Oral Abstract Session-12

Wednesday, March 12, 2025

193 - Estimation of Prevention-Effective CAB-LA Concentrations Among MSM/TGW in HPTN 083

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Disclosure: Dr Hanscom has no financial relationships with ineligible companies to disclose.

CROI 2025

Estimation of prevention-effective CAB-LA concentrations among MSM/TGW in HPTN 083

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*Fred Hutch Cancer Center, Seattle, WA, USA

CROI 2025, 3/12/2025

HPTN HIV Prevention Trials Network

Introduction

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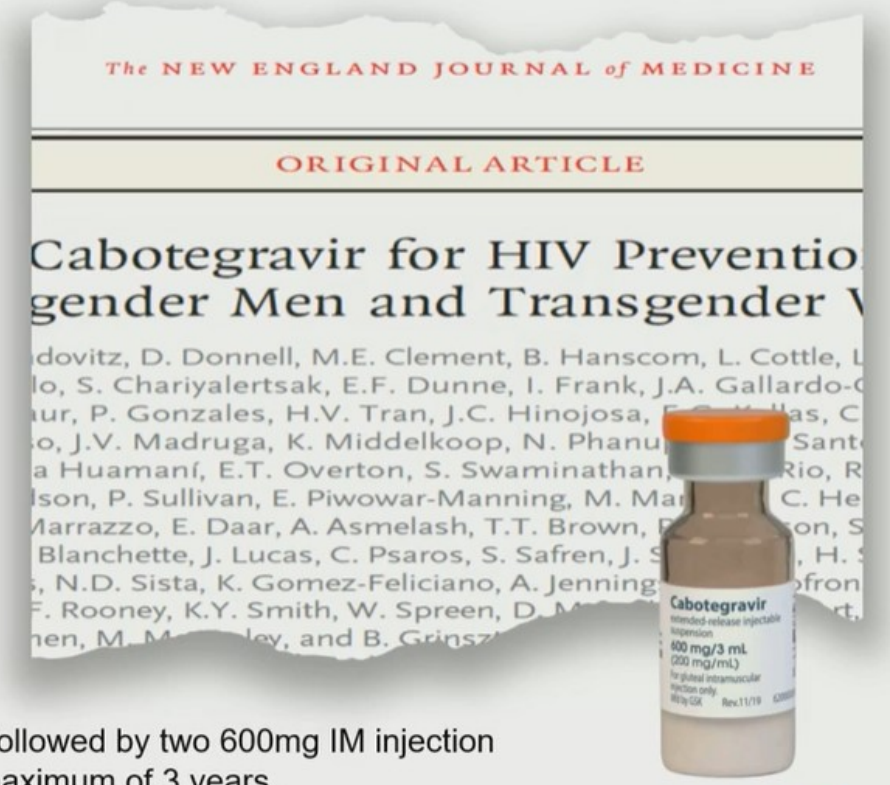
- HIV Prevention Trials Network (HPTN) 083 demonstrated that Cabotegravir (CAB) is highly effective for HIV prevention and superior to TDF/FTC in men who have sex with men (MSM) and transgender women (TGW).



The study regimen consisted of daily oral 30mg tablets for 5 weeks, followed by two 600mg IM injection 4 weeks apart and 600mg injections every 8 weeks thereafter for a maximum of 3 years.

Landovitz R et al. NEJM. 2021.

Objective

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- **Objective:** Estimate the plasma CAB concentration associated with protection against HIV infection in HPTN 083

- **Challenges:**
  - The trial only studied a single treatment regimen.
  - CAB concentrations assessed at discrete, sparse time points
  - HIV-exposure and infection timing unknown

