

CROI 2025 Update: Co-Occurring Conditions

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CROI Updates: Co-Occurring Conditions

- Updates in HIV and TB management
- Updates in ART and weight gain
- Updates in HBV vaccination

HIV and TB co-infection

DOLPHIN-Moms: PK of Dolutegravir and HIV Viral Suppression with 1HP or 3HP in Pregnancy

- For women with HIV, active TB risk is highest during and just after pregnancy
- For PWH needing TB preventive therapy (TPT): **3HP (3 months of weekly isoniazid and rifapentine with daily DTG)** and **1HP (1 month of daily isoniazid and rifapentine with BID DTG)** have similar efficacy, increased adherence, and fewer adverse events compared to 6H (6 months of daily isoniazid)
 - **Pregnant women excluded from all trials**
 - **Pregnant women have 25-30% lower DTG troughs than non-pregnant**
- Both WHO and US CDC recommend daily isoniazid for TB preventive therapy in pregnant women with HIV
 - BUT: Increased adverse pregnancy events with 6H in pregnant versus post partum

What happens to PK of dolutegravir in 1HP and 3HP in pregnant women?

DOLPHIN-Moms: PK of Dolutegravir and HIV Viral Suppression with 1HP or 3HP in Pregnancy

- **Phase II RCT of 1HP and 3HP and pharmacokinetics of DTG**

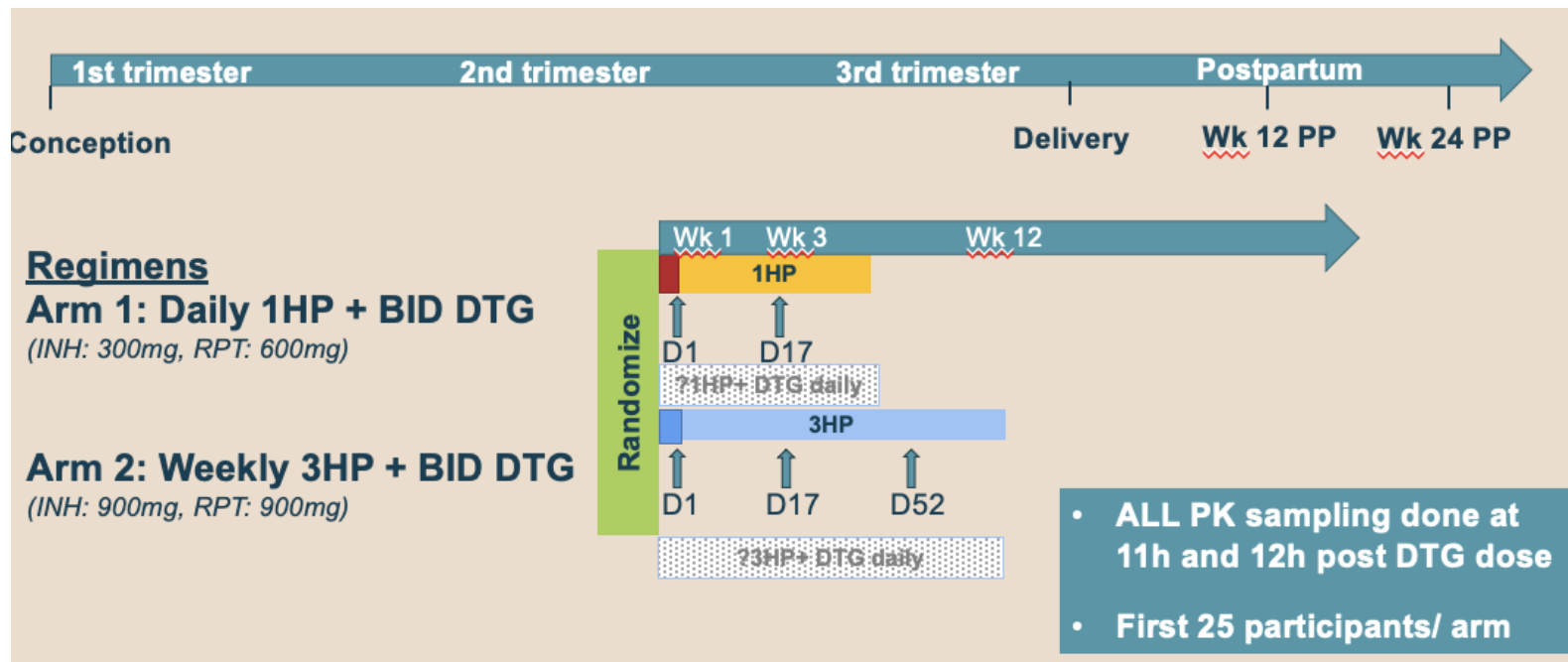
- Ongoing study in South Africa
- Pregnant women at 20-34 weeks of gestation
- ART: DTG based for a month or more with VS

