REGIONAL DIFFERENCES IN HBV VACCINE HISTORY AND RESPONSE IN ACTG A5379: AFRICA, ASIA, BRAZIL AND USA

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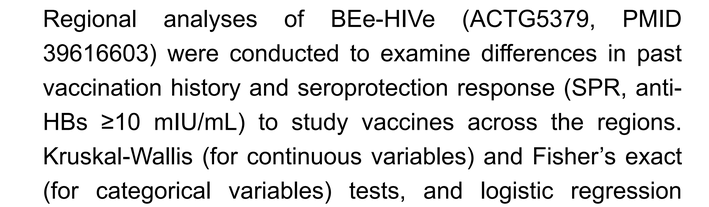
BACKGROUND

As use of long-acting (LA) ART without HBV activity increases, optimizing HBV prevention in PWH is increasingly important. HepB-CpG, an adjuvanted HBV vaccine, has superior immunogenicity to HepB-alum. Understanding regional variation in revaccination outcomes may inform tailored vaccine strategies.

METHODS

A5379 (BEe-HIVe) Study Design

Phase III, prospective, randomized, open label study comparing HepB-CpG and Hep B-alum vaccines for prior nonresponders to conventional HBV vaccine



Regional analyses of BEe-HIVe (ACTG5379, PMID 39616603) were conducted to examine differences in past vaccination history and seroprotection response (SPR, anti-HBs ≥10 mIU/mL) to study vaccines across the regions. Kruskal-Wallis (for continuous variables) and Fisher's exact (for categorical variables) tests, and logistic regression models with stepwise variable selection (for associations between SPR and host factors) were used.

RESULTS

Of 1098 screened, 561 (51%) eligible participants were randomized at 41 sites in:

- Africa, n=117 (Botswana, Kenya, Malawi, South Africa, Uganda)
- Asia, n=95 (Philippines, Thailand, Vietnam)
- Brazil, n=37
- USA, n=312

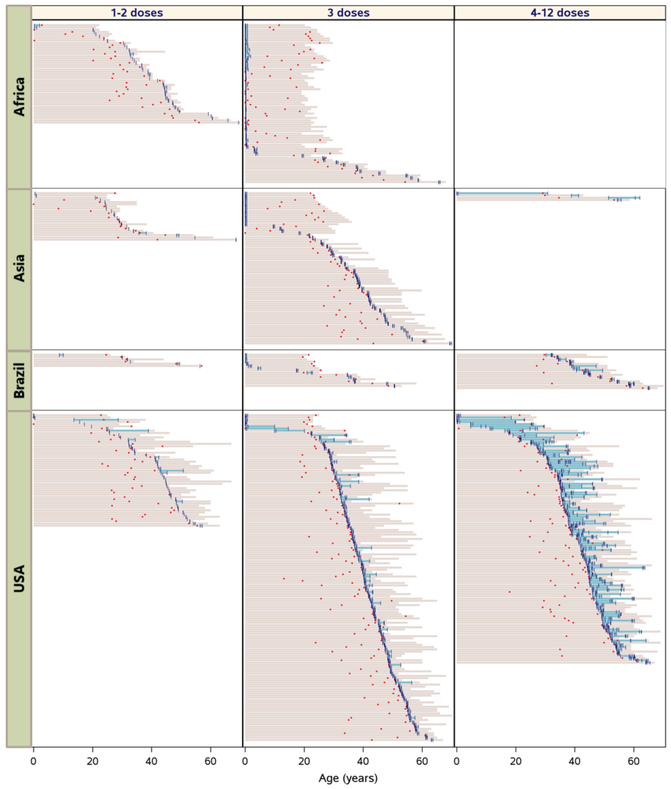
Median age at enrollment was 46 yrs (range 18–70), with substantial regional variation (p<0.0001)

- Youngest in Africa (median 26 yrs)
- Oldest in USA (53 yrs)

HepB-CpG consistently achieved higher seroprotection response than HepB-alum across regions.