Example / Challenges

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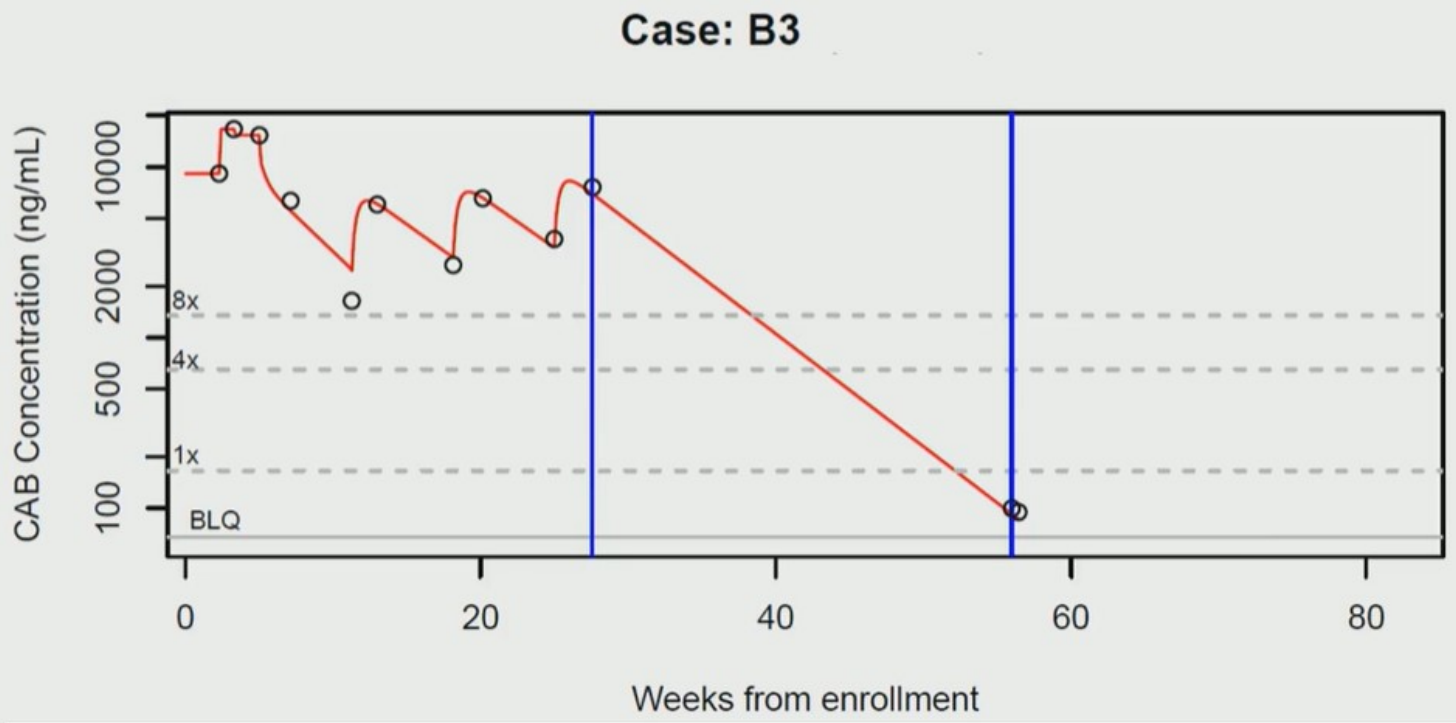

*Architect Ag/Ab testing, Geenius IFA confirmatory testing, m2000 Abbott quantitative viral load testing with a LLOQ of 40 c/mL, and Hologic Aptima Qualitative viral load testing; on select cases SCA (single copy assay) viral load .

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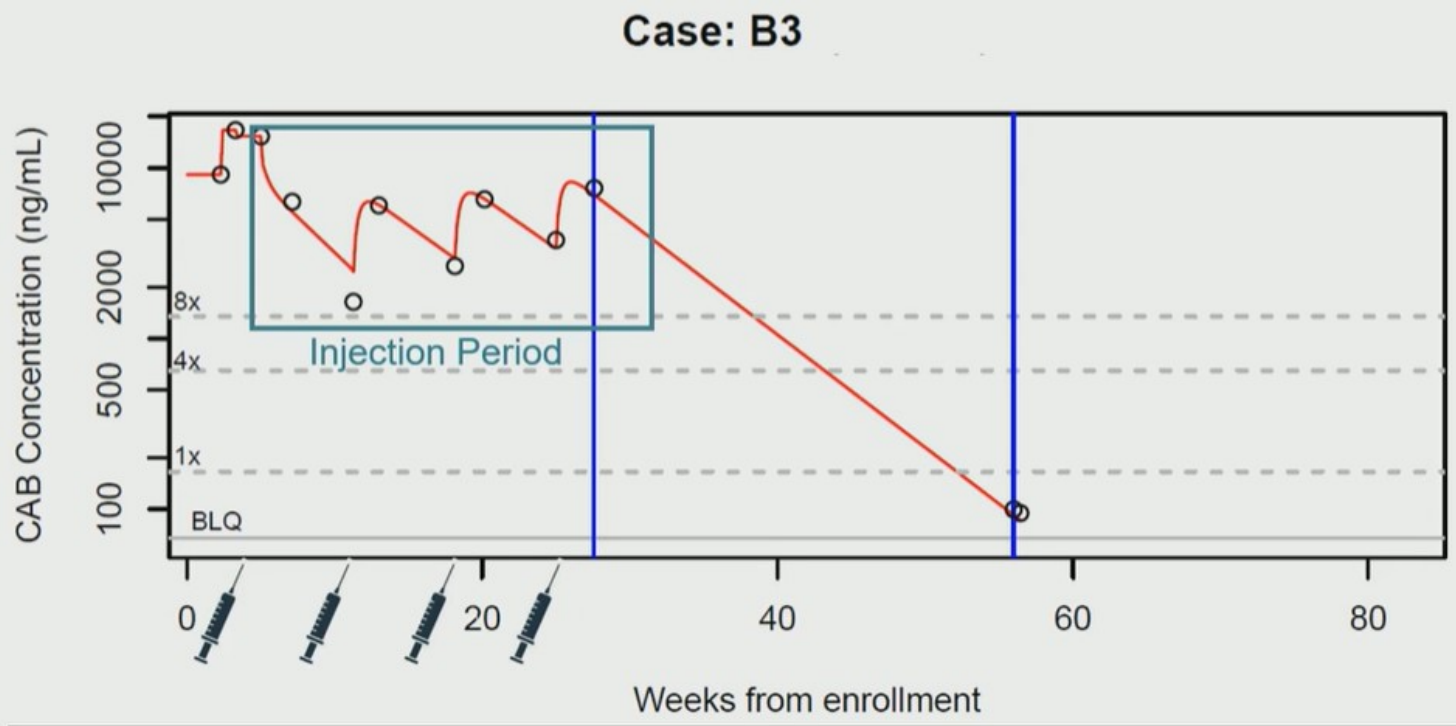

