HIV update : 2021

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- The activity planners and speaker do not have any financial relationships with commercial entities to disclose.

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Objectives

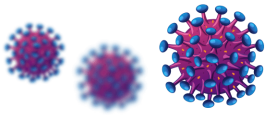
- Recognize the global, national and local epidemiology of HIV
- Discuss “Ending the HIV Epidemic: A Plan for America”
- Describe the indications for HIV screening and characteristics of the HIV antibody test
- Recognize the role of test and treat in rapid initiation of antiretroviral therapy and current HIV treatment guidelines
- Report new HIV therapy options
- Identify current HIV prevention

HIV

- Retrovirus that infects and destroys CD4 cells
- CD4 count: normal range is ~460-1600 cells/mm^3
- HIV viral load (VL): goal once patient is on medications is <20 "undetectable"

WHAT IS HIV?

Human Immunodeficiency Virus (HIV) is a virus that attacks cells that help the body fight infection.



There's no cure, but it is **treatable** with medicine.

HIV.gov

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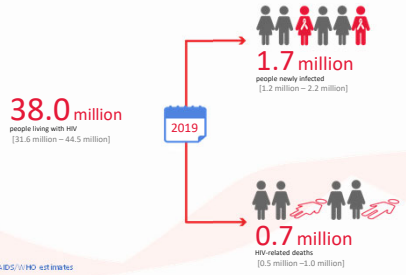
Summary of the global HIV epidemic, 2019



Source: UNAIDS/WHO estimates

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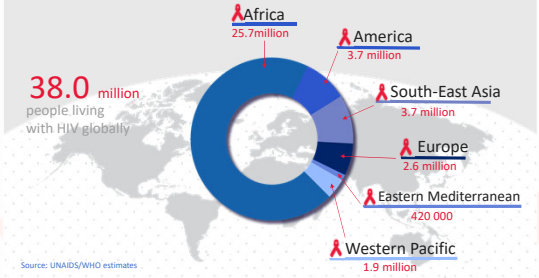
People living with HIV by WHO region, 2019



Source: UNAIDS/WHO estimates

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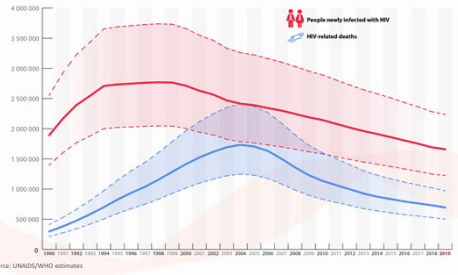
Decline in HIV incidence and mortality over time



Source: UNAIDS/WHO estimates

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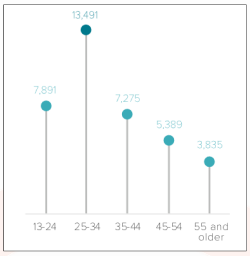
HIV in the US

- In 2018, there were 37,286 new HIV diagnoses in the US
- 69% were among gay and bisexual men, 24% heterosexuals, 7% people who inject drugs (PWID)



Number of new HIV diagnoses was highest among people aged 25 to 34.

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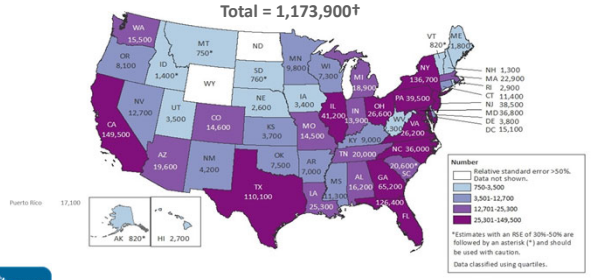
https://www.cdc.gov/hiv/pdf/statistics/overview/cdc-hiv-us-ataglance.pdf

Estimated HIV Prevalence among Persons Aged ≥13 years, by Area of Residence 2018—United States

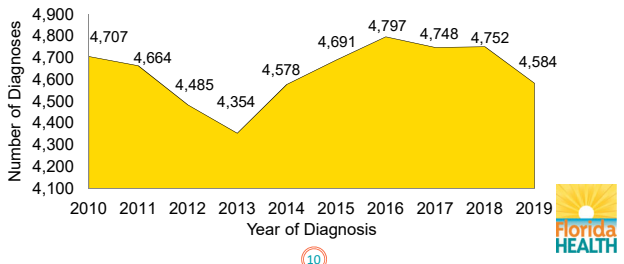
Total = 1,173,900†



Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Estimates rounded to the nearest 100 for estimates >1,000 and to the nearest 10 for estimates ≤1,000 to reflect model uncertainty. Estimates for the year 2018 are preliminary and based on deaths reported to CDC through December 2019. Estimates for Alabama, Oklahoma, and South Carolina should be interpreted with caution due to incomplete death ascertainment.
†Total estimate for the United States does not include data for Puerto Rico.