- **Primary PK Outcome**

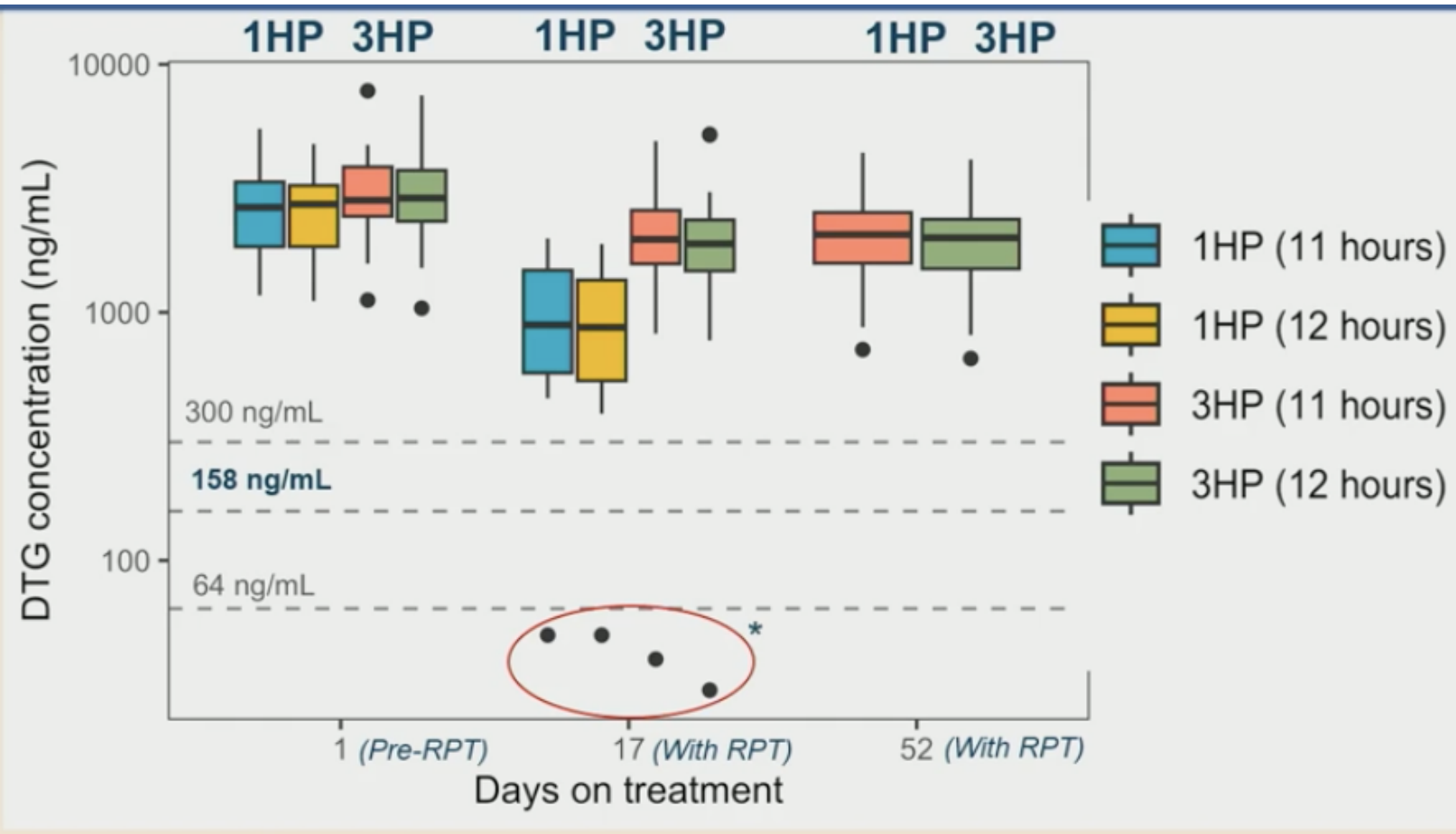
- Population plasma PK parameters of DTG +/- 1HP or 3HP

- **Secondary Outcomes**

- Viral suppression
- Daily versus BID DTG with 1HP or 3 HP



DOLPHIN-Moms: PK of Dolutegravir and HIV Viral Suppression with 1HP or 3HP in Pregnancy



