AETC AIDS Education & Training Center Program Mountain West

PrEP for Prevention of HIV – HIV Nucleic Acid Testing

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Disclaimer

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Disclosures

Only FTC/TDF (Truvada), FTC/TAF (Descovy), and CAB-LA (Apretude) are approved by the U.S. FDA and only for use in some, but not all, populations. This talk may include discussion of other options for PrEP.

Resources

CDC/HHS

- https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2021.pdf
- https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-provider-supplement-2021.pdf

IAS-USA

- https://www.iasusa.org/resources/guidelines/

Clinicians Consultation Center PrEPLine (855-448-7737)

- For questions or ambiguous test results

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Summary of guidance for daily oral PrEP

	Sexually-Active Adults and Adolescents[1]	Persons Who Inject Drug[2]
Identifying substantial risk of acquiring HIV infection	Anal or vaginal sex in past 6 months AND any of the following: • HIV-positive sexual partner (especially if partner has an unknown or detectable viral load) • Bacterial STI in past 6 months[3] • History of inconsistent or no condom use with sexual partner(s)	HIV-positive injecting partner OR Sharing injection equipment
Clinically eligible →	**ALL OF THE FOLLOWING CONDITIONS ARE MET:** • Documented negative HIV Ag/Ab test result within 1 week before initially prescribing PrEP • No signs/symptoms of acute HIV infection • Estimated creatinine clearance ≥30 ml/min[4] • No contraindicated medications	
Dosage	• Daily, continuing, oral doses of F/TDF (Truvada®), ≤90-day supply OR • For men and transgender women at risk for sexual acquisition of HIV; daily, continuing, oral doses of F/TAF (Descovy®), ≤90-day supply	
Follow-up care →	**Follow-up visits at least every 3 months to provide the following:** • HIV Ag/Ab test and HIV-1 RNA assay, medication adherence and behavioral risk reduction support • Bacterial STI screening for MSM and transgender women who have sex with men[3] – oral, rectal, urine, blood • Access to clean needles/syringes and drug treatment services for PWID **Follow-up visits every 6 months to provide the following:** • Assess renal function for patients aged ≥50 years or who have an eCrCl <90 ml/min at PrEP initiation • Bacterial STI screening for all sexually-active patients[3] – [vaginal, oral, rectal, urine- as indicated], blood **Follow-up visits every 12 months to provide the following:** • Assess renal function for all patients • Chlamydia screening for heterosexually active women and men – vaginal, urine • For patients on F/TAF, assess weight, triglyceride and cholesterol levels	

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Summary of guidance for Cabotegravir

	Sexually-Active Adults	Persons Who Inject Drugs[1]
Identifying substantial risk of acquiring HIV infection	Anal or vaginal sex in past 6 months AND any of the following: • HIV-positive sexual partner (especially if partner has an unknown or detectable viral load) • Bacterial STI in past 6 months[2] • History of inconsistent or no condom use with sexual partner(s)	HIV-positive injecting partner OR Sharing injection equipment
Clinically eligible	**ALL OF THE FOLLOWING CONDITIONS ARE MET:** • Documented negative HIV Ag/Ab test result within 1 week before initial cabotegravir injection • No signs/symptoms of acute HIV infection • No contraindicated medications or conditions	
Dosage	• 600 mg cabotegravir administered as one 3 ml intramuscular injection in the gluteal muscle o Initial dose o Second dose 4 weeks after first dose (month 1 follow-up visit) o Every 8 weeks thereafter (month 3,5,7, follow-up visits etc)	

p48: "Because of the long duration of drug exposure following injection, exclusion of acute HIV infection is necessary with the most sensitive test available, an HIV-1 RNA assay."