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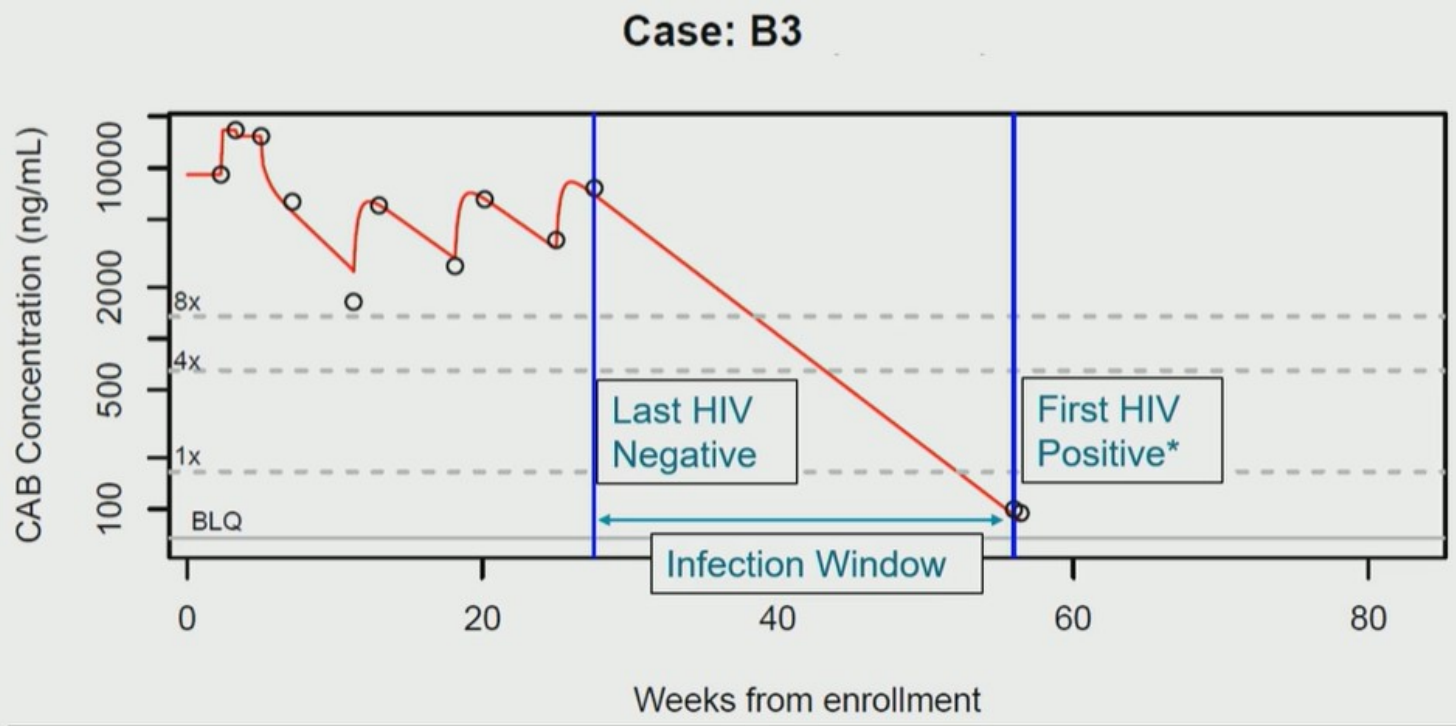

