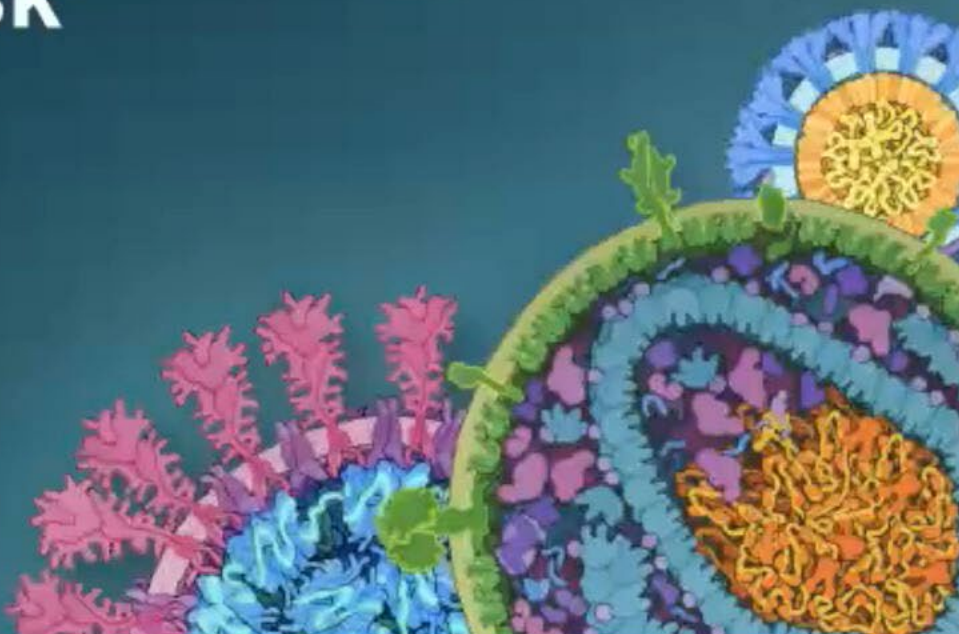


CAB-LA PrEP: Early detection of HIV infection may reduce INSTI resistance risk

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Disclosure: Research collaborations:
Monogram Biosciences
Abbott Laboratories



Background

HPTN 083 and HPTN 084 demonstrated that long-acting injectable cabotegravir was superior to oral TDF/FTC for HIV prevention

- HPTN 083: MSM and TGW - US, Latin America, Asia and Africa
- HPTN 084: Cisgender women - sub-Saharan Africa

In Dec 2021, the US FDA approved CAB-LA to reduce the risk of sexual HIV transmission



Landovitz, NEJM 2021; 385:595
Delany-Moretlwe, R4P 2021



Impact of CAB-LA on detection of HIV infection

CAB suppresses viral replication and delays antibody production

- Rapid tests and Ag/Ab assays often fail to detect infection
- Supplemental Ab tests may be negative/indeterminate for many months
- HIV RNA levels often remain low or undetectable for long periods

Marzinke, JID 2021; 224:1581

Eshleman, JID 2022, In Press

Delayed detection of HIV infection

- Delayed ART initiation
- Emergence of INSTI resistance
- Potential to impact personal health or on-going HIV transmission



In this study, we used a low VL INSTI genotyping assay to evaluate the timing of emergence of INSTI resistance

These data were used to assess whether earlier detection of HIV infection using a sensitive RNA assay for HIV screening would reduce INSTI resistance risk



INSTI Genotyping

Prior testing – HPTN 083 CAB arm

- CAB arm: 16 HIV infections among 2,282 enrolled (4 baseline, 12 incident)
- VL >500 c/mL - GenoSure PRIme assay (Monogram Biosciences)
- 5/16 cases had INSTI resistance (includes 1 baseline case)
- 2 cases had no results (VL <500 at all visits)

