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Evaluation of HIV-1 Recency Assays Among Prospectively Observed HIV-1 Seroconversions

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Introduction

- The estimation of HIV incidence is a useful measure for evaluating country-specific HIV epidemics and the effectiveness of interventions
- Recency assays use measurements of HIV antibody (Ab) avidity or quantity to determine whether individuals acquired HIV recently
- When incorporated into a recent infection testing algorithm (RITA), recency assays can be used to estimate population-level HIV incidence rates[1-3]
- HIV-1 RITAs using recency assays are currently being used to determine comparator background HIV incidence rates in Phase 3 pre-exposure prophylaxis (PrEP) trials (NCT04994509, NCT04925752, and NCT04652700)
- The DISCOVER study (NCT02842086), a large Phase 3 randomized controlled trial that demonstrated the noninferiority of emtricitabine/tenofovir alafenamide (F/TAF) to emtricitabine/tenofovir disoproxil fumarate (F/TDF) for PrEP, provides a unique context to evaluate the performance of recency assays in well-documented HIV seroconversion cases

Objective

- To evaluate the performance of recency assays in well-documented seroconversion cases from the DISCOVER study

Methods

- The performance of 3 different recency assays was evaluated on 42 uniquely dated plasma samples from 25 participants from the DISCOVER study
  - HIV testing was conducted at screening, baseline, and every 12 weeks during DISCOVER
  - Time in days since infection was determined for each sample by subtracting the date of the sample from the date of the last negative HIV test (Day 0)
  - This duration of time between the positive and negative tests determined recent vs long-term infection, and was used as the reference against which to compare the recency assays
  - Of 25 participants with available samples, 15 had samples from a single visit and 10 from multiple visits over a period allowing evaluation of recent and long-term samples from the same participant

Recency Assays

Recency Platform	Method	Unit of Measurement	IA Threshold	MDRI
LAg-EIA*	Ab avidity, EIA	Normalized ODn	1.5 ODn	130 d[4]
ARCHITECT†	Ag/Ab chemiluminescent IA	Signal–cutoff ratio (S/CO)	200 S/CO	186 d[5]
Asante‡	Ab avidity, lateral flow IA, interpreted with electronic reader	LT/R band intensity	3.0 LT/R	180 d[6]

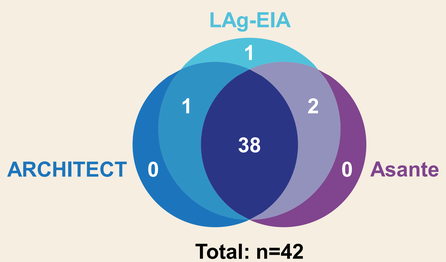
*Sedia® HIV-1 Limiting Antigen Avidity EIA (Sedia Biosciences Corporation, Beaverton, OR); †Abbott™ ARCHITECT™ HIV Ag/Ab Combo assay (Abbott, Abbott Park, Chicago, IL); ‡Asante® HIV-1 Rapid Recency® Assay (Sedia). Ag, antigen; EIA, enzyme immunoassay; IA, immunoassay; MDRI, mean duration of recent infection; ODn, optical density.

- The determination of recent or long-term infection was based on assay-specific IA threshold and MDRI
  - IA threshold: assay result cutoff defining recent infection (below IA = recent; above IA = long term)
  - MDRI: average time post-infection that individuals were classified as recently infected; differs based on the assay used
- The number of days since infection determined for each DISCOVER sample was compared with the MDRI for each assay to make the recent vs long-term determination

Results

Samples Evaluated by Assay

Samples Evaluated in:	LAg-EIA	ARCHITECT	Asante	Samples Tested
3 recency assays	38	38	38	38
2 recency assays				
LAg EIA + ARCHITECT	1	1		1
LAg EIA + Asante	2		2	2
1 recency assay				
ARCHITECT		1		1
Total	41	40	40	42



- Of 42 samples, 38 were tested by all assays, 3 were available for testing by 2 assays, and 1 sample was tested by only 1 assay
- Samples were predominantly subtype B (22/25 participants); 2 participants were subtype F1 and 1 was AG