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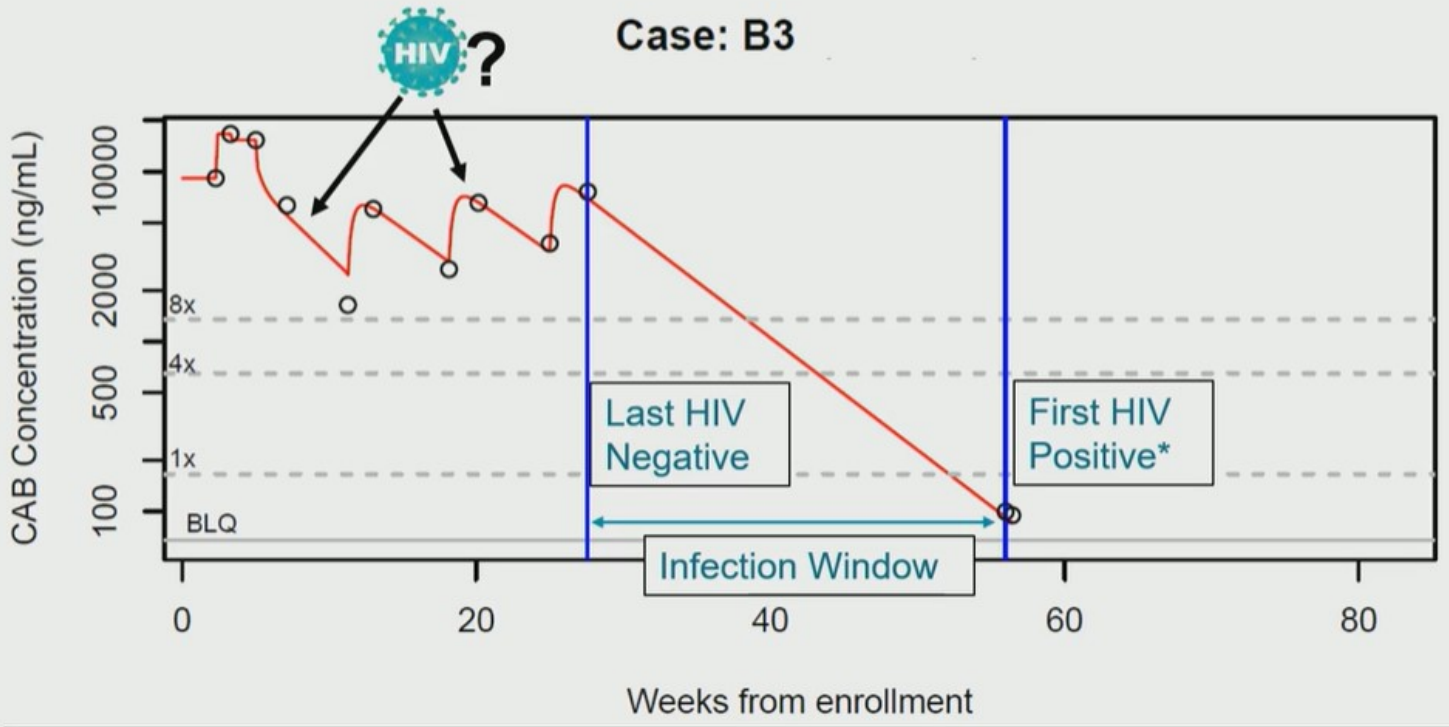