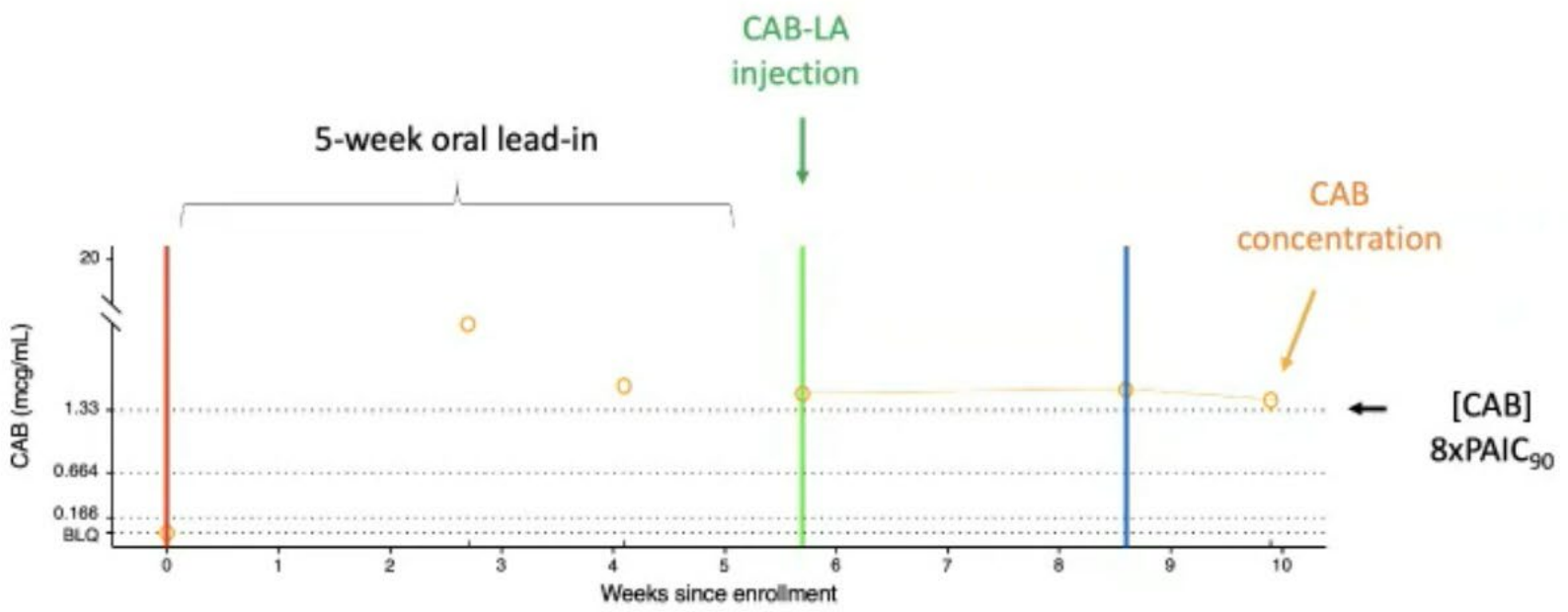
Marzinke, JID 2021; 224:1581

Low VL INSTI resistance testing

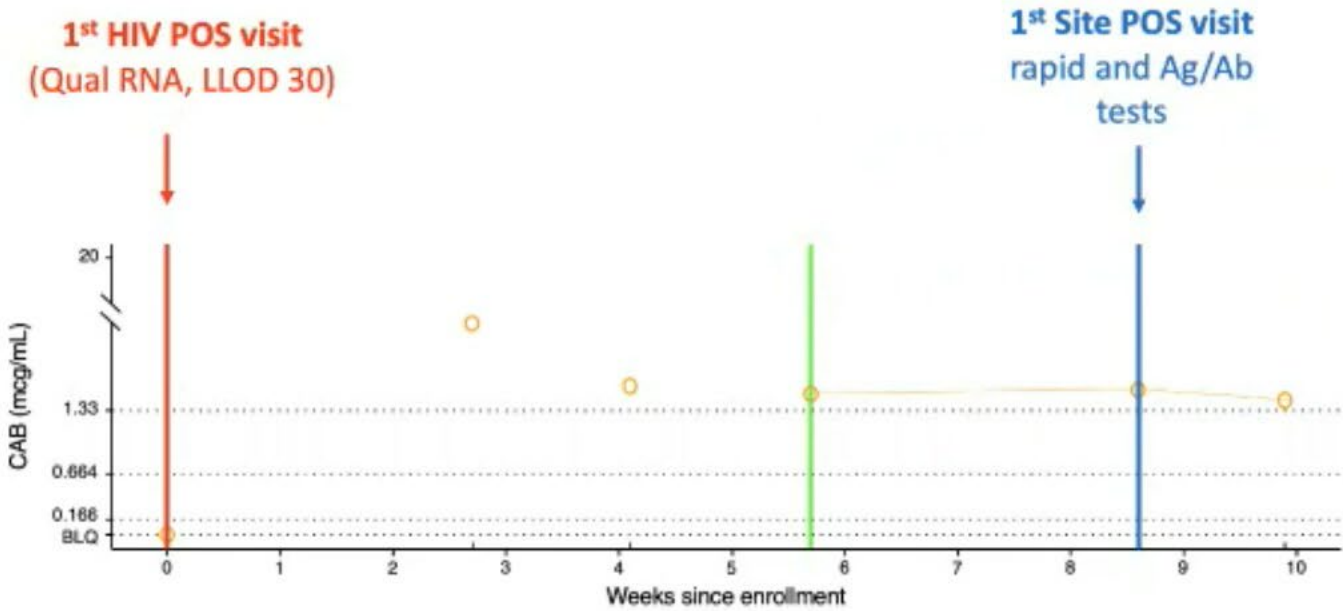
- Qualitative RNA test positive (LLOD 30 copies/mL), VL <500 c/mL
- Single genome sequencing assay (Univ of Pittsburgh)
Halvas, J Clin Invest 2020; 130:5847
- INSTI RAMs - Stanford HIV Resistance Database



