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How low can you go?
Diagnosis of acute HIV infection at very low HIV RNA levels

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Background

- Diagnosis of acute HIV infection (AHI) prior to development of HIV antibodies (Ab) in blood can be challenging.
- In the earliest stages of AHI, diagnosis may be made solely by the detection of HIV RNA in plasma. Guidelines caution that HIV RNA <5,000 copies/ml may be a false positive result. However, those recommendations are based on data from >15 years ago, when testing methodologies were less specific than current technology.
- We reviewed data on diagnosis of AHI in Bangkok, Thailand, to determine if false-positive diagnoses were an issue when the initial diagnosis was made solely on the basis of HIV RNA <5,000 copies/ml

Methods

- The RV254 SEARCH010 cohort has recruited participants with AHI in Thailand since 2009.
- A total 230,036 screening tests were done and 462 AHI cases enrolled through April 2017 (Figure 1).
- We longitudinally examined participants diagnosed with HIV infection based on initial low viral load (LVL: detectable plasma HIV RNA <5,000 copies/ml) with HIV Ab test results negative or inconclusive.
- HIV RNA (qualitative and quantitative) and HIV antibody [4th-generation (4thG) and 3rd-generation (3rdG) immunoassays (IA)] were performed at baseline, 12 and 24 weeks.
- Antiretroviral therapy (ART) was started at baseline.

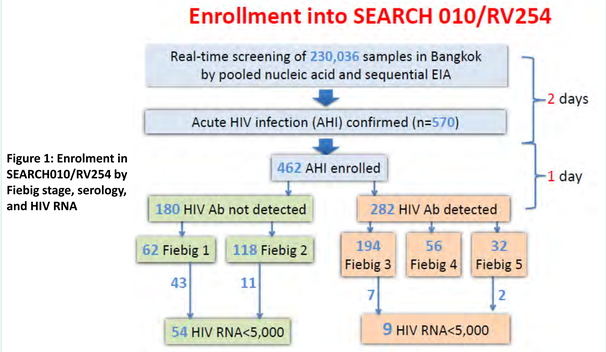
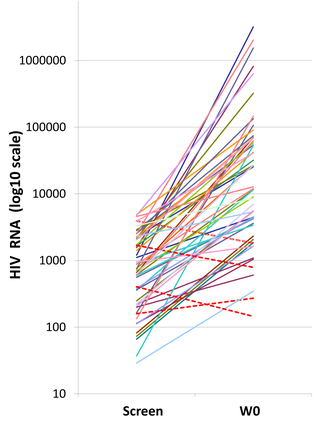


Figure 1: Enrolment in SEARCH010/RV254 by Fiebig stage, serology, and HIV RNA

Results

- 54 (12%) participants were diagnosed with AHI based on LVL alone with negative or inconclusive HIV serology.
- Initial HIV RNA at screening was median 753 (range 29-4865) copies/ml; 57% were <1,000 copies/ml.
- Testing was repeated concurrently with starting ART at W0 after median 3 (range 1-6) days with a median change of +1.3 (-0.4 to +3.4) $\log_{10}$ copies/ml (Figure 2). 57% had HIV RNA >5,000 cps/mL. Only 3 participants had a fall in HIV RNA: all had started 3-drug post-exposure prophylaxis (PEP) on the day of the initial test.
- No false positive HIV RNA tests were identified; all tests were confirmed by repeat HIV RNA, of which 65% were >5,000 copies/ml.
- HIV serology with 3rdGIA showed HIV Ab seroconversion in 87% (46/53) at 12 weeks and 85% (45/53) at 24 weeks.
- Surprisingly, 4thGIA was less sensitive: 58% (31/53) and 47% (25/53) were positive at 12 and 24 weeks, respectively.
- Only 3 participants, 2 of whom received PEP, had both repeat HIV RNA <5,000 copies/ml and negative HIV Ab at 12 weeks.

Figure 2: HIV Viral load change from screening to ART initiation (n=54). Dashed red lines denote PEP users (n=4).



	Median (range)
# Days Screen-W0	3 (1-6)
ΔVL (log10)	+1.3 (-0.4 , +3.4)

PEP as very early ART

- 4 participants started 3-drug PEP after high-risk exposure and negative 4thGIA HIV Ab . The screening sample later tested HIV RNA positive. They transferred to ART without stop in ARV drugs.
- Only 3 participants had fall in HIV RNA from screening (DO) to WO: all had started 3-drug PEP at the screening visit
- One PEP user had rising VL from 159 at screening to 272 on W0.
- Of 3 PEP users with serologic data, 2/3 remained sero-negative at 12 and 24 weeks.

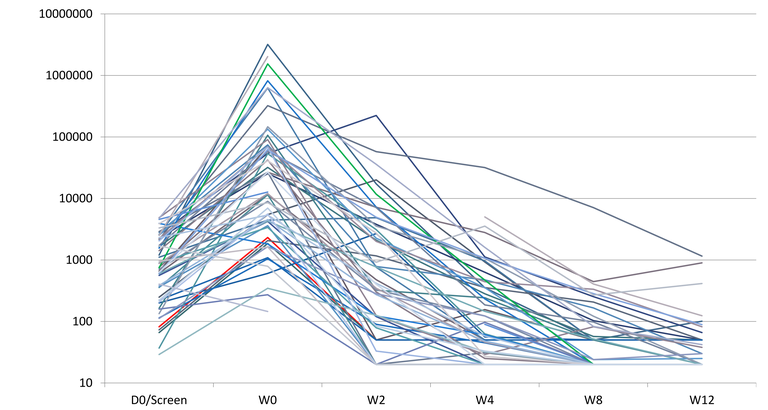
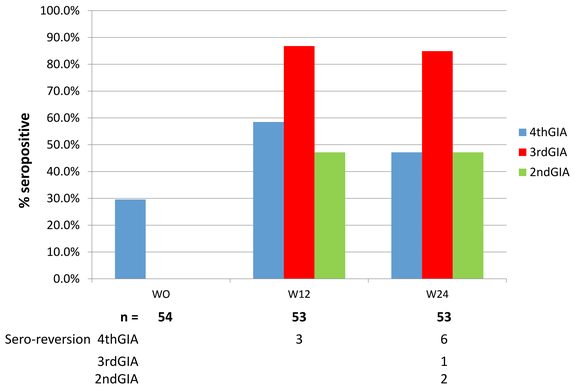


Figure 3: longitudinal HIV RNA from screening through 12 weeks of ART

- Participants start ART at W0 or within 48 hours
- Limited sampling at days 2 through 7 (31 samples from 17 participants) all had detectable HIV RNA
- 11/54 (20%) had undetectable HIV RNA at week 2 after ART
- HIV RNA became undetectable at median 4 (IQR 2-8) weeks on ART .
- 35/53 (66%) undetectable at 8 weeks
- 46/53 (87%) undetectable at 12 weeks

Figure 4: HIV Serology by time point (n=54).



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Conclusions

- Diagnosis of AHI based on HIV RNA <5,000 copies/mL alone had a positive predictive value of 100%
- No false positive tests were identified.
- ART can safely be started in these individuals concurrently with confirmatory HIV RNA and Ab testing.
- Repeat HIV RNA testing, if performed for diagnostic confirmation, should be drawn within 7 days of ART initiation. By 14 days, some patients will have undetectable viral load.
- HIV serology can be repeated at 12 weeks, by which time seroconversion has occurred in the majority of those likely to become seropositive.
- The diagnosis of HIV may be more challenging with the use of PEP, and potentially PrEP, which may blunt or delay the HIV Ab response.

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