Diagnoses of HIV, 2010–2019, Florida

2018–2019 = -4% change; 2015–2019 = -2% change



Florida HEALTH

10

Impact of COVID-19 on HIV diagnoses in Florida

- From January 1-September 25 2020, there were 3217 cases of HIV reported to the Florida Department of Health
- This is a 14% decrease in the number of HIV cases

Table 2: Reported HIV Diagnoses by Race/Ethnicity and Year of Report, Florida (2019–2020)

Race/Ethnicity	2019 YTD N	2019 YTD % of Total	2020 YTD N	2020 YTD % of Total	2019–2020 % Change
White	901	24.1%	836	26.0%	-7.2%
Black	1,451	38.8%	1,217	37.8%	-16.1%
Hispanic	1,315	35.2%	1,085	33.7%	-17.5%
Other	72	1.9%	79	2.5%	9.7%
Total	3,739	100.0%	3,217	100.0%	-14.0%

*Provisional data as of 9/25/20

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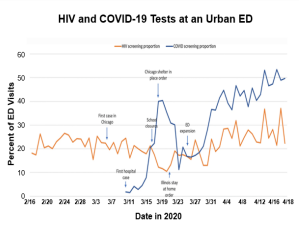
Coronavirus Disease 2019 (COVID-19) and the HIV Epidemic in Florida, Year to Date 2020

Routine Screening for HIV During the COVID-19 Pandemic

- Urban ED preparations
  - Established a large temporary space for screening, testing, and treatment of patients with influenza-like illness who were considered likely to be discharged home
  - Continued HIV screening of patients was incorporated into the design of this secondary ED space, with a station for lab draws designated for HIV screening
- HIV testing (percent of ED visits) was maintained during first 1.5 months
  - Through 4/18: 6 persons tested positive for HIV
- It is important to maintain HIV screening and linkage to care, even in the face of the COVID-19 pandemic
  - HIV elimination initiatives nationwide require expansion and intensification of HIV screening and linkage to care efforts



- Stanford KA, Friedman EE, Schmitt J, et al *AIDS Behav*. 2020;24:2757-2759.

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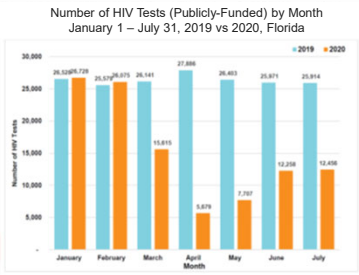
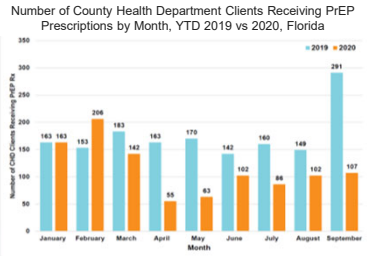
Florida HIV Testing

- Publicly-funded HIV testing in Florida ranges from 310,000-340,000 annually
- Average tests/month for 2019: 26,346
- Average test/month for 2020: 15,217



PrEP Prescriptions

- **2019**: 1574 prescriptions
- **2020**: 1026 prescriptions
- 34.8% decrease in number of prescriptions Jan-Sept 2019 vs 2020



What's next?

- Continue to monitor the impact COVID-19 is having on testing, diagnosis and treatment of HIV
- Evaluate innovative strategies/activities to help reduce disruptions in HIV care

Ending the HIV Epidemic: A Plan for America

GOAL:

75% reduction in new HIV infections in 5 years and at least **90%** reduction in 10 years.

HHS will work with each community to establish local teams on the ground to tailor and implement strategies to:

- **Diagnose** all people with HIV as early as possible.
- **Treat** the infection rapidly and effectively to achieve sustained viral suppression.
- **Prevent** new HIV transmissions by using proven interventions, including pre-exposure prophylaxis (PrEP) and syringe services programs (SSPs).
- **Respond** quickly to potential HIV outbreaks to get needed prevention and treatment services to people who need them.

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When should I test for HIV?

- In 2006, the CDC issued guidelines advocating routine voluntary HIV screening of all patients aged 13 to 64 years as a normal part of medical care, without the need for signed consent or counseling:

  "Opt-out Testing"

- On July 1, 2015, a Florida law went into effect that removed need for written consent for HIV testing in healthcare settings

CDC defines opt-out screening as: "Performing HIV screening after notifying the patient that 1) the test will be performed and 2) the patient may elect to decline or defer testing. Assent is inferred unless the patient declines testing" [Branson, Handsfield, et al. 2006

New Orders

HIV 1/2 ANTIGEN/ANTIBODY, FOURTH GENERATION W/RFL
Routine, ONCE First occurrence Today at 1345

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Some Need More Frequent Screening

- Screen at least annually
  - People who inject drugs and their sex partners
  - People who engage in transactional sex
  - Sex partners of people with HIV infection
  - Sexually active gay, bisexual, and other men who have sex with men (every 3-6 month testing may be beneficial)
  - Heterosexuals who themselves or whose sex partners have had ≥1 sex partner since their most recent HIV test

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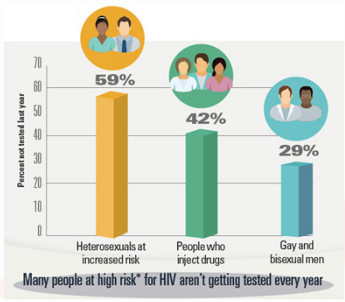
HIV Screening in Pregnant Women

- Universal Opt-out screening
- Address reasons for declining test
  - Document declinations in the medical records
- Timing of HIV test
  - Early during pregnancy
  - Repeat in third trimester, ideally < 36 weeks gestation
  - Rapid testing at time of delivery if indicated

MMWR 2006;55(RR14):1-17.
ACT AGAINST AIDS
ONE TEST TWO LIVES
Get tested for HIV. For you and baby.™

HIV Testing



CDC.gov. Vital Signs, November/December 2017.

How Do We Test For HIV Infection?

