

# Improving Health of Persons With HIV: Understanding the Impact of HIV Resistance

October 28, 2020



### **Upcoming Webinars**

- Identify, Link, and Expand: Care Coordination to Advance HIV Health Outcomes
  - November 10, 2020 at 2PM EST
- Empowering the Care Team to Collaboratively Address Treatment Resistance
  - November 23, 2020 at 2PM EST



### Goals for Today's Webinar

- Today we will address:
  - Recent Advances in HIV Treatment
  - The Diversity of Patients and Treatments
  - Improving Patient and Provider Communications
  - Understanding HIV Labs and Tests for Viral Resistance
  - Viremia and Associated Health Risks
  - Empowering Patients with Health Care Engagement



### **Learning Objectives**

- By the end of today's session, participants will be able to:
  - Better understand viremia and concepts related to viral resistance to HIV medications
  - Describe available options for treatment of HIV resistance to medications
  - Identify ways to engage with your medical provider about treatment options for HIV resistance to medications



## **Faculty**



W. David Hardy, MD, AAHIVS (he/him/his)
An infectious diseases/HIV specialist, researcher and patient advocate. Cared for persons with HIV since 1982 and conducted research on HIV and related diseases since 1984.



Scott Bertani, MPA
Director of Advocacy, HealthHIV

Guides advocacy and policy from a shared lived experience, as both a long-term and graying consumer of HIV services and front-line leader in the care as prevention field. Previously was at Lifelong AIDS Alliance and Evergreen Wellness Advocates.