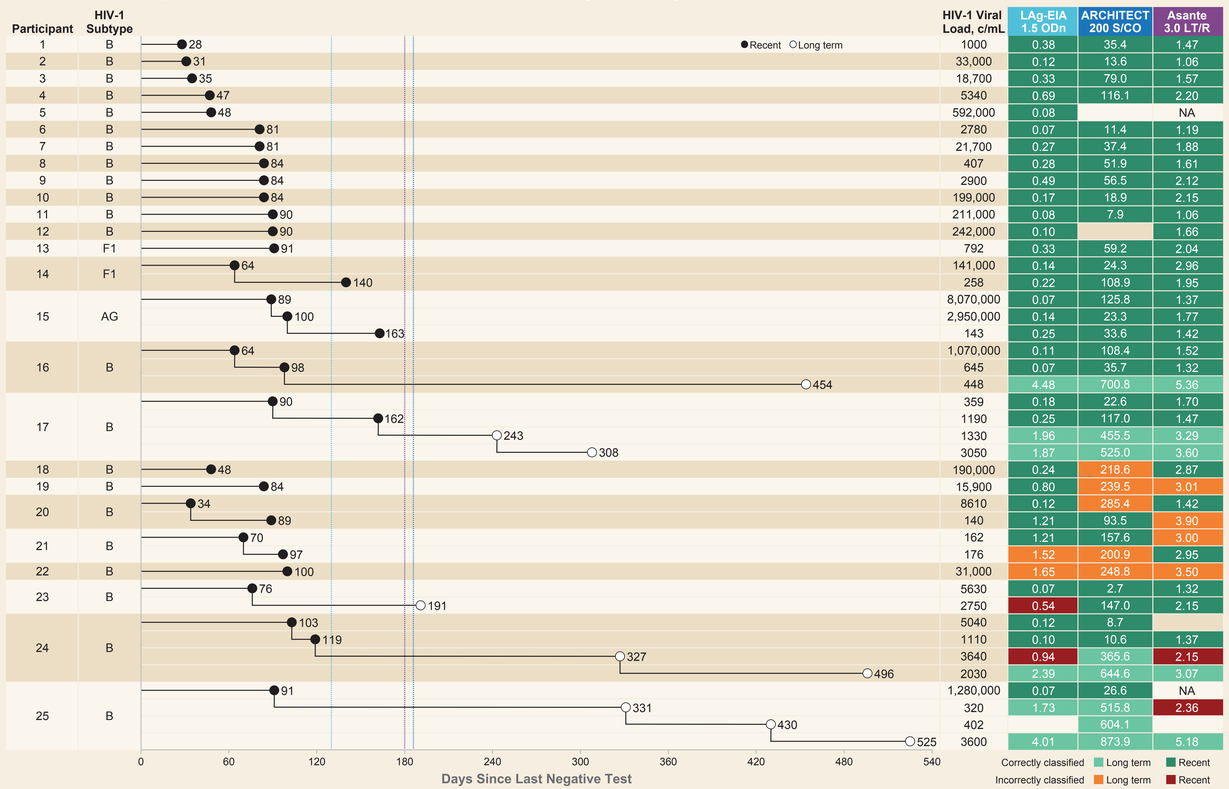
Recency Assay Results

	LAg-EIA n=41	ARCHITECT n=40	Asante n=38*
Classified correctly, n (%)	37 (90)	35 (88)	32 (84)
Classified incorrectly, n (%)	4 (10)	5 (12)	6 (16)
Recent called long term, n	2	5	4
FRR (long term called recent), n	2	0	2

*2 samples were called negative for HIV-1 by Asante. FRR, false recency rate.

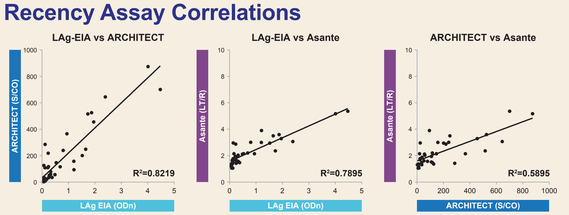
- LAg-EIA correctly classified the most samples (90%); all assays correctly classified >84% of samples
- Similar numbers of incorrectly classified samples were seen between assays (10–16%)
- Of the 3 samples that were incorrectly classified as recent, 1 was incorrectly classified by 2 assays; all participants had documented history of antiretroviral use (on antiretroviral therapy after diagnosis) while in the trial
- Of the 5 participants' samples that were incorrectly classified as long term, 2 had samples from 2 different visits that were incorrectly classified by ≥1 assay, possibly suggesting a participant-specific attribute
- Of the 3 remaining incorrectly classified samples, 2 were incorrectly classified as long term by 2 assays

Timeline of Samples Since Infection and Classification by 3 Assays*



*Day 0 is date of last negative HIV test; numbers to *right of circles* are days since last negative test; MDRI for LAg-EIA in *light blue dotted line*, ARCHITECT in *dark blue dotted line*, and Asante in *purple dotted line* demonstrating cutoff for recent vs long-term infections for each assay; any samples that were close to MDRI cutoff were considered recent as infection most likely did not occur at Day 0; *raw* IA call found in *right columns* for each assay; *blank cells* indicate samples were not tested by assay. NA, not applicable (Asante assay determined sample to be HIV-1 negative so assay call is NA).

Recency Assay Correlations



- Strong correlations were seen between LAg-EIA and ARCHITECT, and Asante
- Less correlation was seen between ARCHITECT and Asante

Conclusions

- LAg-EIA, Asante, and ARCHITECT recency assays were able to distinguish between recent and long-term infections observed during the DISCOVER study
- All 3 assays identified the recent infections with similar high degrees of accuracy
- While HIV incidence was unable to be determined with these assays in sites where DISCOVER was conducted due to lack of appropriate screening of the entire population, use of well-documented seroconversion samples from the DISCOVER study allowed for a thorough analysis of 3 recency assays
- Overall, these analyses support the use of recency assays in determining the counterfactual background HIV incidence rates in future PrEP trials

References: 1. Duong TY, et al. AIDS Res Hum Retroviruses 2019;35:896-905. 2. Kassanjee R, et al. Epidemiology 2012;23:721-8. 3. Parkin N, et al. IAS 2021, abstr 2322 . 4. Duong YT, et al. PLoS One 2015;10:e0114947. 5. Grebe E, et al. J Acquir Immune Defic Syndr 2017;76:547-55. 6. Paresh B, et al. IAS 2017, abstr TUPEC0849. **Acknowledgments:** We extend our thanks to the participants, their families, and all participating investigators. This study was funded by Gilead Sciences, Inc. Editing and production assistance were provided by BioScience Communications, New York, NY, funded by Gilead.