- HIV Antigen/Antibody Test (4th generation testing)
  - Can detect acute HIV infection
- HIV Antibody Test (3rd generation)
- Rapid HIV Test
  - Blood or sputum
  - Requires confirmation
- HIV viral load
  - Can detect acute HIV infection

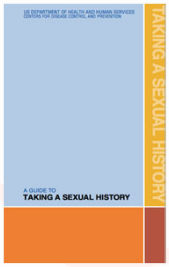
Starting the Conversation

- **" I'm going to ask you a few questions** *about your sexual health. Since sexual health is very important to overall health, I ask all my patients these questions.*
- **Before I begin,** *do you have any questions or sexual concerns you'd like to discuss? "*

Taking a Sexual Health History

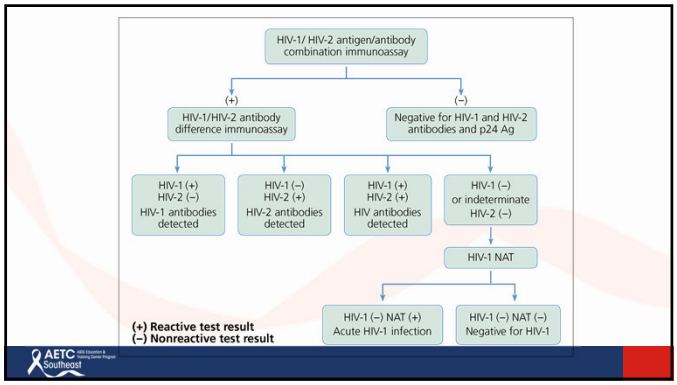
- Assess your own comfort
- Make your patient feel comfortable
- Use neutral and inclusive terms
- Avoid assumptions
- Try not to react overtly
- Rephrase your questions
- Ask for correct pronouns and terminology

Taking a Sexual History



- Make it a normal part of each visit
- The Five "P"s
  - Partners
  - Practices
  - Protection from STDs
  - Past history of STDs
  - Prevention of pregnancy

CDC.gov. Available at https://www.cdc.gov/std/treatment/sexualhistory.pdf



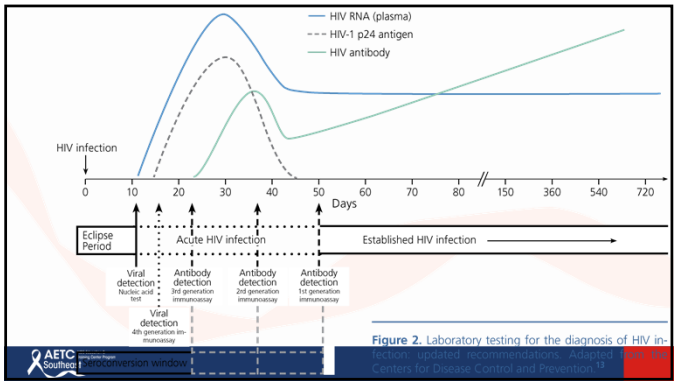


Figure 2. Laboratory testing for the diagnosis of HIV infection: updated recommendations. Adapted from the Centers for Disease Control and Prevention.[13]

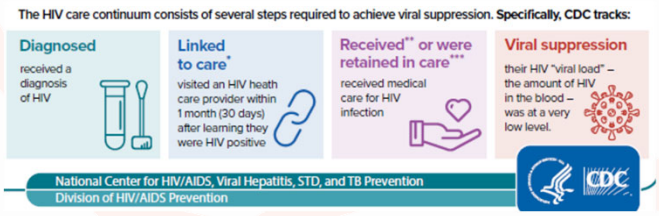
What if the HIV test is negative?

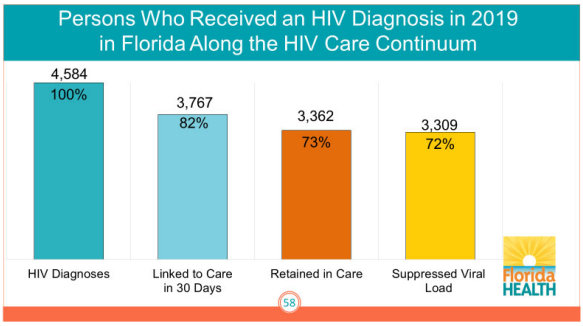
- Face to face notification of negative test result is not required
- Consider if patient at ongoing risk of HIV acquisition
  - Counsel on risk reduction strategies
  - Provide condoms
  - PrEP evaluation and offer
  - Make aware of HIV Post-exposure prophylaxis (PEP)

What happens if the test is positive?

- Positive rapid tests require confirmation
- Results should be communicated confidentially through personal contact
- Provide counseling
  - HIV is a manageable disease
  - Discuss HIV risk reduction
  - Discuss ways to handle the emotional consequences of a positive result
- Inform the patient that they might be contacted by health department staff

The HIV Care Continuum





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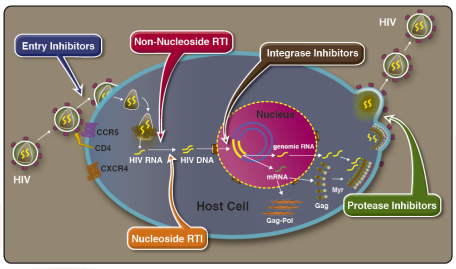
Update – HIV Treatment