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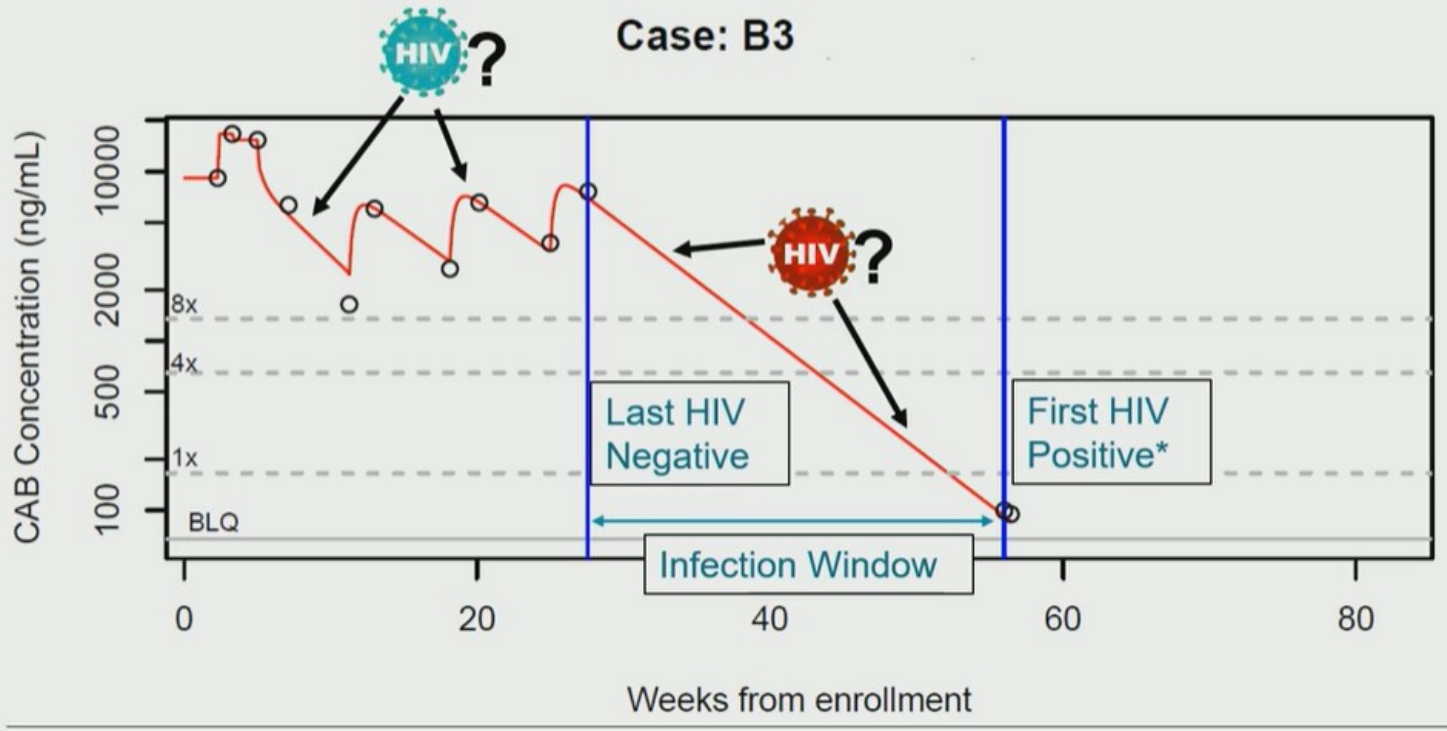

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Nested Case-Control Design

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- Cases: all incident HIV cases from the primary and year-one analyses whose infection occurred within 3 years from enrollment
- Controls: selected at a 4:1 ratio
- Matching factors
  - Region (Africa, Asia, Latin America, US)
  - Gender identity (Cisgender MSM, TGW)
  - Race (Black, Non-black)
  - Duration of follow-up at least as long as the case prior to detection[1] of HIV
- Final count: 25 cases, 99 controls[2]

[1] First-positive HIV date as determined by sensitive testing at the central lab and confirmed by the EAC.
[2] One of the initially selected control participants later was found to be HIV-positive and was excluded from the analysis.

PK Assessment / Categorization

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- CAB concentrations assessed in stored samples for cases and controls
- Full concentration-time curves estimated for all participants
- Participants classified according to CAB concentrations during the infection window