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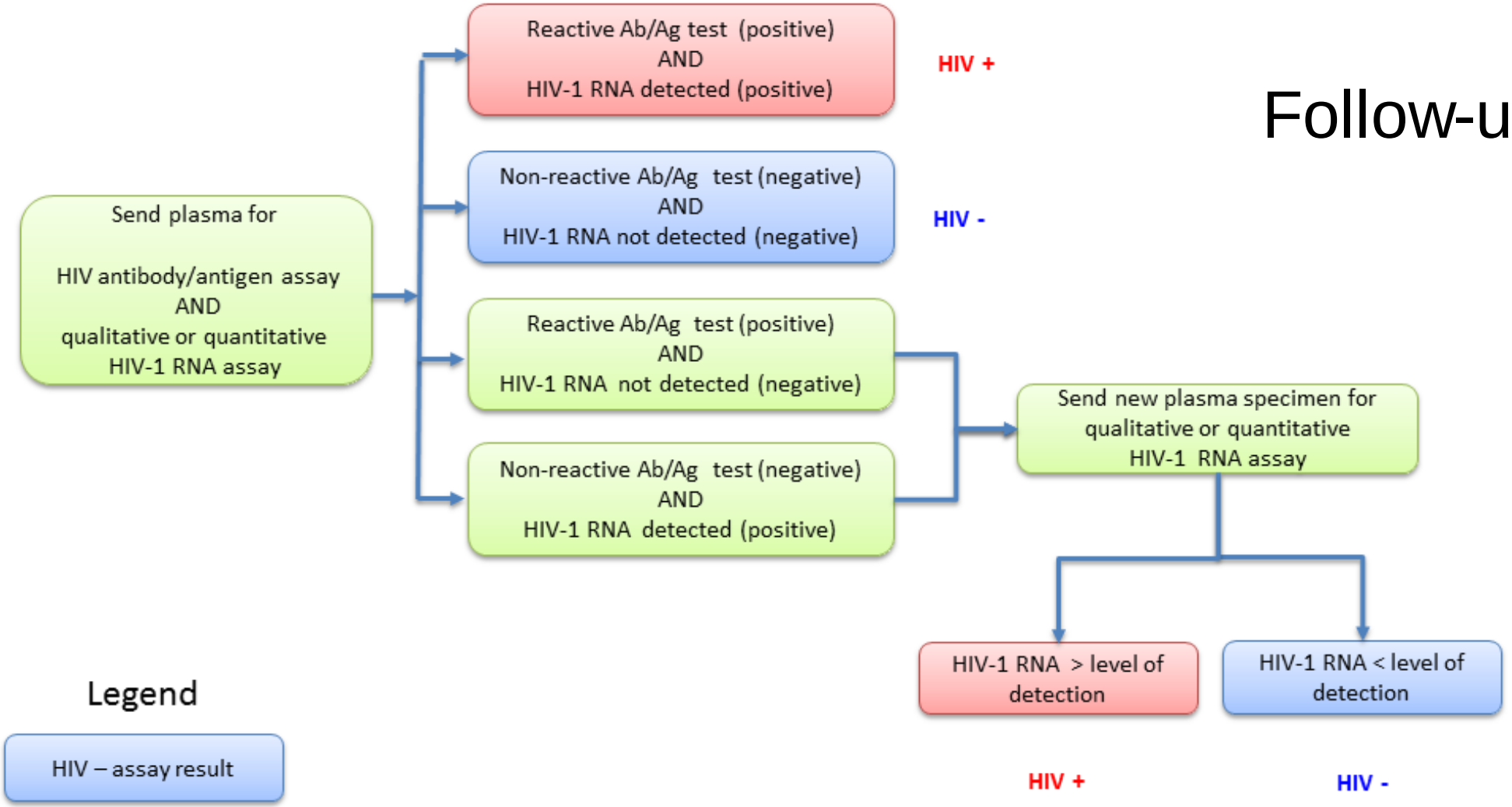
Summary of guidance for Cabotegravir