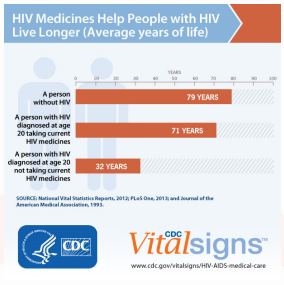
Antiretroviral Mechanism of Action



http://depts.washington.edu/nwaetc/Pill_Chart.pdf

Treatment Goals

- Maximally and durably suppress plasma HIV RNA
- Restore and preserve immunologic function
- Reduce HIV-associated morbidity and prolong the duration and quality of survival
- Prevent HIV transmission *"Treatment as Prevention"*



https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv/9/treatment-goals

Predictors of Virologic Success

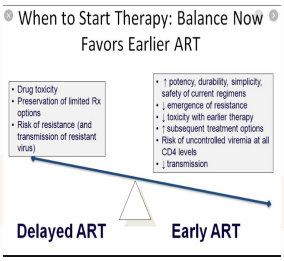
- Low baseline viremia
- High potency of the ARV regimen
- Tolerability of the regimen
- Convenience of the regimen
- Excellent adherence to the regimen

Considerations When Starting Antiretroviral Therapy

- Who to start on antiretroviral therapy-
- When to start antiretroviral therapy –
- What antiretroviral to start
- When to switch antiretroviral therapy
- What to switch to

Who to Start on Antiretroviral Therapy?

	AID's symptoms	CD4<200	CD4 200-350	CD4 350-500	CD4 350-500
US DHHS 2018		Recommended			
IAS-USA 2018		Recommended			
EACS 2018		Recommended			
UK 2016		Recommended			
WHO 2016		Recommended			



Current Recommendations for Same-Day ART Initiation

- Rapid start or initiating ART on same day as HIV is diagnosed is an emerging strategy to **reduce loss to follow-up and decrease time to viral suppression**
- Evidence base limited but growing, and outcomes favorable thus far

DHHS[1]	Recommended	
	WHO[2]	IAS-USA[3]
▪ **Investigational** – Resource intensive – Long-term benefits not yet proven in the US	▪ **Recommended** where feasible	▪ Start ART as soon as possible**, including immediately after diagnosis,** if patient is ready

Slide credit: clinicaloptions.com

Florida's Test and Treat Program:

- Instituted in February 2017 at community health departments
- Provides:

1. Immediate linkage to HIV care
2. Initiation of antiretroviral therapy (ART) at time of diagnosis and/or at the time of returning to care after a gap in services

FDOH HIV/AIDS Section Test and Treat Protocol February 2018

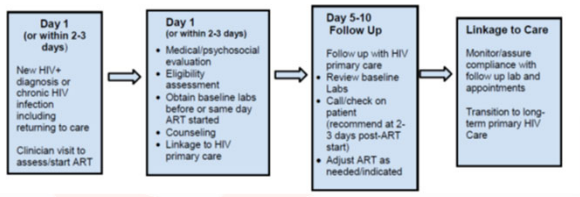
Eligibility for Test and Treat:

Newly diagnosed HIV patients defined as:

- Acute Infection: antibody (-)/RNA (+)
- Recent Infection: antibody (+) with last documented antibody (-) within prior 6 months
- Chronic Infection: antibody positive with no prior HIV test result or last documented antibody (-) > 6 months ago (inclusive of patients lost to follow up and returning to care)

FDOH HIV/AIDS Section Test and Treat Protocol February 2018

Test and Treat Timeline:



FDOH HIV/AIDS Section Test and Treat Protocol February 2018

What Antiretroviral Therapy to Start –Considerations:

- Viral load and CD4 count
- HIV resistance test result
- Drug interactions
- Potential side effects
- Pill burden
- Access and Cost

T&T MEDICATIONS

Brand Name	Generic Name	Therapeutic Class	Pharmacologic Class
BIKTARVY	bictegravir/emtricitabine/tenofovir alafenamide	antiretroviral	INSTI/NRTI combo
DESCOVY	emtricitabine/tenofovir alafenamide	antiretroviral	NRTI Combo
SYMTUZA	darunavir/cobicistat/emtricitabine/tenofovir alafenamide	antiretroviral	PI/NRTI Combo
TIVICAY	dolutegravir	antiretroviral	INSTI
TRUVADA[1]	emtricitabine/tenofovir disoproxil fumarate	antiretroviral	NRTI Combo
ISENTRESS[1,2]	raltegravir	antiretroviral	INSTI

Test and Treat and Retain in Care Guidance (floridahealth.gov)

Table 6a. Recommended Antiretroviral Regimens for Initial Therapy

Recommended Initial Regimens for Most People with HIV

Recommended regimens are those with demonstrated durable virologic efficacy, favorable tolerability and toxicity profiles, and ease of use.

INSTI plus 2 NRTIs:
Note: For individuals of childbearing potential, see Table 6b before prescribing one of these regimens.

- BIC/TAF/FTC **(AI)**
- DTG/ABC/3TC **(AI)**—**if HLA-B*5701 negative**
- DTG plus (TAF or TDF)* plus (FTC or 3TC) **(AI)**
- RAL plus (TAF or TDF)* plus (FTC or 3TC) (**BI** for TDF/[FTC or 3TC], **BII** for TAF/FTC)

INSTI plus 1 NRTI:

- DTG/3TC **(AI)**, except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available

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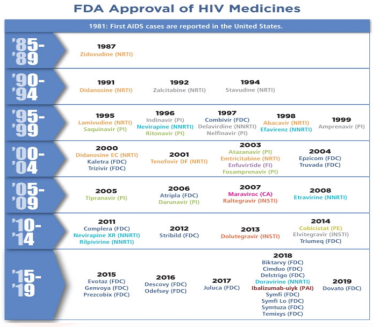
https://clinicalinfo.hiv.gov/sites/default/files/inline-files/AdultandAdolescentGL.pdf



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Single Tablet Combination Regimens