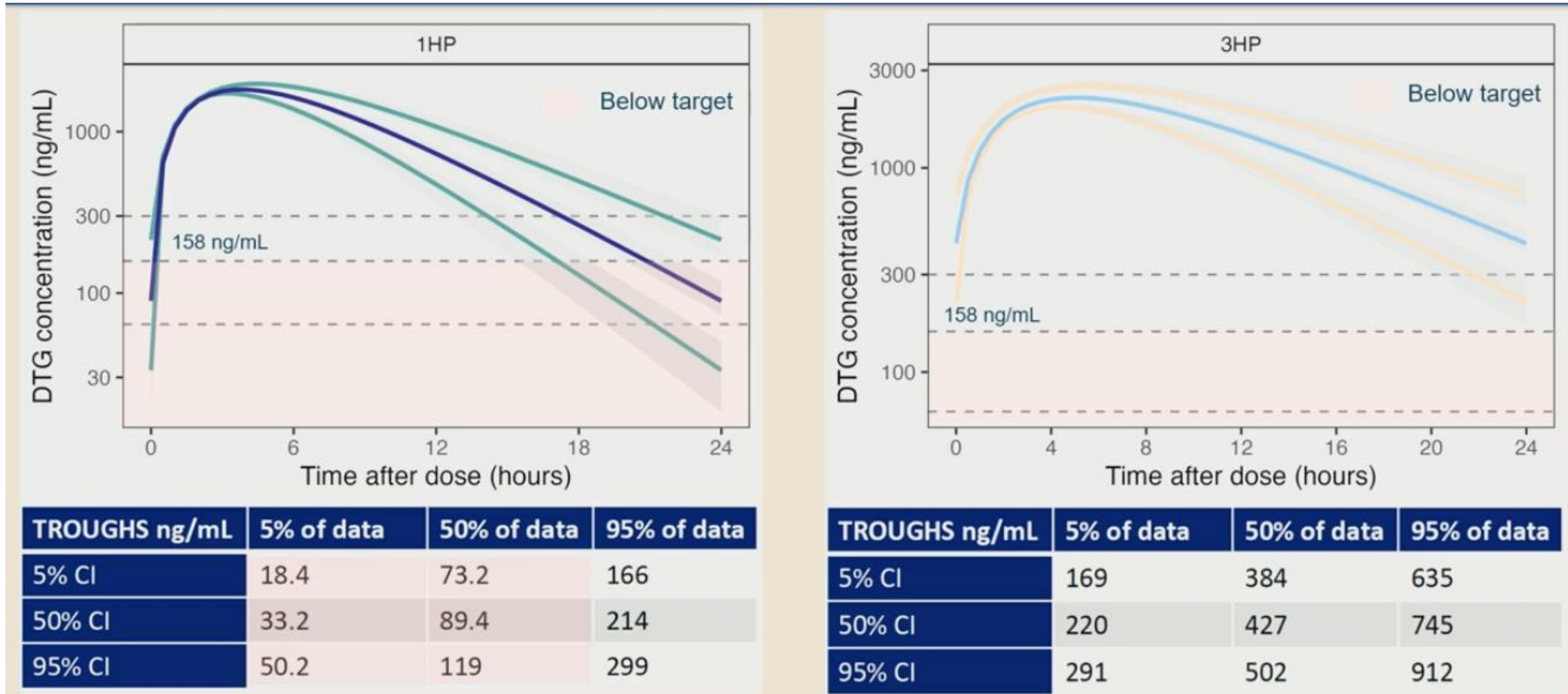
Day 1: **No difference** in [DTG] between arms

Day 17: **Significant difference** in [DTG] as compared to day 1 AND between arms

Day 52: Stable levels (3HP)

***All therapeutic DTG levels except for those with adherence difficulties**

DOLPHIN-Moms: Simulations of DAILY DTG with 1HP and 3HP



Takeaways

- In pregnant women with HIV, **BID DTG with either 1HP or 3HP resulted in appropriate DTG troughs and continued viral suppression**
- In simulation models of daily DTG:
 - 1HP: DTG troughs below acceptable threshold, suggesting need for BID DTG with this regimen in pregnancy
 - 3HP: All DTG troughs above acceptable threshold, suggesting that daily DTG can be given with this regimen in pregnancy
- **Ongoing**: enrollment of an additional 25 women on **3HP and once daily DTG with PK sampling**

TAF Achieves Adequate Intracellular Tenofovir-DP Concentrations with Rifampicin Based TB therapy

- FDA labeling recommends against coadministration of TAF + rifampin
- Open label, three period sequential PK study in people with VS on rifampin containing TB therapy
- Standard dosed TAF achieved **higher TFV-DP intracellular concentrations compared to TDF (standard of care)** in patients with HIV-associated, rifampicin sensitive TB