Follow-up care	**At follow-up visit 1 month after first injection** • HIV Ag/Ab test and HIV-1 RNA assay **At follow-up visits every 2 months (beginning with the third injection – month 3) provide the following:** • HIV Ag/Ab test and HIV-1 RNA assay • Access to clean needles/syringes and drug treatment services for PWID **At follow-up visits every 4 months (beginning with the third injection- month 3) provide the following:** • Bacterial STI screening[2] for MSM and transgender women who have sex with men[2] – oral, rectal, urine, blood **At follow-up visits every 6 months (beginning with the fifth injection – month 7) provide the following:** • Bacterial STI screening[1] for all heterosexually-active women and men – [vaginal, rectal, urine - as indicated], blood **At follow-up visits at least every 12 months (after the first injection) provide the following:** • Assess desire to continue injections for PrEP • Chlamydia screening for heterosexually active women and men – vaginal, urine **At follow-up visits when discontinuing cabotegravir injections provide the following:**

Follow-up HIV testing

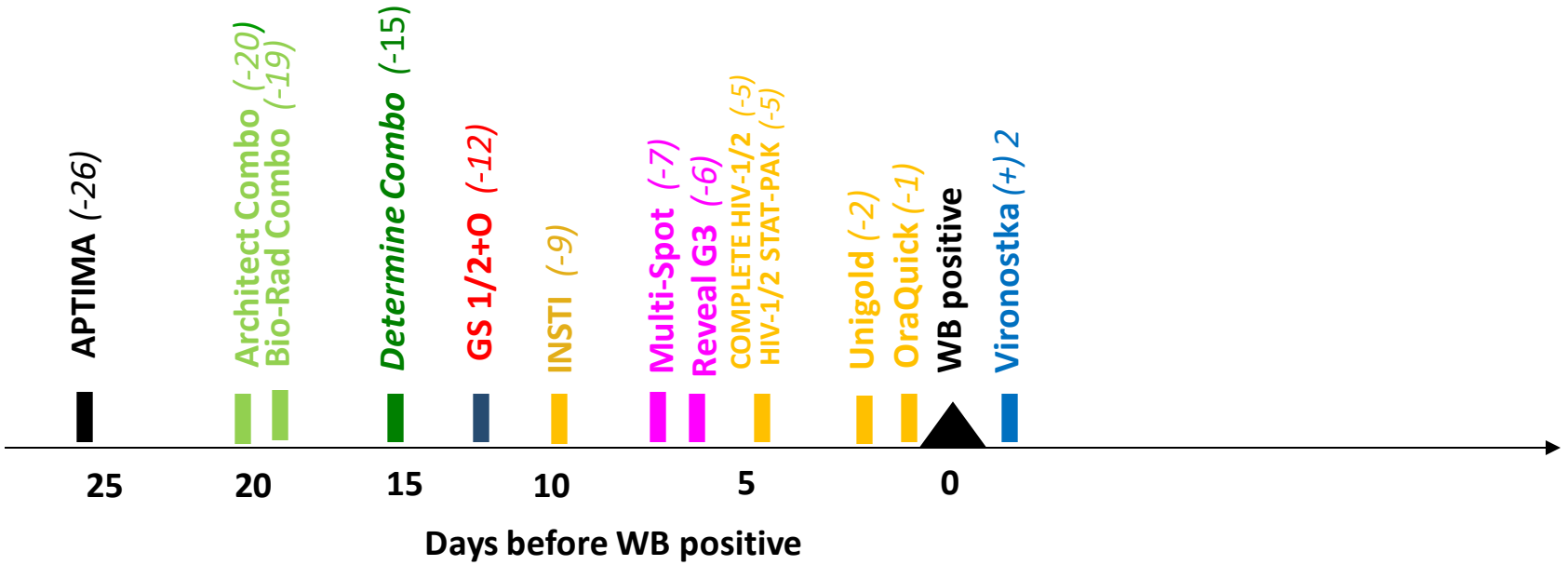
If the patient has taken oral PrEP or PEP medication in the past 3 months
OR
has received a cabotegravir injection in the past 12 months