- Atripla® (EFV/TDF/FTC)
- Biktarvy® (BIC/TAF/FTC)
- Complera® (RPV/TDF/FTC)
- Delstrigo™ (DOR/TDF/3TC)
- Dovato® (DTG/3TC)
- Genvoya® (EVG/c/TAF/FTC)
- Juluca® (DTG/RPV)
- Odefsey® (RPV/FTC/TAF)
- Stribild® (EVG/c/TDF/FTC)
- Symfi™ and Symfi Lo® (EFV/TDF/3TC)
- Symtuza® (DRV/c/TAF/FTC)
- Triumeq® (DTG/ABC/3TC)

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Example of Studies of Recommended INSTIs as First-Line ART Regimens

Trial	INSTI Regimen	Comparator	Wks	Results	Outcome vs Comparator
GS-1489[1]	**BIC**/FTC/TAF	DTG/ABC/3TC	96	88 vs 90%	Noninferior
GS-1490[2]	**BIC**/FTC/TAF	DTG + FTC/TAF	96	84 vs 86%	Noninferior
SINGLE[3]	**DTG** + ABC/3TC	EFV/FTC/TDF	144	71 vs 63%	Favors INSTI
FLAMINGO[4]	**DTG** + 2 NRTIs	DRV + RTV + 2 NRTIs	96	80 vs 68%	Favors INSTI
SPRING-2[5]	**DTG** + 2 NRTIs	RAL + 2 NRTIs	96	81 vs 76%	Noninferior
GEMINI[6]	DTG + 3TC	DTG plus TDF/FTC	96	86 vs 89.5%	Noninferior

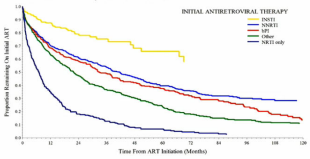
- No resistance mutations (INSTI or NRTI) in treatment naïve studies of dolutegravir or bictegravir
- Rates of discontinuation for AEs numerically lower with INSTIs vs PIs or NNRTIs
- Modest difference in adverse events between arms in head-to-head comparisons of dolutegravir with bictegravir if dolutegravir given with abacavir

1. DA Wohl et al. Lancet HIV 6 (6), e355-e363. Jun 2019. 2. HJ Stellbrink et al. Lancet HIV 6 (6), e364-e372. Jun 2019. 3. Walmsley. JAIDS. 2015;70:515. 4. Molina. Lancet HIV. 2015;2:e127. 5. Raffi. Lancet Infect Dis. 2013;13:927. 6. Cahn. IAS 2019. Abstr WEAB0404LB.

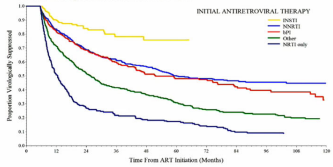
Increased Persistence Of Initial Art With INSTI-containing Regimens

Thibaut Davy, Sonia Napravnik, Oksana Zakharova, Joseph J. Eron

Time on Initial ART, UCHCC 1996-2015



Time to Virologic Failure, UCHCC 1996-2015



	Discontinuation HR (95% CI)	Virologic failure HR (95% CI)
INSTI	0.49 (0.35, 0.69)	0.70 (0.46, 1.06)
bPI	1.24 (1.05, 1.47)	1.24 (1.01, 1.53)
Other	1.47 (1.24, 1.75)	1.21 (0.99, 1.46)
NRTI	2.98 (2.38, 3.74)	1.72 (1.35, 2.19)
NNRTI	Ref.	Ref.

Davy-Mendez T, Eron JJ, Zakharova O, Wohl DA, **Napravnik S.** J Acquir Immune Defic Syndr. 2017 Oct 1;76(2):111-115.

Low Virologic Failure and Treatment Emergent Resistance with Dolutegravir and Bictegravir

Trial Name	Follow-up, Wks	Treatment Arm	Virologic Failure, n (%)	Treatment-Emergent Primary Mutations, n
SPRING-2[1]	96	DTG + 2 NRTI (n = 411)	22 (5)	0
		RAL + 2 NRTIs (n = 411)	29 (7)	1 (INSTI), 4 (NRTI)
SINGLE[2]	144	DTG + ABC/3TC (n = 414)	39 (9)	0
		EFV/TDF/FTC (n = 419)	33 (8)	1 (NRTI),6 (NNRTI)
FLAMINGO[3]	96	DTG + 2 NRTI (n = 242)	2 (< 1)	0
		DRV/R + 2 NRTI(n = 242)	4 (2)	0
GS-1489[4]	96	BIC/F/TAF (n =316)	3 (1)	0
		DTG/ABC/3TC (n= 315)	8 (2.5)	0
GS-1490[5]	96	BIC/F/TAF (n =320)	14 (4)	0
		DTG + TAF/FTC (325)	4 (1)	0
Gemini 1 and 2[6]	144	DTG/3TC (n= 716)	6	0
		DTG + TDF/FTC (n = 717)	4	1

Raffi F, et al. *Lancet Infect Dis.* 2013;13:927-935. 2. Pappa K, et al. ICAAC 2014. Abstract H-647a. 3. Molina JM, et al. Glasgow HIV 2014. Abstract O153. DA Wohl et al. Lancet HIV 6 (6), e355-e363. Jun 2019. 5. HJ Stellbrink et al. Lancet HIV 6 (6), e364-e372. Jun 2019. 6. Cahn. IAS 2019. Abstr

Integrase Inhibitors Considerations

- There maybe transmitted resistance with integrase resistance but very rare
- Women of childbearing potential – risk of birth defects continues to fall
- Possible weight gain – now convincingly associated with weight gain

