National HIV Curriculum

Mini-Lecture Series

ID Week 2022 Report Back

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Disclaimer

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Disclosures

Dr. Budak has no financial conflicts of interests to disclose.

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]

[1] Kim NH, et al. Int J STD AIDS. 2009; 20:595-600.
[2] Schnittman S, et al. JAIDS; 86: 445-449.

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/mm^3
  - 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)

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

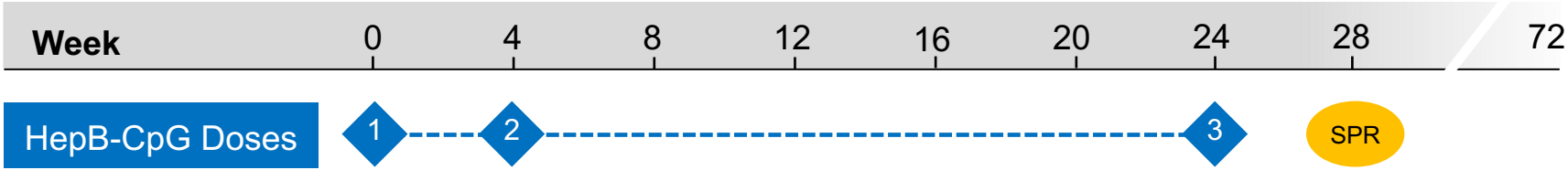
Arm B: HBV Vaccine Naive	
HepB (CpG)	3 doses: 0, 4, and 24 weeks

Source: Marks K, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster LB749.

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



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

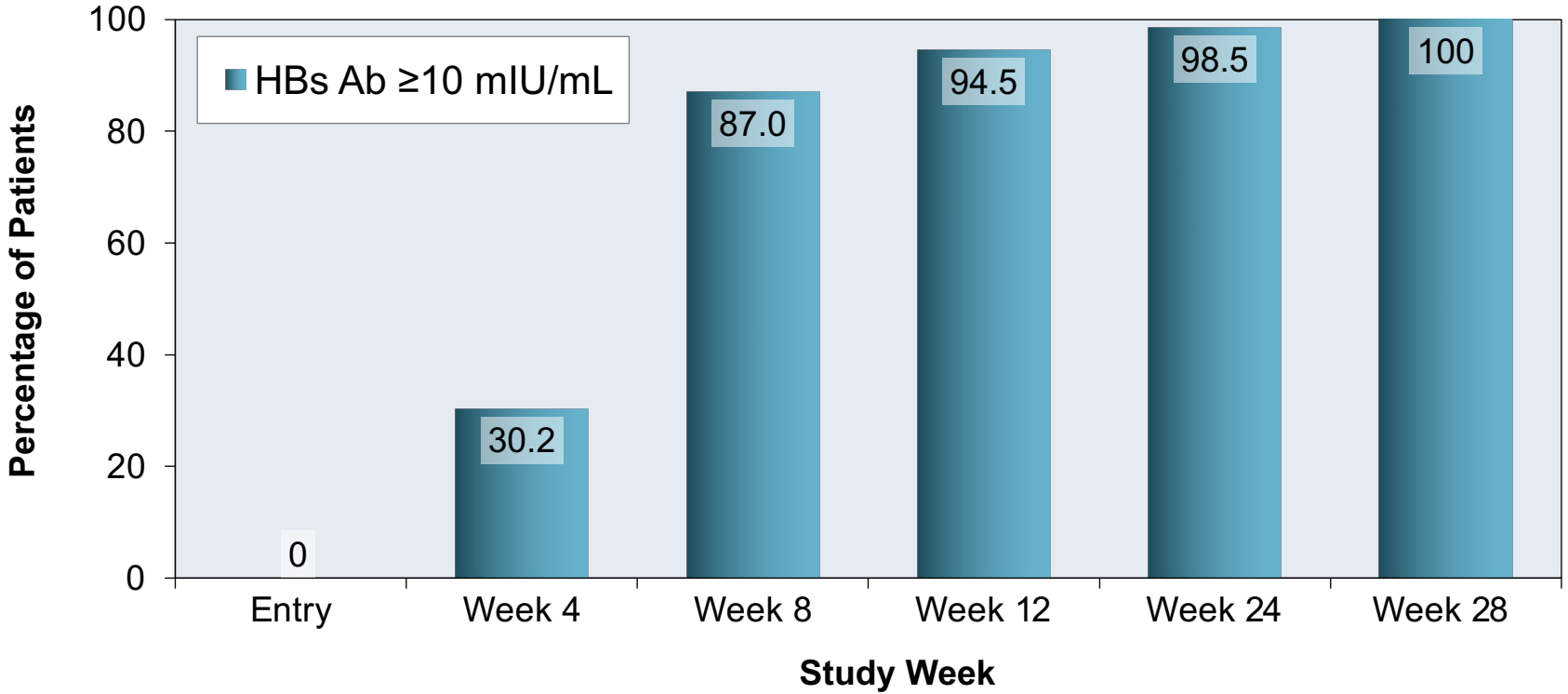
Source: Marks K, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster LB749.

