the road to a cure

February 18, 2021

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Clinical Trials

- Phase 1. Safety, safety dosage, Side Effects. 20-80 (subjects)
- Phase 2. Effectiveness, dosage trial. 100-200
- Phase 3. Effectiveness, Side Effects, Compare with other products. 300-3000
- FDA approval
- Phase 4. Further observation of effectiveness, Side Effects, Safety etc 1000 +
Clinical Trials of the currently available anti-HBV drugs we have conducted at Jefferson 1996-present

- Lamivudine (Epivir-HBV) 8 trials 1998 (FDA approved)
- Lobucavir 3 trials halted
- Adefovir (Hepsera) 4 trials 2002 (FDA approved)
- Entecavir (Baraclude) 4 trials 2005 (FDA approved)
- Telbivudine (Tyzeka) 3 trials 2006 (FDA approved)
- Tenofovir Disoproxil Fumarate (Viread) 3 trials 2008 (FDA approved)
- Tenofovir Alafenamide
- (Vemlidy) 3 trials 2016 (FDA approved)
- ABI (HBV Cure drug?)
Antiviral Therapy Suppresses Development of Hepatocellular Carcinoma in Chronic Hepatitis B (Lamivudine)

HCC cumulative incidence rates at 5 years between **Entecavir-treated** and the control group

![Graph showing cumulative development rates of HCC](image)

log-rank test: $P < 0.001$

Hosaka et al. HEPATOLOGY, 2013; 58: 98-107
Incidence of HCC in patients on TDF in Studies 102/103 was lower than predicted by the REACH-B model.

In non-cirrhotic patients, the effect of TDF becomes noticeable between 2–3 years of therapy, became statistically significant at 5 years and remained statistically significant at 6 years of therapy (55% reduction). REACH-B is a risk calculator developed in non-cirrhotic patients so it may underestimate the risk in cirrhotics.
## Worldwide HCC

<table>
<thead>
<tr>
<th>Etiology</th>
<th>1985</th>
<th>2000</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td>80-85%</td>
<td>60%</td>
<td>50%</td>
</tr>
<tr>
<td>HCV</td>
<td>The rest</td>
<td>25%</td>
<td>25%</td>
</tr>
<tr>
<td>ALD</td>
<td></td>
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<tr>
<td>NASH</td>
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</tbody>
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El-Serag HB. Gastroenterology. 2004;127(5, Supplement 1):S27-S34
Ha et al. Cancer 2016;122:2512-23 (used SEER Data)