Tenofovir alafenamide (TAF)

- Tenovofir alafenamide (TAF) (Vemlidy®) is an oral prodrug of tenofovir, which is hydrolyzed to tenofovir in plasma then converted to its active form intracellularly
- This results in lower plasma concentrations and higher intracellular concentrations than tenofovir disoproxil fumarate (TDF) (Viread®)
- TAF: Lower potential for adverse kidney issues and bone effects

Effect of Switching ART on Weight and Metabolic Changes

Study	Switch	Weight/Metabolic Changes
OPERA (observational) Mallon AIDS 2020, OAB0604	TDF to TAF	2-4.5 kg/yr; greatest in those also switching to newer INSTI (DTG, BIC)
TRIO (observational) McComsey, IDWeek, 2020, LB7	TDF or ABC to TAF	Greater weight gain after switching from TDF to TAF than after switching from ABC to TAF
TANGO (randomized) van Wyk AIDS 2020 #0606	TAF-based regimen to DTG/3TC	Weight: no difference DTG/3TC: Improved lipids, insulin resistance, especially after switching from boosted regimen

Dual therapy

- GEMINI-1,-2 and TANGO: Virologic Outcomes With DTG + 3TC as Initial or Switch Therapy
- **GEMINI-1,-2:** Initial therapy with DTG + 3TC noninferior to DTG + TDF/FTC for primary endpoint of HIV-1 RNA < 50 c/mL
- **TANGO:** Switch to DTG/3TC noninferior to continued TAF-based ART for primary endpoint of HIV-1 RNA ≥ 50 c/mL

Dual Therapy Treatment Option

Dolutegravir/lamivudine→Dovato®

- Treatment naïve
- Switch from three drug regimen
- No Hep B, NRTI/Integrase mutations or history of treatment failure

Dovato
dolutegravir 50 mg/
lamivudine 300 mg tablets

How Commonly Will 2 drugs Be Used

- Multiple unboosted combinations approved or in development (DTG/3TC. DTG/ RPV and cabotegravir/RPV)
- Few differences yet in AE or long term outcomes
- No substantial cost differences
- Fewer metabolic effects – no TAF?

When to switch antiretroviral therapy ?

Reasons

- adverse events,
- drug-drug or drug-food interactions
- pill burden, cost, simplification
- virologic failure

When to switch antiretroviral therapy ?

Virologic failure

- VL undetectable – drug resistance unlikely
- VL <200 – controversial; one large retrospective analysis found no increased risk of failure
- VL persistently >200 –drug resistance often associated (particularly >500)
- Caution with change to newer VL assays and “blips”

Guideline Recommendations for Switching ART in Virologically Suppressed Patients

- Principle of switching: Maintain viral suppression without jeopardizing future treatment options
- In general, if the older regimen is well tolerated without evidence of toxicity, there is little

DHHS[2]	IAS-USA[3]	EACS[4]	WHO[5]
Consider switching: ▪ Simplify regimen ▪ Enhance tolerability and/or decrease toxicity ▪ Prevent/mitigate DDIs ▪ Eliminate food or fluid requirements ▪ Reduce costs	*Proactive switching:* ▪ From TDF- to TAF-based ART if high risk of renal/bone toxicity *Consider switching:* ▪ If evidence of/potential for chronic toxicity, DDIs, or emergent AEs ▪ From 3-drug to 2-drug regimens if no prior VF	*Indications:* ▪ Documented toxicity ▪ Prevention of long-term toxicity ▪ DDIs (including with DAAs for HCV) ▪ Planned pregnancy ▪ Aging and/or comorbidity ▪ Simplification	▪ Consider substitution according to national recommendations in the context of drug supply and patient choice

What antiretroviral therapy to change to

- Review ART history
- Assess adherence, tolerability, and drug interactions
- Perform resistance testing while on ART (or within 4 weeks of d/c of ART)
- Identify susceptible drugs/drug classes
- Consider newer agents (expanded access or clinical trials)
- Design a regimen with 2 (preferably 3) fully active agents

ART: What NOT to use as Initial therapy

Nucleosides (NRTI)
- 3 or 4 all NRTI combination regimens
- older drugs (didanosine,stavudine, zidovudine)

Non-nucleosides (NNRTI)
- older drugs (delavirdine,nevirapine)
- etravirine in initial regimens

Protease Inhibitors (PI)
- unboosted PIs
- older drugs (fosamprenavir,indinavir, lopinavir,nelfinavir, ritonavir [except as booster], saquinavir

Entry inhibitors (EI)
- enfuvirtide, maraviroc, ibalizumab

ART: What NOT to use (EVER)

- all monotherapy
- all-NRTI regimens
- 2-NNRTI regimens
- unboosted PIs
- older drugs: delavirdine (DLV), didanosine (ddI), indinavir (IDV), nelfinavir (NFV), and stavudine (d4T)
- two of the same thing: cobi + RTV, FTC + 3TC, TDF + TAF
- nevirapine in women (CD4>250), men (CD4 >400)
- ETR + [FPV/r or TPV/r] (unfavorable drug interactions)

Why Does Treatment Fail Patients?