Case presentation



Case presentation

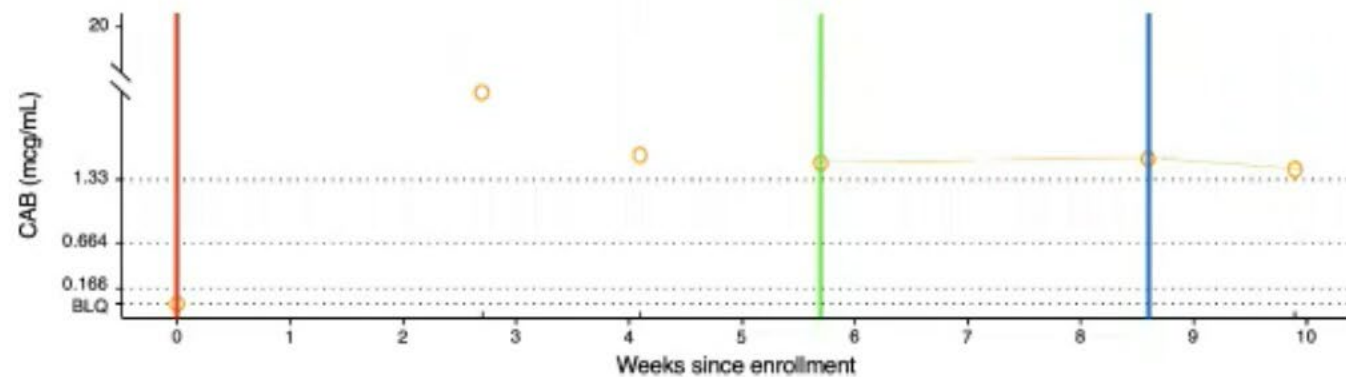


Case presentation

Retrospective testing
HPTN Lab Center



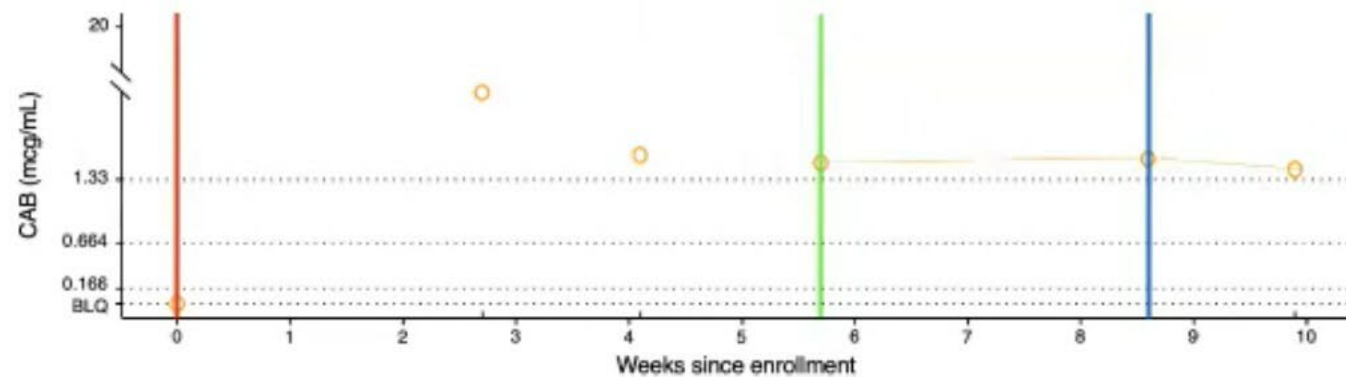
Ag/Ab test	-	-	-	-	+	+
Qualitative RNA test	+	+	+	+	+	+
Confirmatory Ab test					+	+
Viral load test	50,080	20,760	700	204	1,660	4,829



