ID Week 2022 Report Back

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Disclaimer

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ID Week Summary: Outline

1. Hepatitis B Vaccination with HepB-CpG (*Heplisav-B*): BEE-HIVE preliminary results

2. Real World Outcomes with Injectable Cabotegravir-Rilpivirine (*Cabenuva*)
BEE-HIVE Preliminary Results
Background

• HBV vaccine seroprotection rates (SPR) in persons with HIV (PWH) are lower (range 18-71%) than in adults without HIV (range 60-80%)\(^1\)

• HepB-CpG vaccine, FDA approved in 2017, is a 2-dose series for adults ≥18 years
  – In immunocompetent adults, SPRs with Hep B vaccine (Engerix-B or Recombivax-B) ranged from 65-80% vs. 90-95% with HepB-CpG\(^1\)

• A single center study of 51 PWH, without immunity to hepatitis B, receiving HepB-CpG demonstrated overall SPRs of 82%, with higher SPR in those with higher CD4 cell counts\(^2\)

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B-Enhancement of HBV Vaccination in Persons Living With HIV (BEe-HIVe): Study Design

- **Entry Criteria Arm A and B**
  - PWH and age 18-70 years
  - On ART & HIV-1 RNA <1,000 copies/mL
  - CD4 >100 cells/mm³
  - Negative HBV surface Ab (sAb)
  - No history of hepatitis B
  - Not pregnant

- **Arm A (Vaccine Non-Responders)**
  - Serum Hep B sAb <10 mIU/mL
  - HBV vaccination (>168 days prior)

- **Arm B (Vaccine Naïve)**
  - Hep B sAb negative (<45 days)

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**Arm A: HBV Vaccine Non-Responders**

- HepB (CpG) 2 doses: 0, 4 weeks
- HepB (CpG) 3 doses: 0, 4, and 24 weeks
- HepB (Eng-B) 3 doses: 0, 4, and 24 weeks

**Arm B: HBV Vaccine Naïve**

- HepB (CpG) 3 doses: 0, 4, and 24 weeks

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BEe-HIVe Arm B Methods

• Objectives
  1. Determine SPR (HBsAb ≥ 10 mIU/mL) at 28 weeks of 3-dose HepB-CpG in HBV vaccine-naïve PWH
  2. Describe grade ≥3 adverse events

• HepB-CpG given at entry, 4 weeks, and 24 weeks; followed out to 72 weeks

<table>
<thead>
<tr>
<th>Week</th>
<th>0</th>
<th>4</th>
<th>8</th>
<th>12</th>
<th>16</th>
<th>20</th>
<th>24</th>
<th>28</th>
<th>72</th>
</tr>
</thead>
<tbody>
<tr>
<td>HepB-CpG Doses</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>SPR</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

68 of 74 PWH in Arm B completed 3 doses of HepB-CpG vaccine and had an HBsAb measurement

### BEe-HIVe Arm B: Use of HepB-CpG in HBV Vaccine Naïve PWH

#### Key Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Arm B (n = 74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, years (Q1,Q3)</td>
<td>47 (40, 51)</td>
</tr>
<tr>
<td>Male/Female at birth, %</td>
<td>46/54</td>
</tr>
<tr>
<td>HIV RNA &lt;60 copies/mL, %</td>
<td>96</td>
</tr>
<tr>
<td>Median current CD4 count (cells/mm$^3$) (Q1, Q3)</td>
<td>625 (473, 829)</td>
</tr>
<tr>
<td>Median nadir CD4 count (cells/mm$^3$) (Q1, Q3)</td>
<td>247 (140, 429)</td>
</tr>
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BEe-HIVe Arm B Results: Seroprotection Rate by Study Week

BEe-HIVe Arm B Results: Seroprotection Rate by Study Week

61% of participants experienced ≥1 AE(s) related to study treatment
- Grade 1 = 39% of participants
- Grade 2 = 20% of participants
- Grade 3 malaise in 1 participant

<table>
<thead>
<tr>
<th>Adverse Effects</th>
<th>Percent of Participants</th>
</tr>
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<tbody>
<tr>
<td>Injection site reaction</td>
<td>40%</td>
</tr>
<tr>
<td>Malaise</td>
<td>26%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>23%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>22%</td>
</tr>
<tr>
<td>Headache</td>
<td>22%</td>
</tr>
<tr>
<td>Fever</td>
<td>3%</td>
</tr>
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</table>
BEe-HIVe Arm B Preliminary Results: Summary