- ADHERENCE
- Baseline resistance or cross-resistance
- Prior use of antiretroviral therapy
- Less potent antiretroviral regimens
- Drug levels and drug interactions
- Tissue reservoir penetration
- Provider inexperience
- Other

Importance of Adherence to ART

- Adherence is strongly correlated with
  - **Suppression of HIV-1 RNA**: greater adherence associated with higher likelihood of viral suppression
  - **Reduced rates of drug resistance**: poor adherence can allow selective pressure and expansion of resistant virus in the absence of full viral suppression
  - **Increased survival**: lack of adherence to ART a significant predictor of progression to AIDS and death
  - **Improved quality of life**

Enhancing Engagement in Treatment and Care

- **Poor engagement in care is a predictor of higher mortality among patients with HIV infection**
  - Mortality ~ 50% higher among patients with poor retention in care
- Developing an effective patient–provider relationship is key to enhancing patient engagement in care
  - Endeavor to encourage open and frank communication
  - Devote sufficient time to addressing needs of each patient
  - Shorten wait time from patient's request to schedule an initial HIV care appointment until the date of the initial HIV medical visit

Long acting antiretrovirals – cabotegravir

- Now FDA approved
- Integrase inhibitor similar to dolutegravir
- Similar resistance profile
- Initially will require an oral lead in
- Injected into Gluteus Medius
- Exciting -Nanotechnology formulation : SC and IM injections
- Safety- mostly injection site reactions and nodules with SC dosing
- RPV long acting needs cold chain

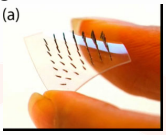
Cabotegravir: Phase 3 trials

Study (reference)	Study population	Design	Result (week 48)
FLAIR Orkin NEJM 2020;382:1124-1135	Rx-naïve adults (N=629)	ABC/3TC/DTG X 20 wks → CAB + RPV (oral X 4 wks, then IM monthly) or continue oral regimen (non-inferiority Δ6%)	VS >93%; CAB + RPV **non-inferior** to oral regimen Glasgow 2020: 144 wks
ATLAS Swindells NEJM 2020;382:1112-1123	Adults with VS on 2 NRTI + PI, NNRTI, or INSTI (N=616)	continue ART or change to CAB + RPV (oral X 4 weeks, then IM monthly) (non-inferiority Δ6%)	VS >92%; CAB + RPV **non-inferior** to oral regimen Glasgow 2020: 96 wks
ATLAS-2M Overton CROI 2020 Abstract 34	Adults on SOC ART or CAB + RPV LA with VL <50 (N=1045)	CAB 400 + RPV 600 LA IM q4 wks or CAB 600 + RPV 600 LA IM q8 wks (non-inferiority Δ4%)	VS >93%; CAB + RPV q8 wks **non-inferior** to q4 wks

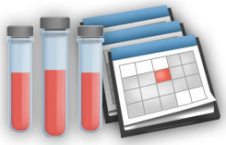
Drugs in the Pipeline

- CAB – Prodrug in Rhesus Macaques – Nano formulated
- Has extended release Q6 month dosing
- Cabotegravir – Micro needle Patches

(a)



Pre-exposure Prophylaxis



PrEP IS AN HIV PREVENTION METHOD IN WHICH PEOPLE WHO DO NOT HAVE HIV INFECTION TAKE A PILL DAILY TO REDUCE THEIR RISK OF BECOMING INFECTED

ONLY PEOPLE WHO ARE HIV-NEGATIVE SHOULD USE PrEP. A NEGATIVE HIV TEST IS REQUIRED BEFORE STARTING PrEP AND THEN EVERY 3 MONTHS WHILE TAKING PrEP.

AETC AIDS Education & Training Center Program Southeast

http://aids.gov/hiv-aids-basics/prevention/reduce-your-risk/pre-exposure-prophylaxis

Why PrEP?

- Estimated 50,000 new HIV infections each year in the US
  - No cure
  - No effective vaccine yet
- In multiple studies, there is a significantly decreased risk of HIV acquisition in those who took PrEP consistently

Transmission Route	Effectiveness Estimate	Interpretation
Sexual	~99%	Very high levels of adherence to PrEP ensures maximum effectiveness.
Injection drug use	74% – 84%	These estimates are based on tenofovir alone and not necessarily when taken daily. The effectiveness may be greater for the two-drug oral therapy and if used daily.

CDC.gov. PrEP FAQs. Available at https://www.cdc.gov/hiv/clinicians/prevention/prep.html. Accessed 12.15.2019.

ESTIMATED NUMBER OF ADULTS WHO COULD POTENTIALLY BENEFIT FROM PREP, UNITED STATES, 2015

	Gay, bisexual, or other men who have sex with men	Heterosexually active adults	Persons who inject drugs	Total by race/ethnicity
Black/African American, non-Hispanic	309,190	164,660	26,490	500,340
Hispanic/Latino	220,760	46,580	14,920	282,260
White, non-Hispanic	238,670	36,540	28,020	303,230
Total who could potentially benefit from PrEP	**813,970**	**258,080**	**72,510**	**1,144,550**

Notes: PrEP=pre-exposure prophylaxis; data for "other race/ethnicity" are not shown

CDC U.S. Department of Health and Human Services Centers for Disease Control and Prevention

Smith, DK., et al. CROI 2018; March 4-7, Boston, MA, USA.