Case presentation

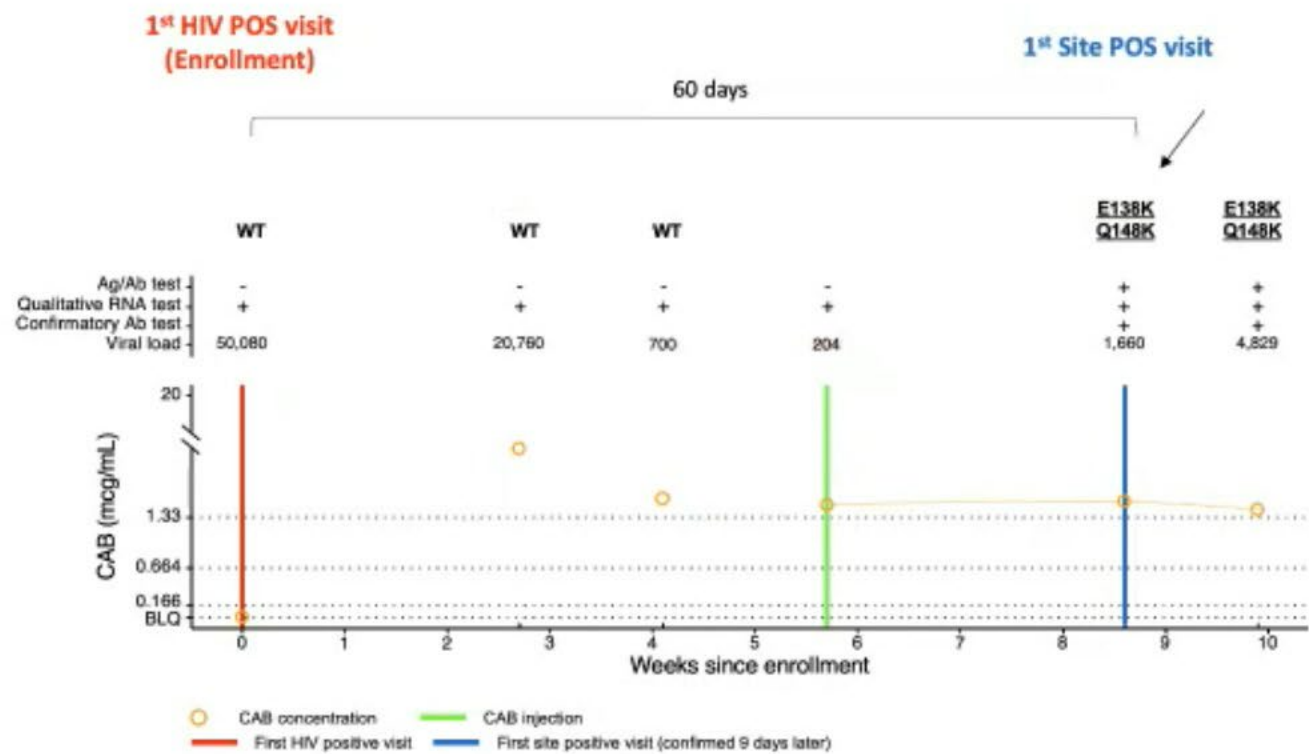
INSTI RAMs

		WT	E138E/K Q148K/R	E138K Q148K	
Ag/Ab test	-	-	-	+	+
Qualitative RNA test	+	+	+	+	+
Confirmatory Ab test				+	+
Viral load test	50,080	700	204	1,660	4,829