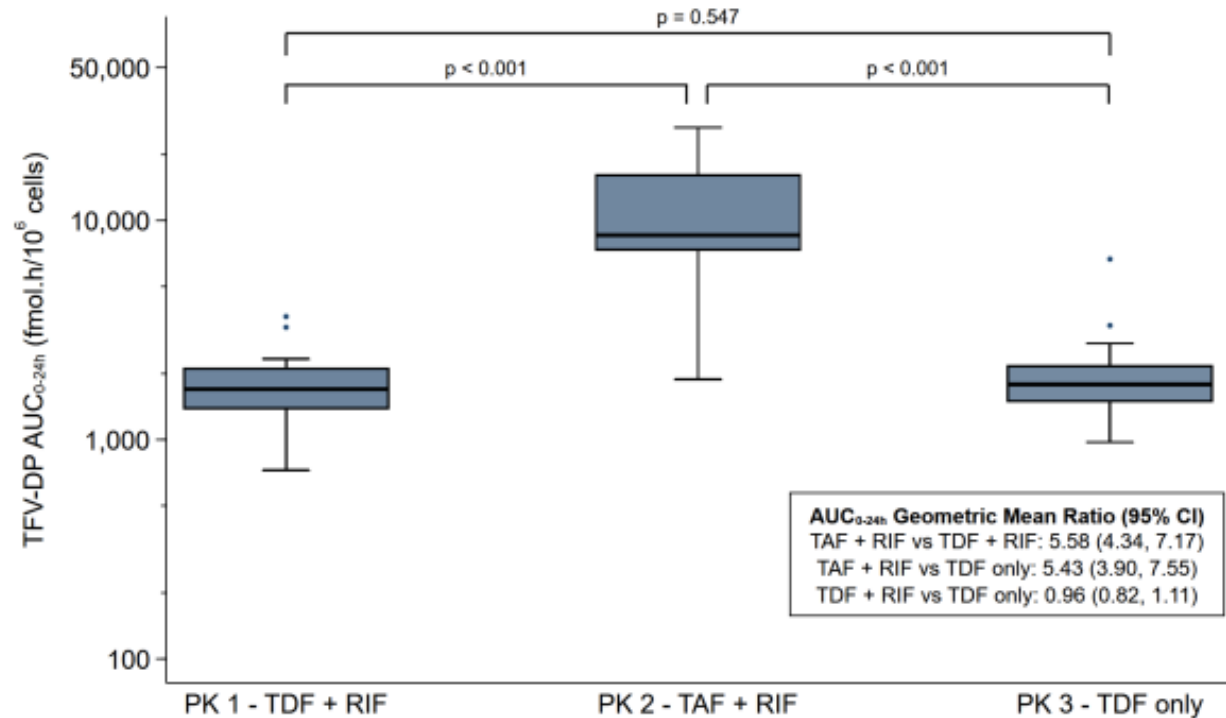


Figure 1: Intracellular Tenofovir Diphosphate 24-Hour Area Under the Concentration-Time Curve by Treatment Period

Weight Gain

Weight Gain on ART

- Some weight gain expected with ART initiation¹
- Signals for independent weight gain effects of INSTI + TAF, with greatest weight gain in combination^{2,3}
 - True in both switch and ART-naïve start
- Mechanism? Unknown!
 - Weight suppressive effects of EFV, TDF
 - Synergy between TAF and INSTIs
- Is weight gain on ART reversible? We don't know! No definitive RCT data

1 Pantazis et al. Lancet HIV 2024

2 Venter et al. NEJM 2019

3 Sax et al. CID 2020

Switch to DTG/3TC vs. B/F/TAF (PASO-DOBLE)

In PASO-DOBLE, switching ART to **DTG/3TC vs B/F/TAF in PWH with VS** was associated with less weight gain.

Poster #661 Tiraboschi et al: Switch to DTG/3TC vs B/F/TAF: Efficacy and Weight Changes by Predefined Subgroups