CAB Exposure Categories

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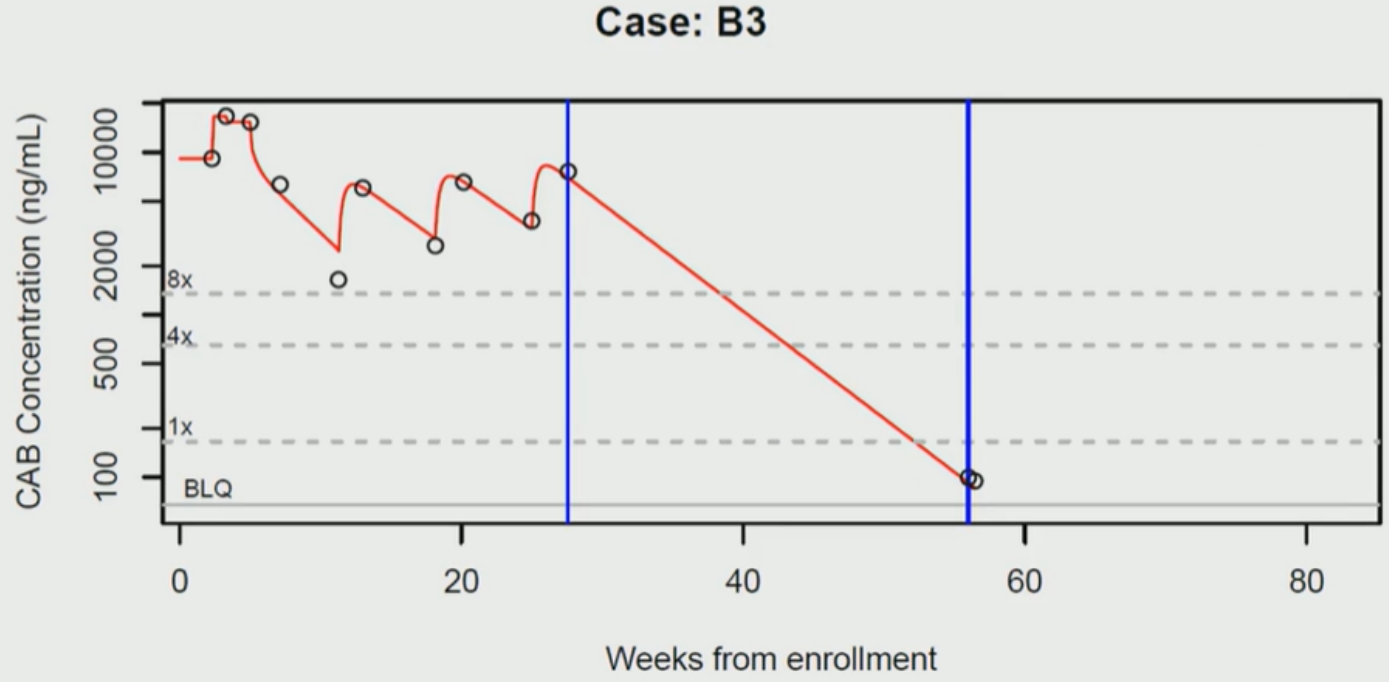
Classification according to minimum CAB concentration during the infection window:



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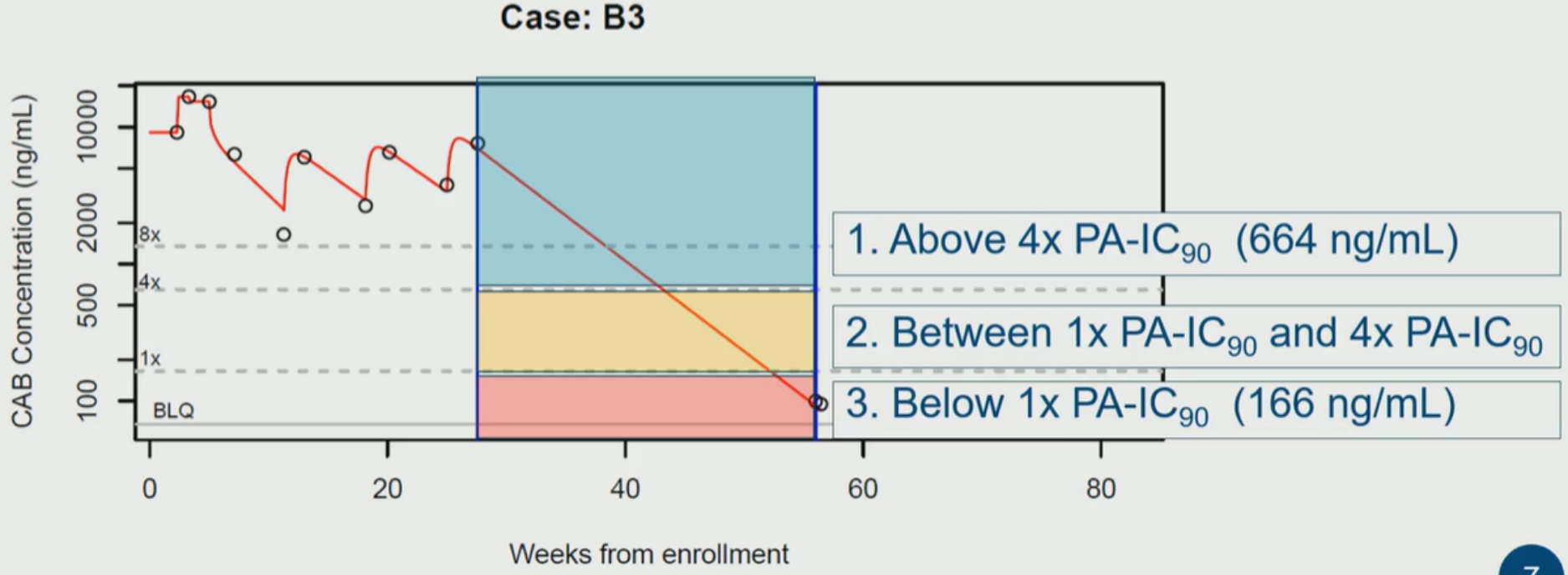