AETC AIDS Education & Training Center Program Southeast

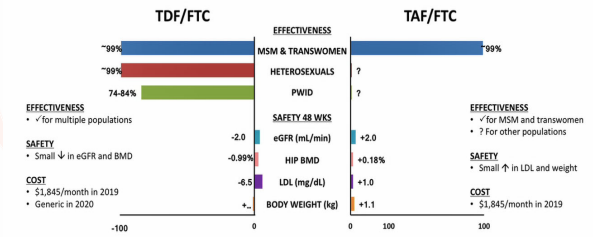
2 FDA-Approved Medications for PrEP

Each consists of two drugs combined in a single oral tablet taken daily

1. Emtricitabine (F) 200 mg combined with tenofovir disoproxil fumarate (TDF) 300 mg (F/TDF – brand name **Truvada**®)
2. Emtricitabine (F) 200 mg combined with tenofovir alafenamide (TAF) 25 mg (F/TAF – brand name **Descovy**®)

Approved to prevent HIV infection in adults and adolescents weighing at least 77 pounds (35 kg)

Which medication should I prescribe for daily PrEP



F:\da.gov.media\129607\download-cdc.gov\hiv\risk\estimates\prevention strategies.html

Table 1: Summary of Guidance for PrEP Use

	Men Who Have Sex with Men	Heterosexual Women and Men	Persons Who Inject Drugs
Detecting substantial risk of acquiring HIV infection	HIV-positive sexual partner Recent bacterial STI† High number of sex partners History of inconsistent or no condom use Commercial sex work	HIV-positive sexual partner Recent bacterial STI‡ High number of sex partners History of inconsistent or no condom use Commercial sex work In high HIV prevalence area or network	HIV-positive injecting partner Sharing injection equipment
Clinically eligible	Documented negative HIV test result before prescribing PrEP No signs/symptoms of acute HIV infection Normal renal function; no contraindicated medications Documented hepatitis B virus infection and vaccination status		
Prescription	Daily, continuing, oral doses of TDF/FTC (Truvada), ≤90-day supply		
Other services	Follow-up visits at least every 3 months to provide the following: HIV test, medication adherence counseling, behavioral risk reduction support, side effect assessment, STI symptom assessment At 3 months and every 6 months thereafter, assess renal function Every 3-6 months, test for bacterial STIs		
	Do oral/rectal STI testing	For women, assess pregnancy intent Pregnancy test every 3 months	Access to clean needles/syringes and drug treatment services

STI: sexually transmitted infection

Preexposure Prophylaxis for the Prevention of HIV Infection in the United States – 2017 Update Clinical Practice Guideline

Ready, Set, PrEP

- Launched by the US Department of Health and Human Services on 12/3/19
- To qualify, patients must:
  -test negative for HIV
  -have a valid prescription from a healthcare provider
  -not have prescription drug coverage
- Beginning no later than March 30, 2020, patients may obtain PrEP through CVS, Walgreens, Rite Aid or mail order all at no cost
- https://www.getyourprep.com/ or 855-447-8410
- HIV.gov Locator

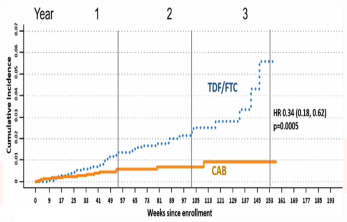
HPTN 083- PrEP with IM CAB vs TDF/FTC

- Phase 3 randomized double blinded HIV PrEP international study
- Study population : High risk adult MSM/TGW (n=4750)
- Study population 67% 30 years
- 12 % TGW
- Cabotegravir oral lead in 5 weeks ->IM q2 months vs TDF/FTC po daily

HPTN 083- PrEP with IM CAB vs TDF/FTC

- Results :
- DSMB stopped study early
- New HIV infections 13 (CAB) vs 39(TDF/FTC)
- HIV incidence 0.41(CAB) vs 1.22(TDF/FTC)

Conclusion CAB non inferior and superior



Original Investigation

Sexual Activity Without Condoms and Risk of HIV Transmission in Serodifferent Couples When the HIV-Positive Partner Is Using Suppressive Antiretroviral Therapy

Alison J. Rodger, MD; Valentina Cambiano, PhD; Tina Bruun, RN; Pietro Vernazza, MD; Simon Collins; Jan van Lunzen, PhD; Giulio Maria Corbelli; Vicente Estrada, MD; Anna Maria Geretti, MD; Apostolos Beloukas, PhD; David Asboe, FRCP; Pompeyo Viciana, MD; Félix Gutiérrez, MD; Bonaventura Clotet, PhD; Christian Pradier, MD; Jan Gerstoft, MD; Rainer Weber, MD; Katarina Westling, MD; Gilles Wandeler, MD; Jan M. Prins, PhD; Armin Rieger, MD; Marcel Stoeckle, MD; Tim Kümmerle, PhD; Teresa Bini, MD; Adriana Ammassari, MD; Richard Gilson, MD; Ivanka Krznaric, PhD; Matti Ristola, PhD; Robert Zangerle, MD; Pia Handberg, RN; Antonio Antela, PhD; Sris Allan, FRCP; Andrew N. Phillips, PhD; Jens Lundgren, MD; for the PARTNER Study Group

- The PARTNER1 study looked at 888 couples where one was HIV positive and on antiretroviral treatment (ART) and who were already having sex without condoms:

-548 heterosexual couples

-340 MSM

- They found that in more than 58,000 acts of condomless sex there were no HIV transmissions from the HIV positive partner among those on treatment with an undetectable viral load
- Couples were followed for a median of 1.3 years

JAMA. 2016;316(2):171-181. doi:10.1001/jama.2016.5148

Partner2 Study:

- Prospective observational study in 14 European countries
- Enrolled 927 homosexual serodiscordant couples between September 2010 and July 2017
- Positive partner was on suppressive ART
- A total of 74568 condomless-sex acts were reported, with 0 cases of within couple HIV transmission

http://programme.aids2018.org/Abstract/Abstract/13470

QUESTIONS?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Southeast
THANK YOU!