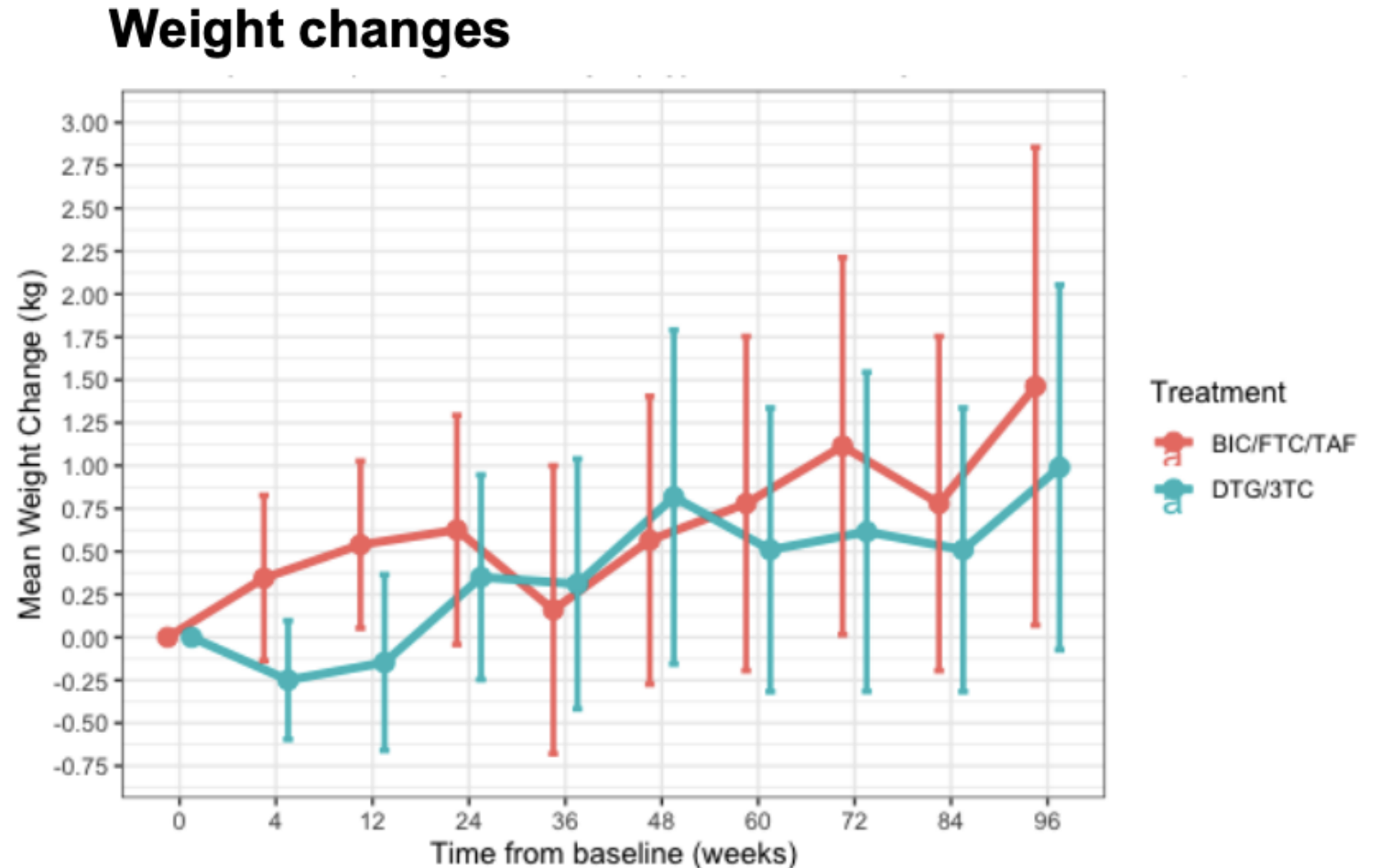
- Subgroup analysis of efficacy and **clinically meaningful weight changes (>5% from baseline)**
- Significant lower proportions of PWH with significant weight gain in DTG/3TC arm in:
 - females, age 35-50 years, Latin-American ethnicity
 - Pre-switch CD4 $\geq 500/\text{mm}^3$
 - TDF, FTC, and NNRTI containing regimens

Poster #897 Di Gregorio et al.: Body Composition Changes in People With HIV Switching to DTG/3TC or BIC/TAF/FTC

- Analysis of body composition in both arms via whole body DXA and abdominal CT
- Significant increase in fat compartments and decrease in lean mass compartments in all groups; changes were greater in BIC/TAF/FTC group versus DTG/3TC group
- TDF and EFV at baseline associated with significant difference in visceral and total fat mass changes

Impact of Switching From DTG/3TC to BIC/FTC/TAF on Weight, Cholesterol, and Inflammation in HIV

- INSTINCT Trial: Effect of switching from DTG/3TC to BIC/TAF/FTC on systemic inflammation up to 96 weeks
- No difference in weight changes between groups



Mean weight at baseline 77 kg and the overall mean weight change was 1.22 kg, (95% CI 0.31-2.13) with no difference between groups.

Weight Gain Rapid Fire

- **Poster #890** Pedersen et al.: Weight and Body Composition After Switch to DTG/3TC from DTG/3TC/ABC
 - Switching to two drug ART (DTG/3TC) by discontinuing abacavir for 48 weeks did NOT change body weight, fat distribution, or metabolic parameters in PWH
- **Poster #893** Milic et al.: Body Composition Changes in PWH Switching From or Maintaining TDF-Based Regimens
 - After 2 years of follow-up, TDF maintenance a/w slight reduction in BMI and total lean mass; switching to TAF a/w increase in BMI and stabilization of lean and fat mass
- **Poster #894** Mavarani et al: Risk Factors Associated With Extreme Weight Gain in PWH
 - Association with higher risk of >10% weight gain within 5 years in PWH: younger age, higher baseline CD4/CD8 ratio, switch to TAF, switch off TDF (trend)