BEe-HIVe Arm B: Use of HepB-CpG in HBV Vaccine Naïve PWH Key Patient Characteristics

BEe—HIVe Key Patient Characteristics	
Characteristic	**Arm B (n = 74)**
Median age, years (Q1,Q3)	47 (40, 51)
Male/Female at birth, %	46/54
HIV RNA <60 copies/mL, %	96
Median current CD4 count (cells/mm^3) (Q1, Q3)	625 (473, 829)
Median nadir CD4 count (cells/mm^3) (Q1, Q3)	247 (140, 429)

Source: Marks K, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster LB749.

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



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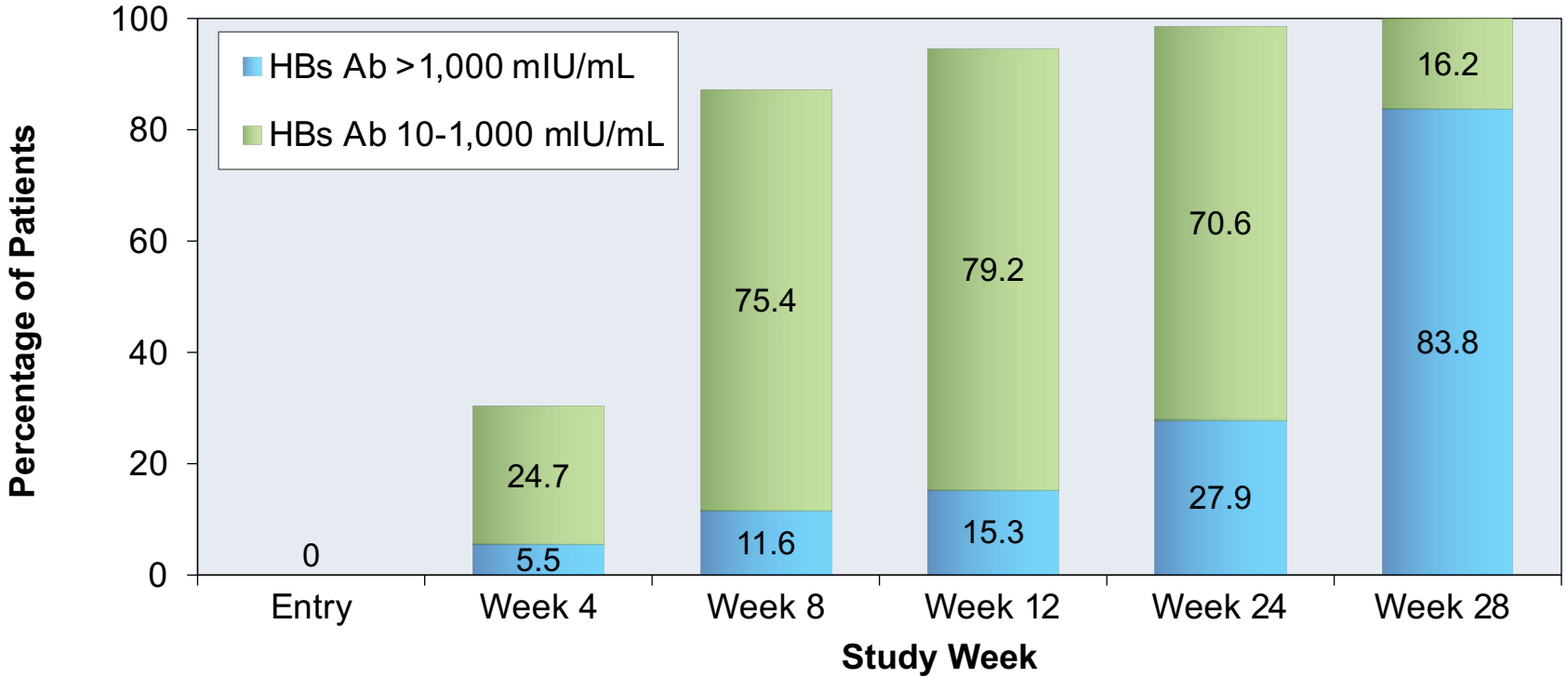

Source: Marks K, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster LB749.

BEe-HIVe Arm B Adverse Effects

- 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

Adverse Effects	Percent of Participants
Injection site reaction	40%
Malaise	26%
Fatigue	23%
Myalgia	22%
Headache	22%
Fever	3%

Source: Marks K, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster LB749.

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**

Source: Marks K, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster LB749.

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
  - Welford EM, et al, Abstract #1583.
- CARISEL: Implementation Effectiveness in EU Clinical Sites
  - De Wit S, et al, Abstract #1584.

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 1st dose long acting injectable (LAI) CAB-RPV

Baseline HIV-1 RNA at 1st dose LAI CAB-RPV	n (%)
HIV-1 RNA <50 copies/mL	321 (84%)
HIV-1 RNA 50-199 copies/mL	27 (7%)
HIV-1 RNA ≥200 copies/mL	28 (7%)
No baseline HIV-1 RNA	7 (2%)

Source: Sension MG, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster 1582.

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

Source: Sension MG, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster 1582.

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

Source: Welford EM, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster 1583.

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

Source: De Wit S, et al. ID Week. October 19-23, 2022; Washington, D.C. Poster 1584.

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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Acknowledgments

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