• In this single arm study, 100% of 68 HBV vaccine naïve PWH after 3-dose HepB-CpG achieved SPR (HBsAb ≥10 mIU/mL)

• There were no unexpected safety issues or deaths

• Low representation from predictors of non-response (low CD4 cell count, viremia, HCV)

• Unfortunately, 2 dose HepB-CpG was not the protocol used in this study

Outcomes with LAI CAB-RPV
Clinical Experience with LAI Cabotegravir-Rilpivirine

• Real World Use and Effectiveness in the US in the OPERA Cohort
  – Sension MG, et al, Abstract #1582.

• Low level HBV Viremia in PWH with HBV Core Ab Positivity After Switch

• CARISEL: Implementation Effectiveness in EU Clinical Sites
Real World Use & Effectiveness of LAI CAB-RPV in OPERA Cohort

- Between 1/2021 and 2/2022, 383 ART experienced PWH in the OPERA cohort received 1\textsuperscript{st} dose long acting injectable (LAI) CAB-RPV

<table>
<thead>
<tr>
<th>Baseline HIV-1 RNA at 1\textsuperscript{st} dose LAI CAB-RPV</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV-1 RNA &lt;50 copies/mL</td>
<td>321 (84%)</td>
</tr>
<tr>
<td>HIV-1 RNA 50-199 copies/mL</td>
<td>27 (7%)</td>
</tr>
<tr>
<td>HIV-1 RNA ≥200 copies/mL</td>
<td>28 (7%)</td>
</tr>
<tr>
<td>No baseline HIV-1 RNA</td>
<td>7 (2%)</td>
</tr>
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</table>

Real World Use & Effectiveness of LAI CAB-RPV in OPERA Cohort

- 89% remained on LAI CAB-RPV at the end of follow up

- Of PWH with HIV-1 RNA <200 copies/mL prior to initiation, 99% had HIV-1 RNA <200 copies/mL at the end of follow up

- Of PWH with HIV-1 RNA ≥200 copies/mL prior to initiation, 91% achieved HIV-1 RNA <200 copies/mL

Low Level HBViremia after Switch to CAB-RPV in HBcAb Positivity

- Retrospective case series of 149 PWH switched to LAI CAB-RPV
- 25.5% (38/149) HBV core antibody positive and surface Ag negative
- 7.9% (3/149) developed HBV DNA ranging from <10 to 101 IU/mL
  - Time to positivity: 2 at time of 1st LAI CAB-RPV, 1 between 1st and 2nd doses
  - 1 had positive HBsAb prior to switch to LAI CAB-RPV
  - 2 switched to BIC/TAF/FTC and achieved HBV viral suppression
  - 1 continued CAB-RPV, HBV DNA level decreased from 14 to <10 IU/mL
- Clinical significance of this HBV low-level viremia is unknown

CARISEL: Implementation of LAI CAB-RPV in the EU

• ViiV sponsored phase 3b multicenter open-label implementation-effectiveness trial examining strategies to support implementation across 5 EU countries
  – 437 participants at 18 clinical sites with 70 staff providers

• Comparing standard arm to enhanced implementation
  – Standard arm = Education resources, virtual injection training, regular support
  – Enhanced arm = Face-to-face injection training, CQI, educational resources

• Month 12 endpoints
  – Viral suppression 87% across both arms

Conclusions

• HepB-CpG is safe and effective in HBV vaccine naïve PWH.\(^1\)
  – Though the 2-dose protocol was not used, we can extrapolate that the vaccine is efficacious (SPR 94%) at 12 weeks after only 2 doses.

• Virologic outcomes early after PWH in OPERA cohort switched to LAI CAB-RPV demonstrated high rates of viral suppression and low rates of virologic failure.\(^2\)

• Of 149 PWH switched to LAI CAB-RPV, 38 were HBcAb-positive, HBsAg-negative, and three developed HBV low-level viremia, the clinical significance of which is unknown.\(^3\)

• Regardless of implementation support and clinical infrastructure across 18 clinical sites in the EU, LAI CAB-RPV is effective for PWH.\(^4\)

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