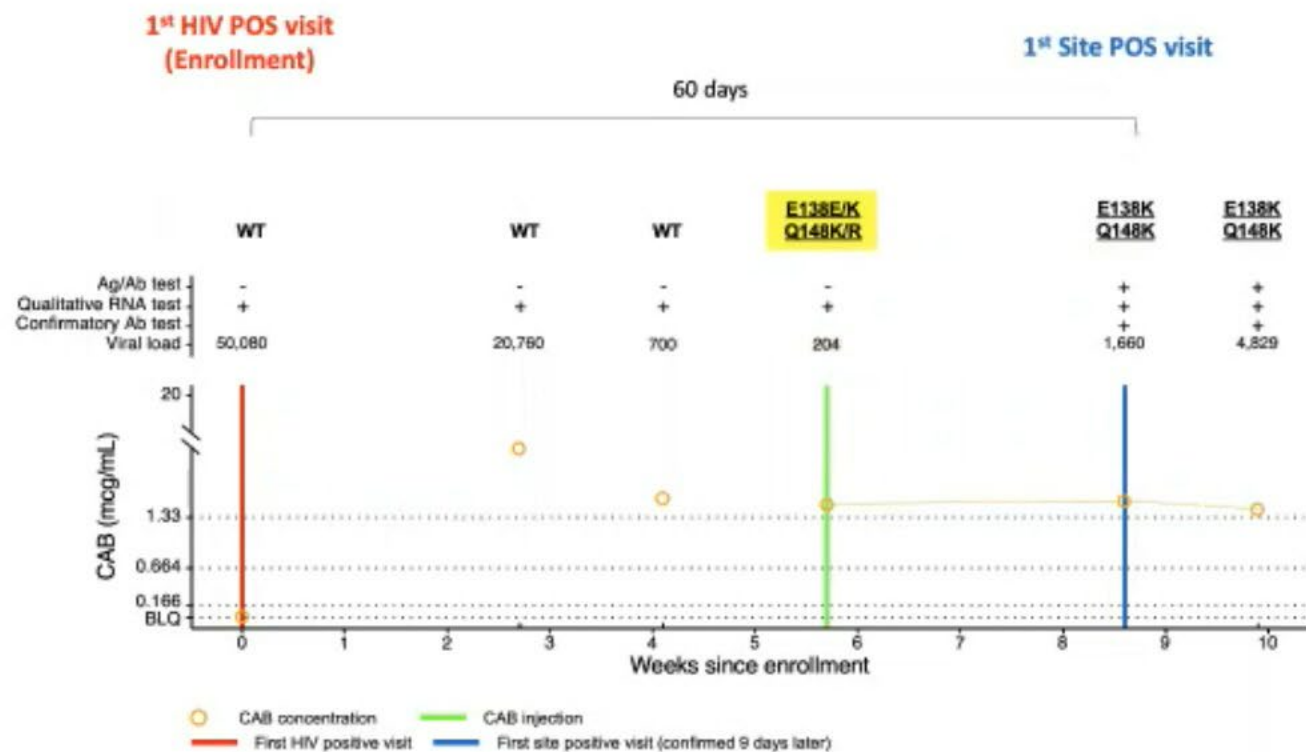
Case A2

Subtype C



Case A2

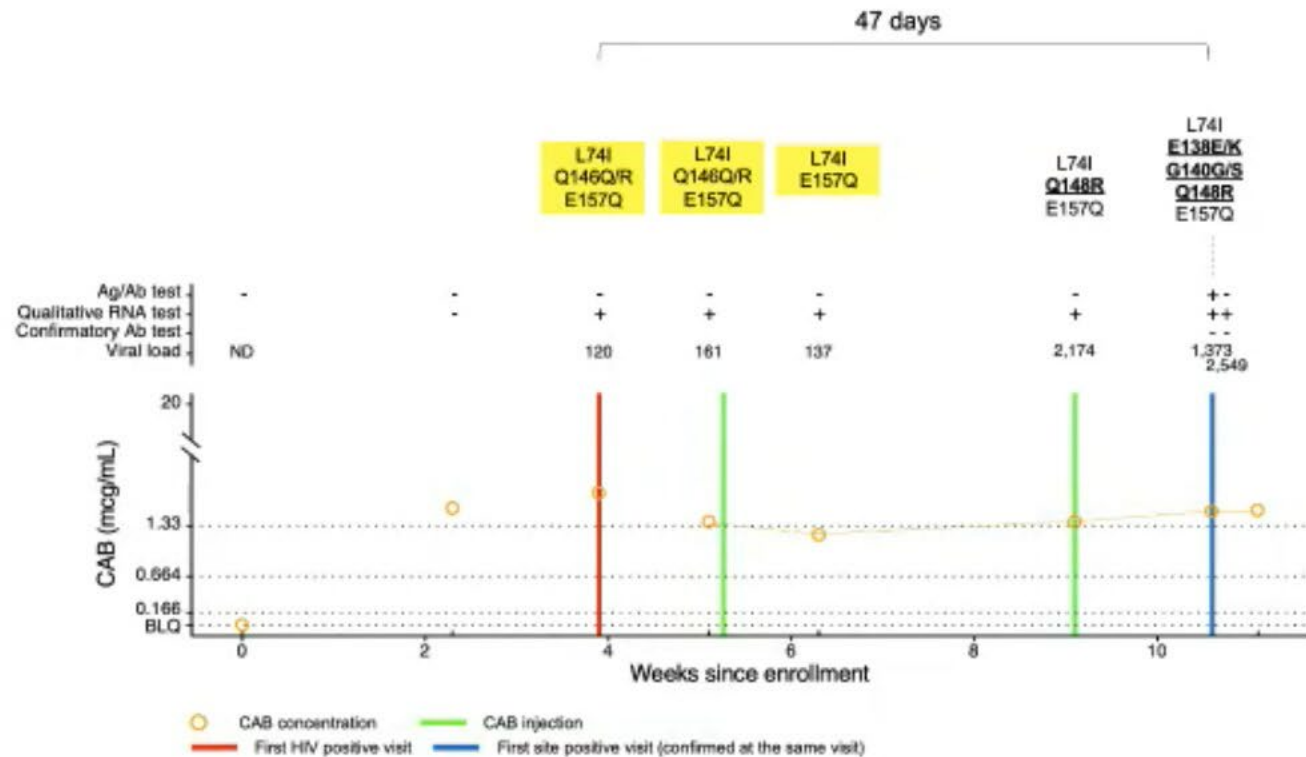
Subtype C



Use of an RNA test for HIV screening would have allowed ART initiation before CAB administration