Legend

- HIV – assay result
- HIV + assay result
- HIV Status Unclear

HIV test window periods relative to WB
166 plasma specimens from 17 seroconverters



Modified from *Masciotra et al, J Clin Virol 2011* and *Owen et al, J Clin Micro 2008*

slide courtesy of Bernie Branson

Delayed detection of HIV infection in oral PrEP

PrEP may lead to delayed seroconversion and false-negative tests, particularly with oral fluid tests

Curlin et al CID 2017; 64(12): 1663-69

- Delayed diagnosis occurred in 80 of 287 seroconverting individuals
- OFOQ conversion delay: median 98.5, range 14.5-547.5 days
- Delay was associated with low plasma RNA level

Donnell et al AIDS 2017; 31(14): 2007-16

- PrEP was associated with more frequent delayed diagnosis >100 days by POC Ab testing (17% v 6%)

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Delayed detection of HIV infection in CAB-LA PrEP (n=11)

	Baseline	Incident infection
Median delay 1st pos (range)	62 (28-72) days	98 (35-185 days)
Median log VL at 1st pos visit	4.4 (3.1-4.7)	2.1 (ND-2.9)
		5 of 7 detectable
Received CAB p infection	4/4	6/7

5 of these participants acquired INSTI resistance.

These 11 are 0.2% of the 4570 participants in the study.

Marzinke JID 2021

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Delayed detection of HIV infection in FTC/TDF in HPTN 083 (n=42)

	Baseline (n=3)	Incident infections (n=39)
Median delay 1st pos (range)	34 (14-36) days	31* (7-68 days*)
Median log VL at 1st pos visit	3.3 (2.1-4.7)	4.1 (NQ-4.3)**
	3/3 detectable	6/7 detectable

*excluding case with visit interval 372 days
**for the 6 participants with detectable VL

4 participants continued to receive oral PreP

5 M184V/I, 1 K65R

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PrEP USE DURING ACUTE HIV INFECTION IN A COMMUNITY SETTING COMPROMISES HIV DIAGNOSIS

Table: Clinical and diagnostic test results from 6 Thai MSM who started PrEP during acute HIV infection.
xG=x generation HIV antibody test, Gn= Geenius, □=nonreactive, ■=reactive, ND=not done

Partici-pant	# days on PrEP	HIV diagnosis	Pre-PrEP VL (cps/mL)	Pre-ART VL (cps/mL)	Pre-ART CD4 (cells/μL)	Week 0			Week 24			Week 48			
						2G	3G	4G	2G	3G	4G	2G	3G	4G	Gn
3145	7	NAAT	16,780	216	685	□	■	□	□	■	□	ND	ND	□	□
4634	2	NAAT	219	2,317	528	□	□	□	□	■	□	□	ND	□	□
5803	29	Ab	58	37,222	302	□	■	□	■	■	□	ND	ND	■	□
6313	91	Ab	223,361	389	690	■	■	□	■	■	□	ND	ND	□	□
6934	2	NAAT	32	276	739	□	□	□	□	□	□	□	□	□	□
7167	15	NAAT	317	8,802	521	□	□	□	■	■	■	ND	ND	ND.	□

WB = Indeterminate or NEG at all time points in all participants

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Colby et al. CROI 2021. Abstract #179