Example Case-Control Set

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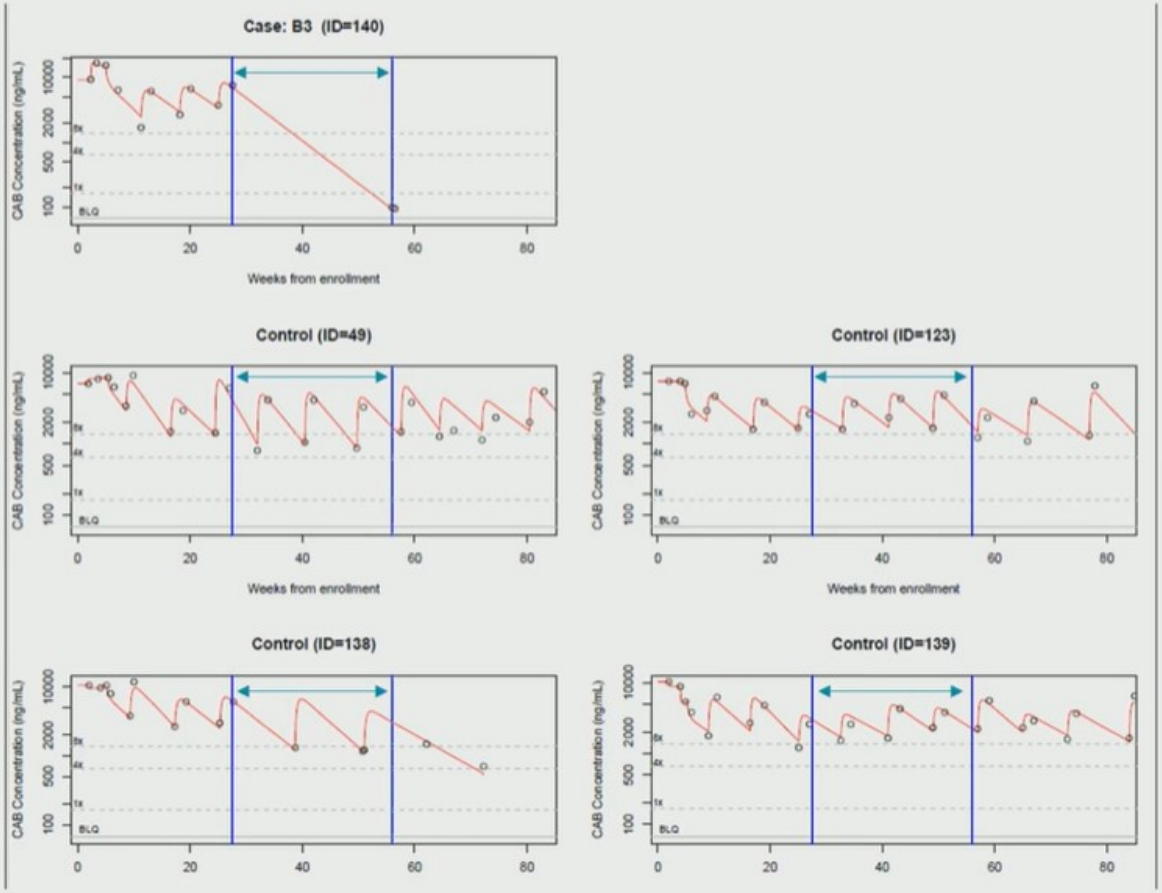