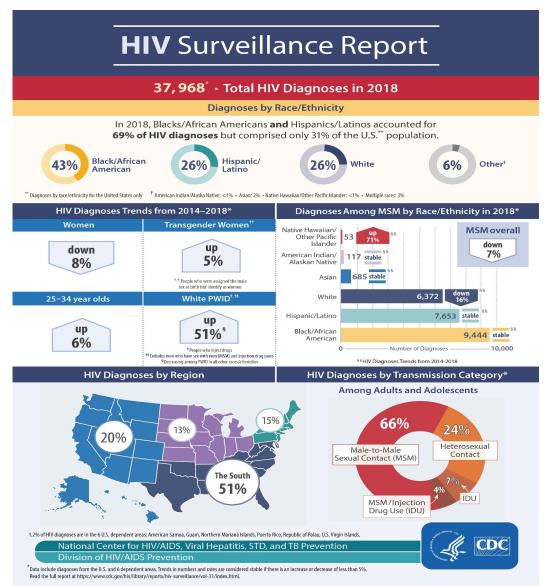




# Improving Health of Persons With HIV: Understanding the Impact of HIV Resistance

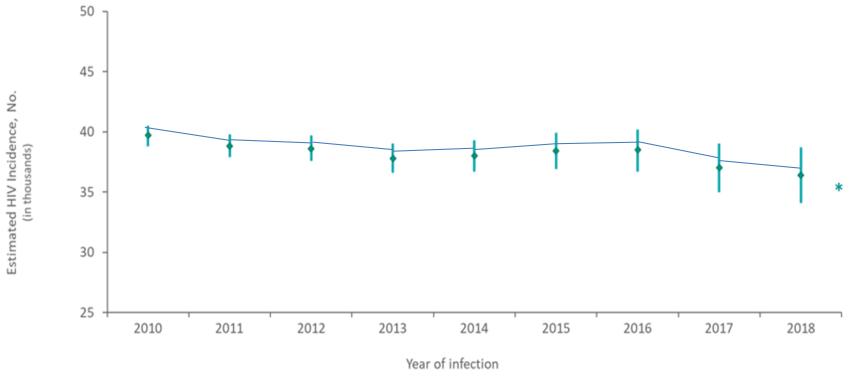
W. David Hardy, MD, AAHIVS





**HealthHIV** 

# Estimated Number of New Persons with HIV Aged ≥13 Years, 2010–2018—United States

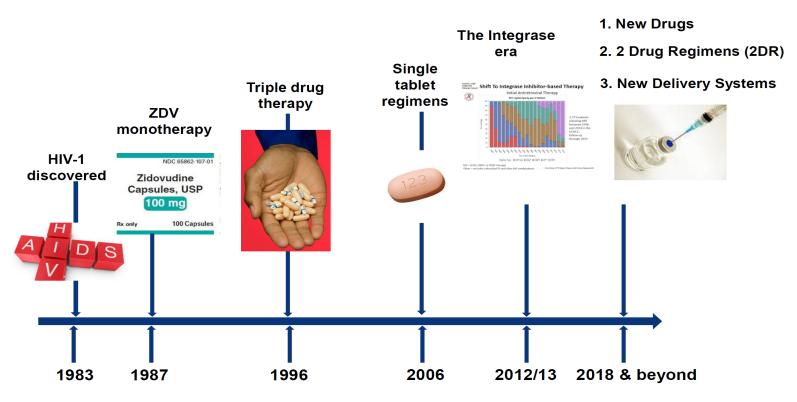


Note. Estimates were derived from a CD4 depletion model using HIV surveillance data. Bars indicate the range of the lower and upper bounds of the 95% confidence intervals for the point estimate.

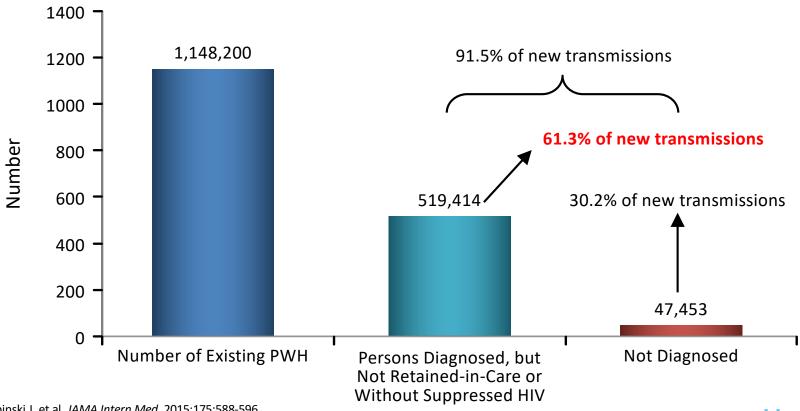
\* Difference from the 2010 estimate was deemed statistically significant (P < .05).

**HealthHIV** 

# Antiretroviral Therapy: Past, Present, and Future



## Why HIV Diagnosis, Retention-in-Care and Treatment Is So Important?



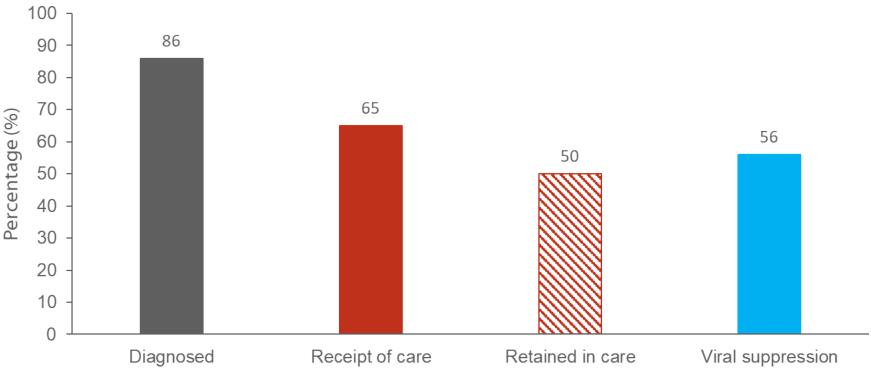
Skarbinski J, et al. JAMA Intern Med. 2015;175:588-596.