Figure 1: Age at prior vaccination and number of vaccine doses prior to A5379 entry by region

Each tan line represents time from birth to individual participant's age at the time of study eligibility. Ages at prior HBV vaccination are marked in blue (|), and multiple vaccine doses are connected by a blue line (—). Age at HIV diagnosis is marked in red (•).



- Age at first HBV vaccination varied across regions (p<0.0001)
  - The first vaccination age was as infants (<1 yr) for 50% in Africa, compared to 19%, 14% and 4% in Asia, Brazil, and USA, respectively.
- Prior HBV vaccine doses ranged from 1 to 12
  - 3 doses in 54%, 1–2 doses in 22%, and ≥4 doses in 24%.
  - Notably, none in Africa had received ≥4 doses, compared to 4% in Asia, 43% in Brazil, and 36% in USA (p<0.0001).

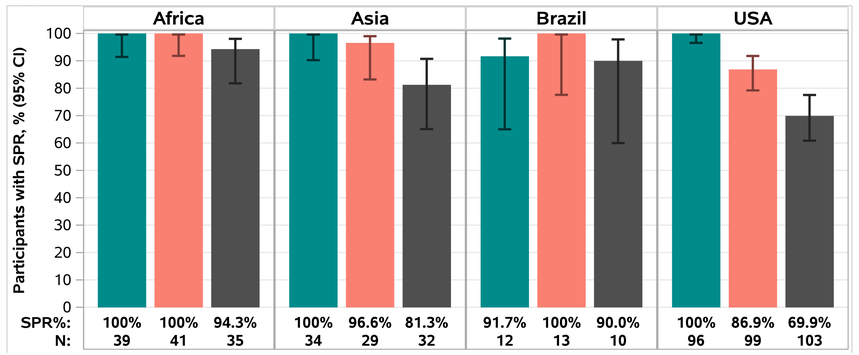
Across all regions, HepB-CpG achieved higher primary SPRs than HepB-alum, particularly with 3 doses except in Brazil, where sample size was small (Figure 2A).

HepB-alum responses varied, being highest in Africa and lowest in the USA; this trend was more evident at the end of study (Figure 2B).

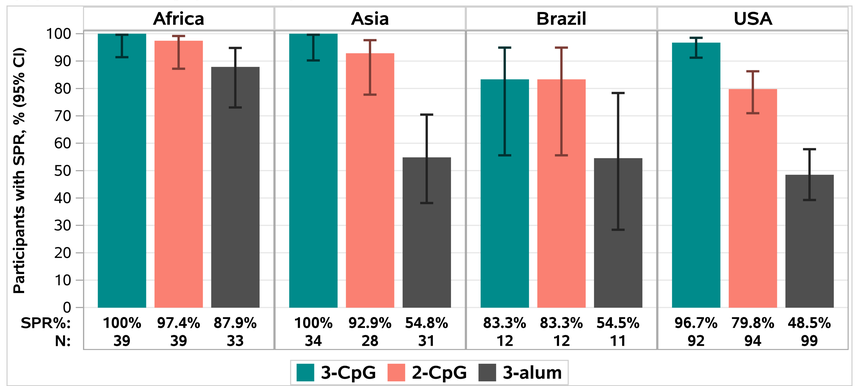
Final regression model identified Black race (which varied by region) to be predictive of primary SPR, along with Hep-CpG, younger age and higher CD4.

Figure 2: SPR proportion (95% Wilson confidence interval [CI]) by region

(A) Primary (4 weeks post series for 3 doses, 8 weeks post series for 2 doses)



(B) End of study (Week 72)



CONCLUSIONS

- HepB-CpG consistently achieved higher SPR than HepB-alum across regions.
- Participant age and timing of initial HBV vaccination likely contribute to regional SPR differences.

These findings underscore the importance of tailoring HBV prevention strategies to regional testing and vaccination practices, particularly in the context of expanding LA ART use.

PLAIN LANGUAGE SUMMARY: In a global study of people with HIV who had not responded to earlier hepatitis B vaccines, more people achieved protective immunity with HepB-CpG than with conventional vaccine across regions. Differences in age and when people had first received hepatitis B vaccination likely explain some of the regional variation in protection rates.