Case C1
Subtype B

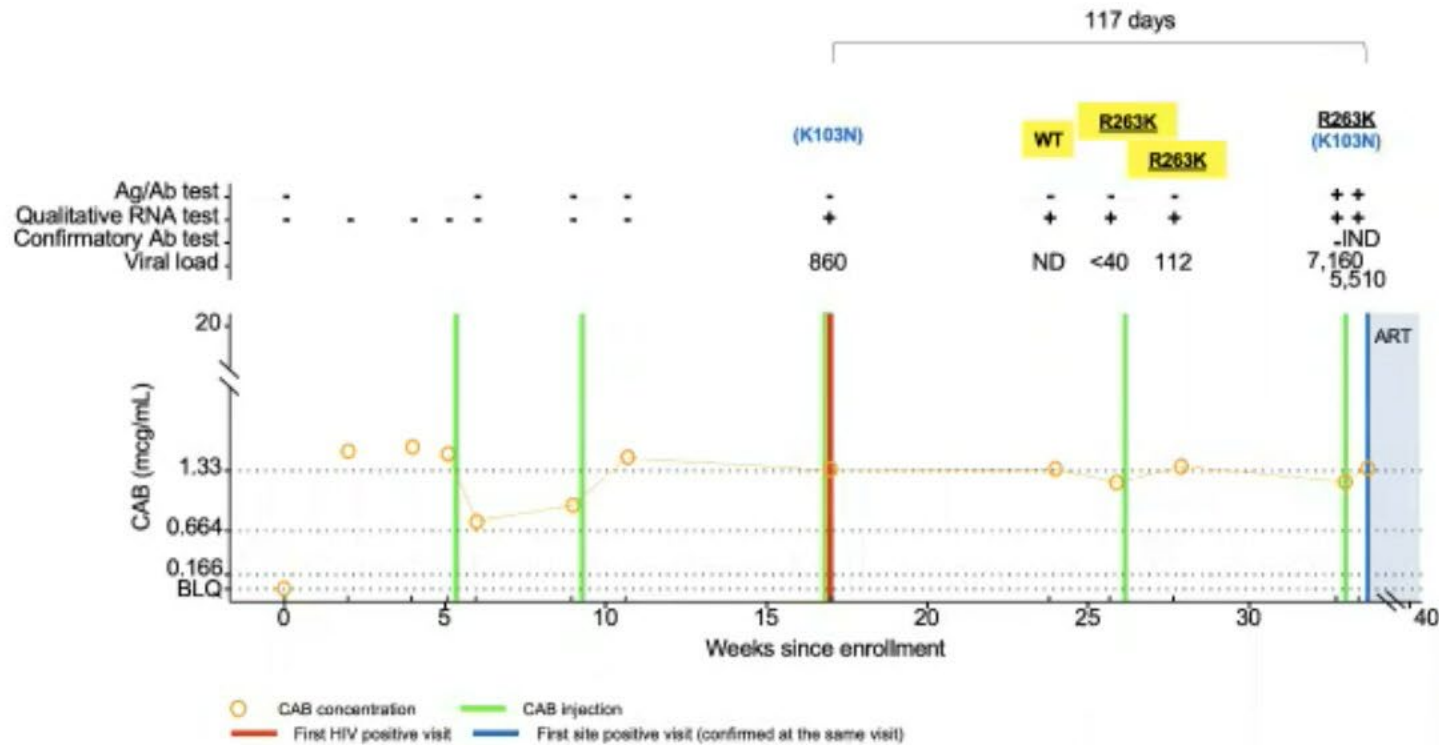


Use of an RNA test for HIV screening would have allowed ART initiation before major INSTI RAMs were detected