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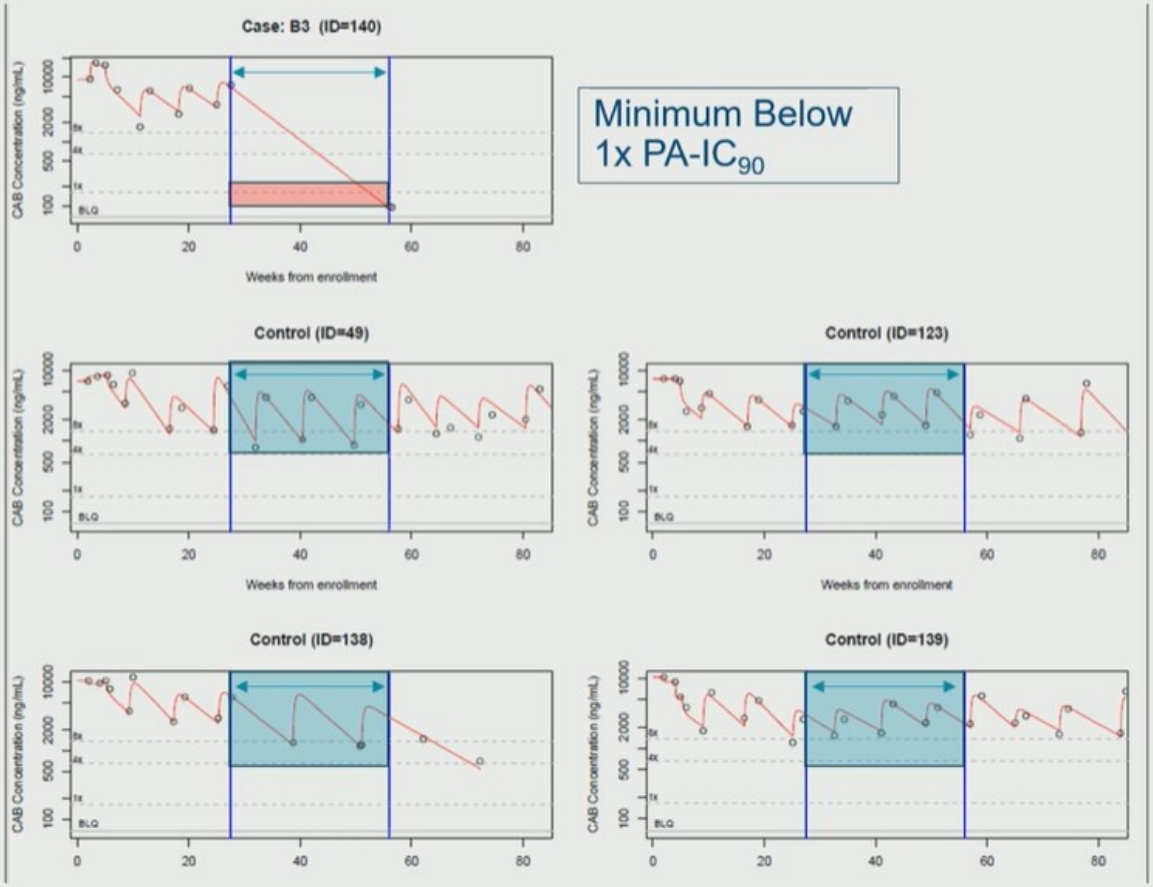

Minimum Below 1x PA-IC_{90}

Minimum Above 4x PA-IC_{90}

Results

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Minimum plasma CAB during acquisition window	Cases (n=25) *n (%)*	Controls (n=99) *n (%)*	Risk Reduction (95% CI)
< 1x PA-IC_{90}	16 (64)	14 (14)	(ref)
≥ 1x PA-IC_{90} and < 4x PA-IC_{90}	2 (8)	10 (10)	79 (-20, 96)
≥ 4x PA-IC_{90}	7 (28)	75 (76)	93 (77, 98)

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Conclusions

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- The approved 8-weekly 600mg dosing has been shown to reliably achieve CAB above 4x PA-IC_{90} (664 ng/mL)
- We observe a strong, statistically significant association between CAB concentrations above 4x PA-IC_{90} and HIV protection
  - These results are consistent with non-human primate model results
- CAB LA is estimated to provide over 90% reduction in the probability HIV acquisition among MSM and TGW

Acknowledgments

Sponsors

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HIV Prevention Trials Network (HPTN)

- Laboratory Center (Johns Hopkins University)
- SCHARP (Fred Hutchinson Cancer Research Center)
- Leadership and Operations Center (FHI360)

Pharmaceutical Support

- ViiV Healthcare
- Gilead Sciences, Inc.

HPTN 083 Study Team

Community Program Managers
Community Educators & Recruiters,
CAB Members

Our 43 study sites in 7 countries

And most of all, our study participants