Takeaways

- HIV and ART related weight gain is multifactorial
- More evidence that initiation of TAF + INSTI (2nd gen) is associated with more weight gain than INSTI alone, suggesting synergistic or additive effect, but-
- Switching from INSTI to combination of TAF + INSTI does not appear to drive further weight gain
- TDF continues to be associated with attenuation of some metabolic and mass effects
- **What do we do about weight gain?**

Hepatitis B Vaccination in PWH

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

HBV vaccine seroprotection rates (SPR) in persons with HIV (PWH) are lower than in adults without HIV with conventional HBV vaccine (HepB-alum)¹

- **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)

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

ACTG 5479 (BEe-HIVe): Prior Results

Arm A (vaccine non response)¹

- PWH with non-response to conventional HBV vaccine achieved **superior SPR** as compared to 3 doses of HepB-alum
- Three doses of HepB-CpG achieved high proportion of SPR with HBsAb titers > 1000 mIU/mL (78%)

Arm B (vaccine naïve)²

- **100% of PWH** receiving 3-dose series HepB-CpG (Heplisav-B) vaccine **achieved seroprotective response** (SPR, HBsAb \geq 10 mIU/mL), 84% HBsAb \geq 1000 mIU/mL
- **98.5% achieved SPR after two doses**, though at lower titers (28% HBsAb \geq 1000 mIU/mL)