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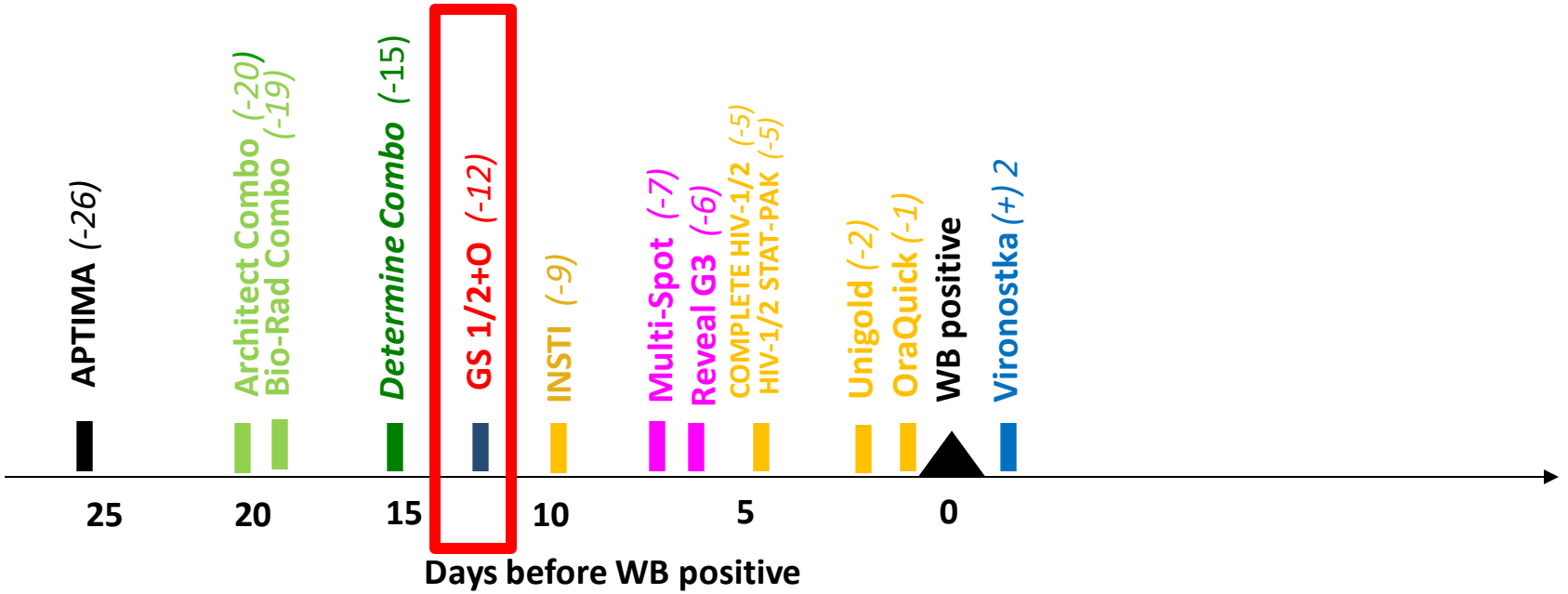

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slide courtesy of Bernie Branson

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Ability of Tests to Detect Acute HIV Cases San Francisco, 2003-2008

Test	Type	Detection of HIV in Screened Ab-/RNA+ specimens
ARCHITECT Ag/Ab Combo	Ag/Ab	48/55 (87%)
Determine Combo	Ag/Ab	31/57 (54%)
GS HIV-1/2 + O	Lab based Ab	20/58 (34%)
Unigold	POC Ab	14/54 (26%)
Multispot	Lab based Ab	11/58 (19%)

Pilcher et al PLoS One 2013

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Real issue: cost and back of envelope cost-effectiveness

- Some payers currently refusing to cover screening with HIV NAT in PrEP.
- CAB $164/test, 2283 participants
  - Baseline testing = 2283 X $164/ 4 participants = additional ~$95,000 per AHI identified
  - Followup = 9 NAT (Q2 months over 17 months) = $3,369,708
  - With 5 of 11 participants acquiring INSTI resistance = ~$700,000/case identified
  - And it is unclear if these cases of resistance could have been prevented.
- FTC/TDF, 2287 participants
  - Follow-up (Q3mo) = 2287 x $164 x 5 tests = $1,875,340
  - With 5 M184V/I = additional ~$375,000/case identified
- CAB-LA is likely not cost effective overall
  - ICER is >$100,000 QALY c/w generic PrEP unless CAB<$4100/yr (currently list $3700/dose)
  - Neilan 2022 Ann Internal Med

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Acknowledgment

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