Case D3

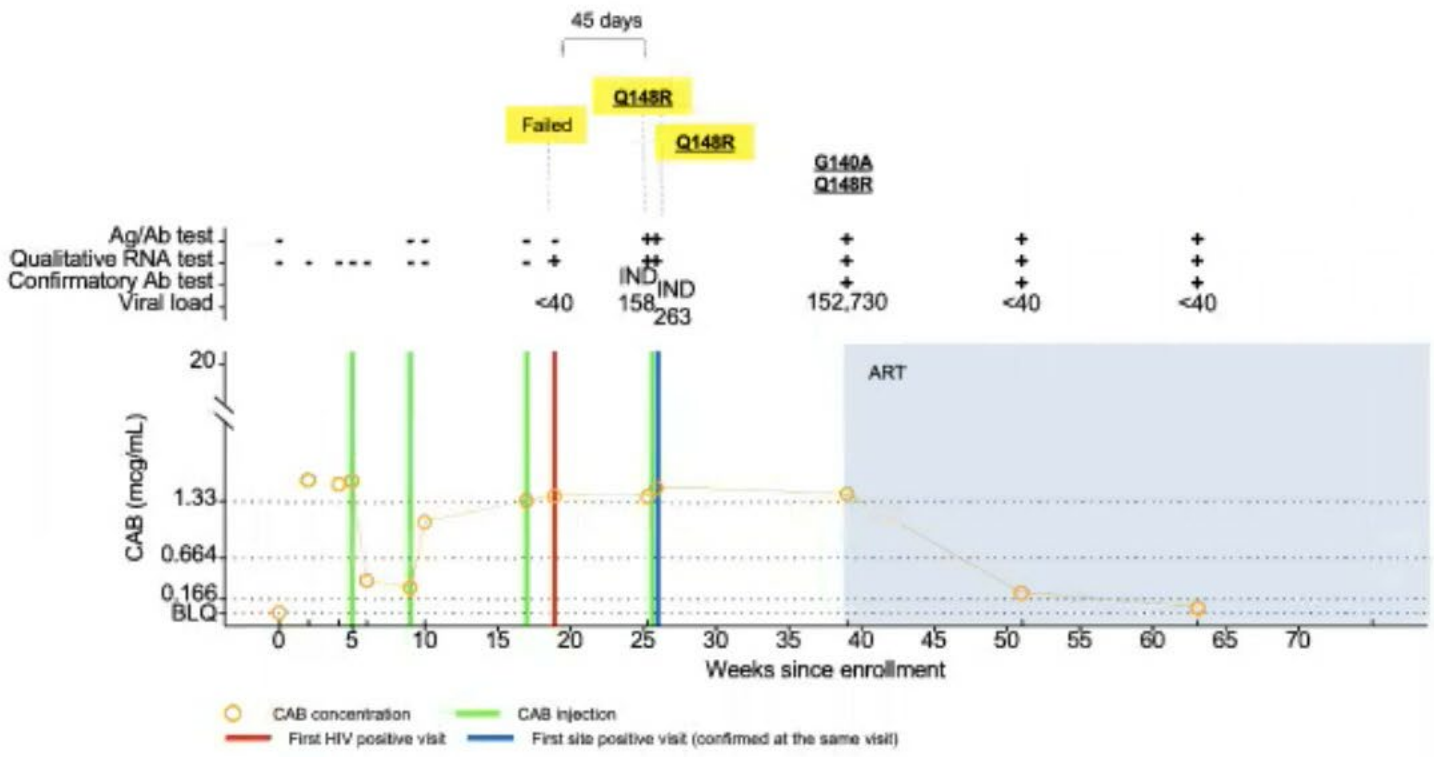
Subtype B/F



Use of an RNA test for HIV screening would have allowed ART initiation before the INSTI RAM was detected



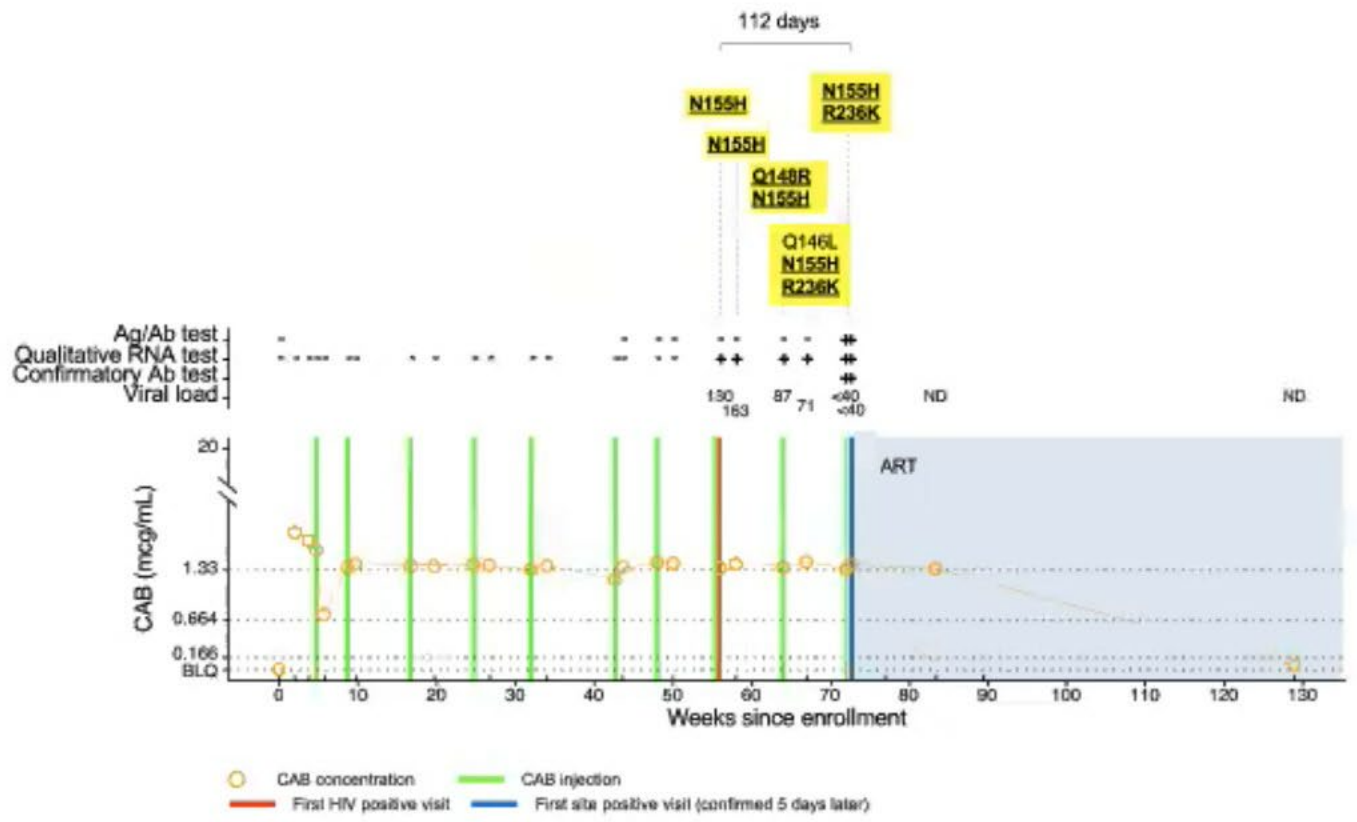
Case D4
Subtype C



Use of an RNA test for HIV screening would have allowed ART initiation before an **additional major INSTI RAM** was detected