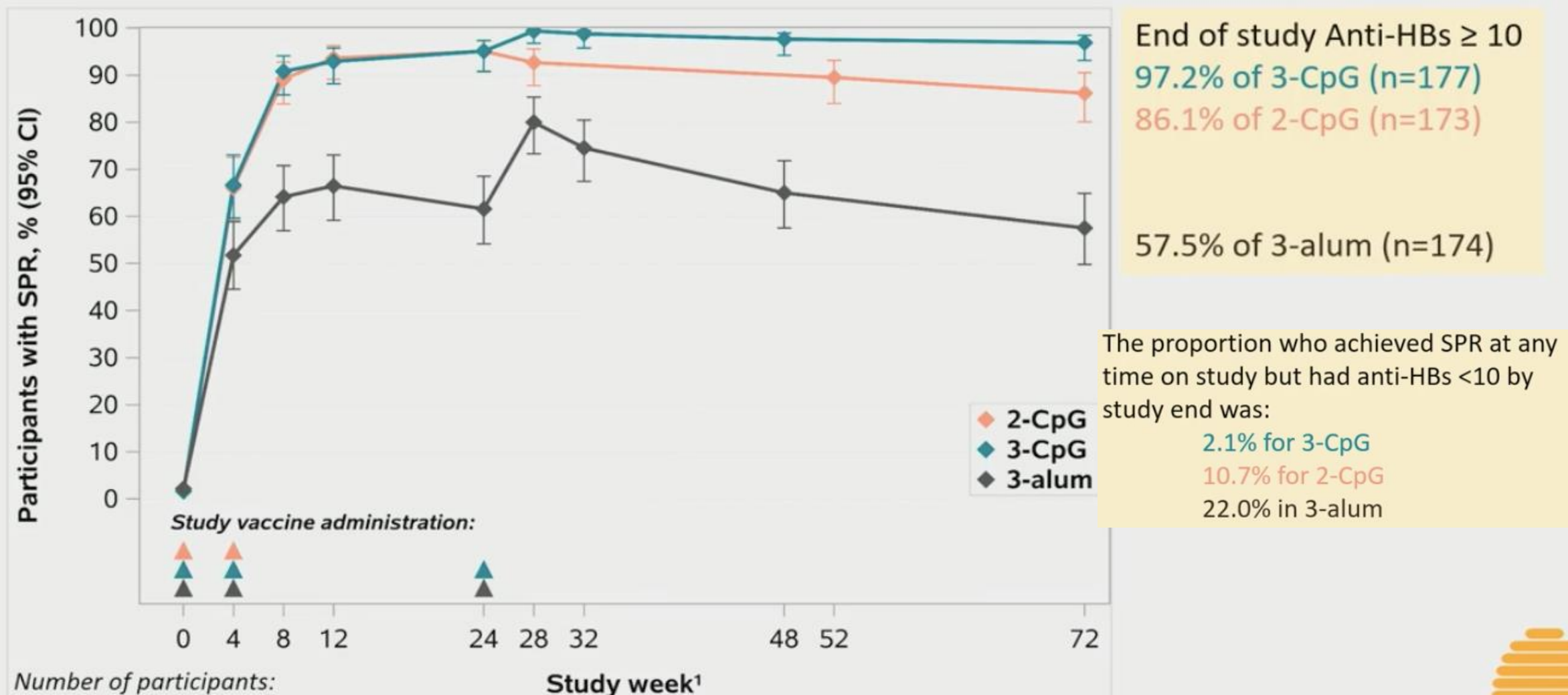
72 week durability data for both arms

¹Marks KM, et al. JAMA 2025

²Marks KM, et al. Clin Infect Dis 2023

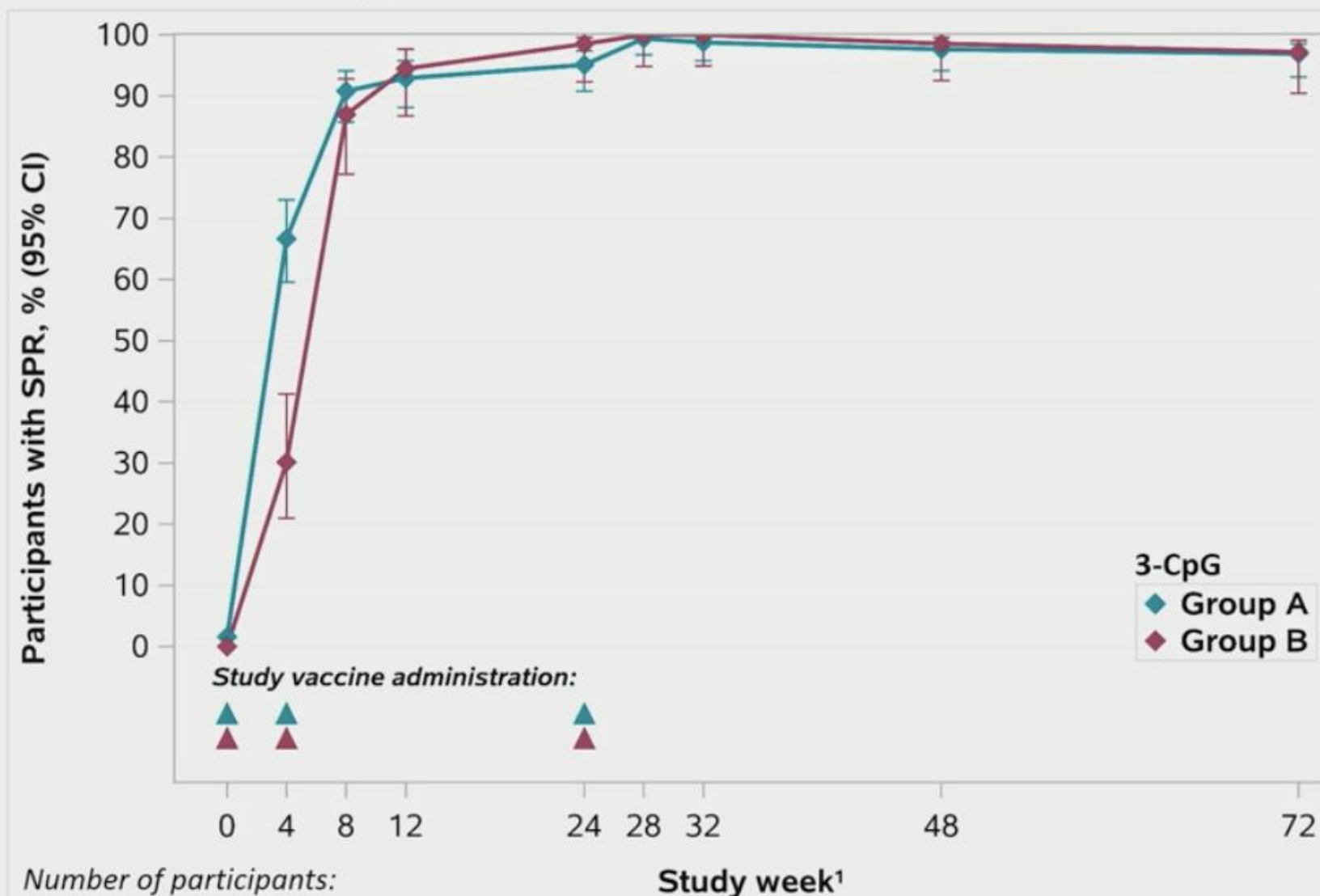
BEe-HIVe: Group A 72 week Results

Group A: Proportion with Anti-HBs ≥ 10 at Study Visits



BEe-HIVe: Group B 72 week Results

Group B: Proportion with Anti-HBs ≥ 10 at Study Visits



End of study anti-HBs ≥ 10
97.3% 3-CpG (n=74)

For comparison,
97.2% in Grp A 3-CpG (n=177)