Case D1 Subtype ND (likely B)

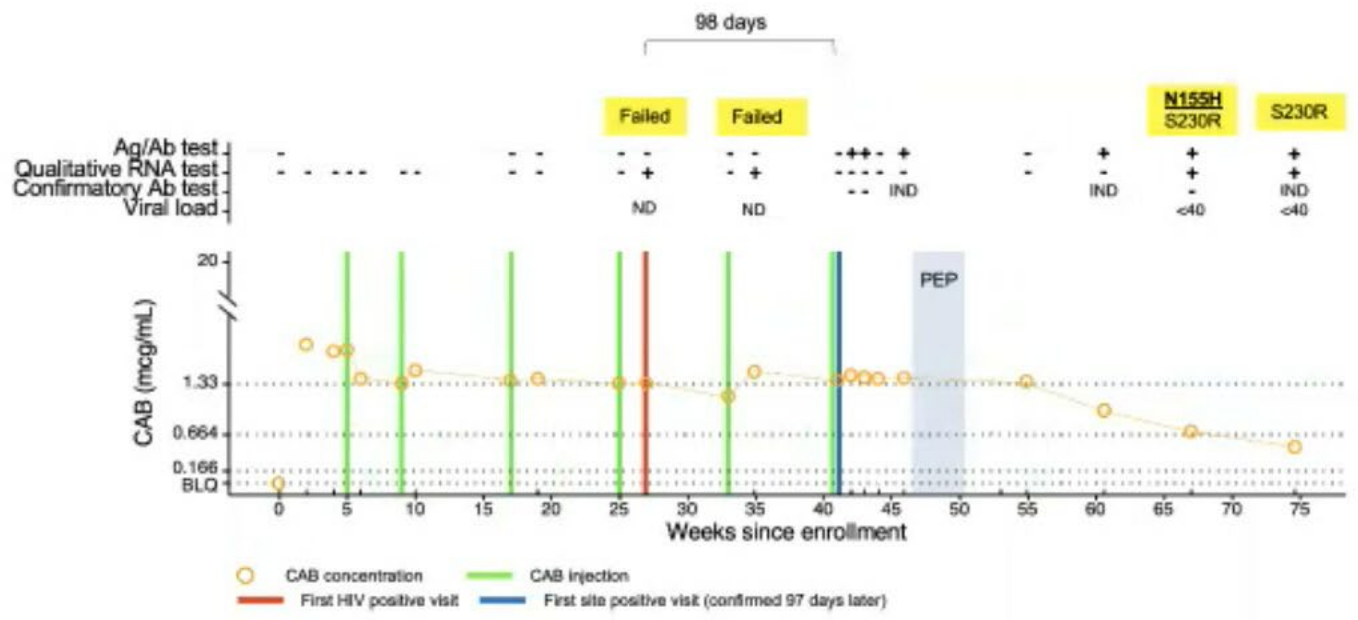


Use of an RNA test for HIV screening would have allowed ART initiation before **multiple** INSTI RAMs were detected



Case D2

Subtype ND
(likely B)



The impact of an RNA test for screening could not be assessed in this case since genotyping results were not obtained near the time of HIV infection



Key Findings

In 5/7 cases, major INSTI RAMs were first detected in samples with low VLs - not just in high VL "breakthrough" samples

Use of a RNA assay for HIV screening would have detected infection before a **major** INSTI RAM was detected (4 cases) or before **additional major** INSTI RAMs accumulated (2 cases)



Conclusions

Use of a sensitive RNA assay for HIV screening will help identify infections earlier
This may allow for earlier ART initiation, potentially reducing the risk of INSTI resistance
This testing should be performed using the most sensitive RNA assay available

These findings support the language in the US Package Insert and recent guidance from the US CDC for HIV testing in the setting of CAB-LA PrEP

Apretude package insert: <https://www.accessdata.fda.gov>

US CDC, DHHS. PrEP for the prevention of HIV infections in the United States – 2021 Update



Additional Considerations

None of the participants was started on an INSTI-based ART regimen
Data are not yet available on use of INSTI-based ART in infections that occur in the setting of CAB PrEP

In the context of proven high efficacy, CAB-LA should also be considered for HIV PrEP in settings where HIV RNA screening is not readily available



Acknowledgments

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