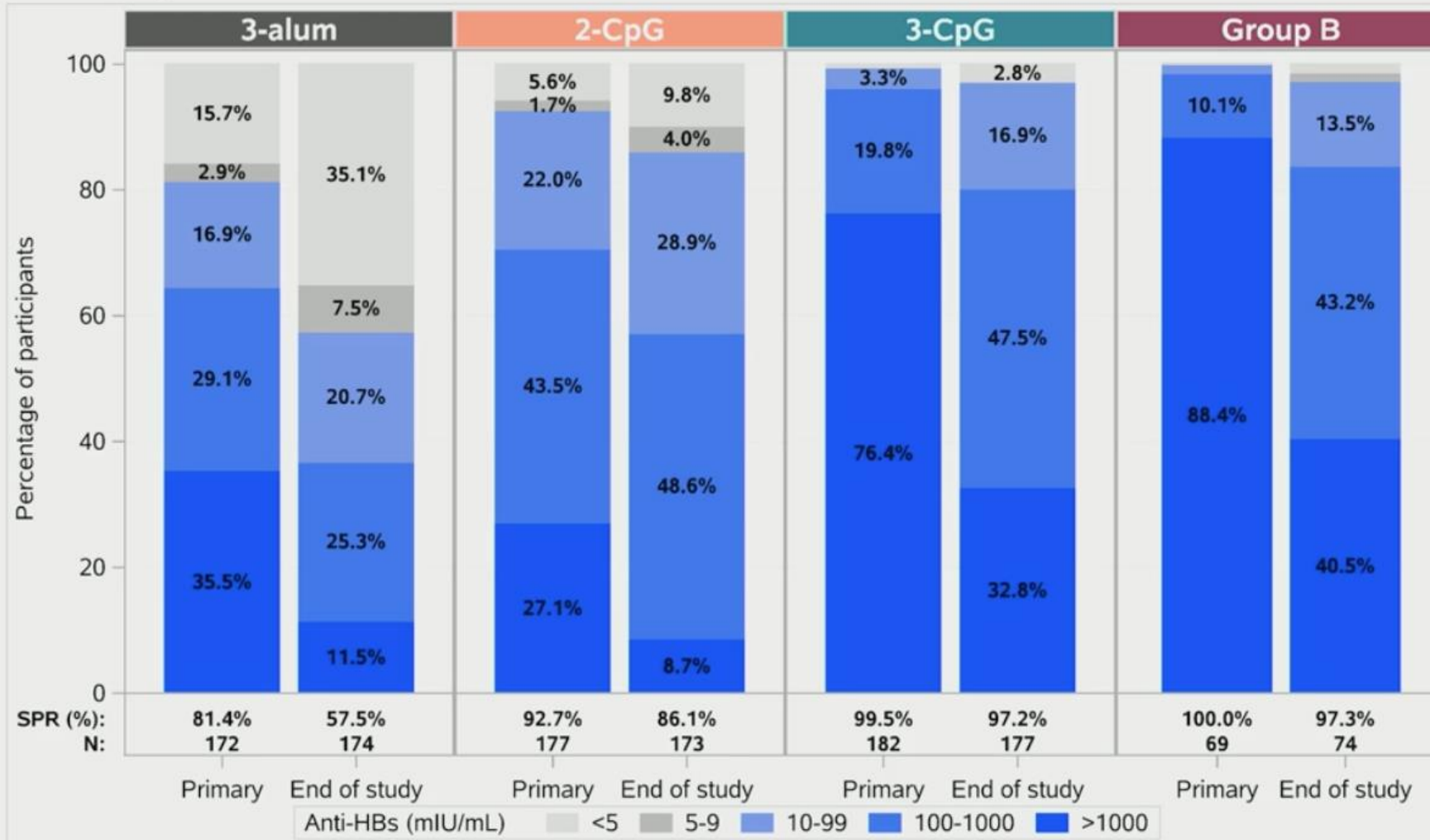
Group B Durability

- Primary SPR proportion
100% (CI: 94.7%, 100%)
- End of study SPR proportion
97.3% (CI: 90.7%, 99.3%)



BEE-HIVE: 72 week Results

Group A & B: Distribution of Anti-HBs titers*



Higher primary anti-HBs titers were more likely to lead to SPR by end of study (EOS).

EOS SPR:

- 100% of those with titers > 1000 at primary response
- 0% with titers <100 in 3-alum at primary response
- 61% with titers <100 in 2-CpG at primary response
- Not enough people with titer <100 at primary response in 3-CpG arms to say!

Takeaways

- In PWH, higher end of study seroprotection was achieved with HepB-CpG over HepB-alum, and among CpG, 3 doses over 2 doses
- HepB-CpG led to durable seroprotection both in vaccine-naïve and prior vaccine non responders
- NB: Low CD4 and HIV viremia not well represented in the study

Co-Occurring Conditions: Take Home Points

- In pregnant women with HIV, BID DTG with either 1HP or 3HP was favorable from a PK perspective- and daily dosing of DTG with 3HP might be
- There is increasing data that ART related weight gain is complex; need more data regarding impact of regimen switch
- HepB-CpG (Heplisav-B) is superior to conventional HBV vaccination in PWH and is highly durable

Questions?

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