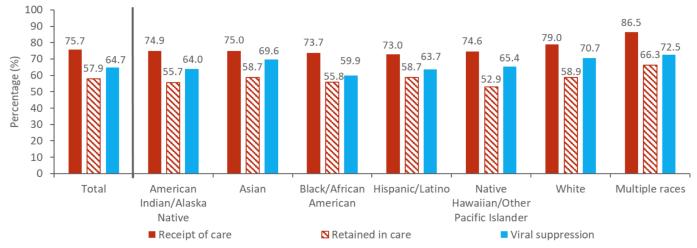
### HIV Care Continuum, 2018 - United States



Note. Receipt of medical care was defined as  $\geq 1$  test (CD4 or VL) in 2018. Retained in continuous medical care was defined as  $\geq 2$  tests (CD4 or VL)  $\geq 3$  months apart in 2018. Viral suppression was defined as < 200 copies/mL on the most recent VL test in 2018.

# People Living with HIV: Accessing Antiretroviral Therapy in the US

Receipt of HIV Medical Care, Retention in Care, and Viral Suppression among Persons Aged ≥13 Years Living with Diagnosed HIV Infection, by Race/Ethnicity 2018—41 States and the District of Columbia



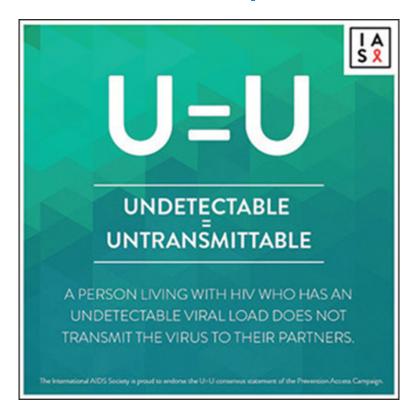


Note. Receipt of medical care was defined as  $\geq 1$  test (CD4 or VL) in 2018. Retained in continuous medical care was defined as  $\geq 2$  tests (CD4 or VL)  $\geq 3$  months apart in 2018. Viral suppression was defined as < 200 copies/mL on the most recent VL test in 2018. Asian includes Asian/Pacific Islander legacy cases. Hispanics/Latinos can be of any race.

Source: CDC. Selected national HIV prevention and care outcomes (slides) pdf icon[PDF – 2 MB].



# The science is clear: with HIV, undetectable equals untransmittable





















BETTER HEALTH

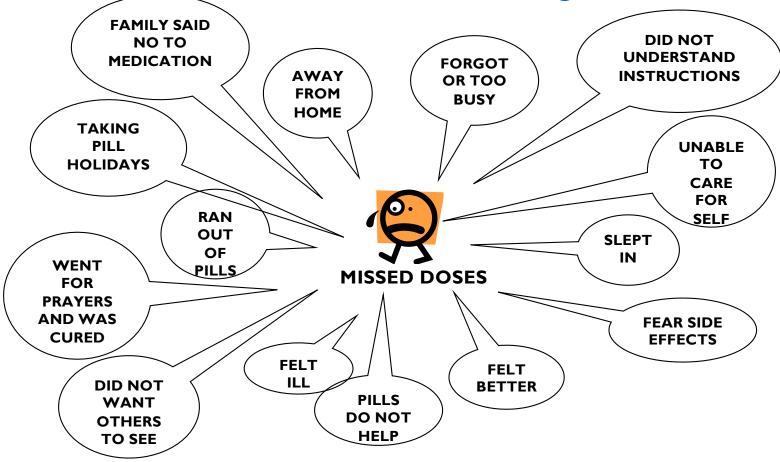


MAINTAINS SUPPRESSION





Adherence Challenges



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# What are some challenges I might face when taking my medication?

- Side effects from my medications
- Interactions with my other medications which change my HIV medications or vice-versa
- My busy work/life schedule that interferes with my medication schedule

- Behavioral or mental health concerns
- My use of alcohol or other drugs which alter my judgement or mood
- Treatment fatigue



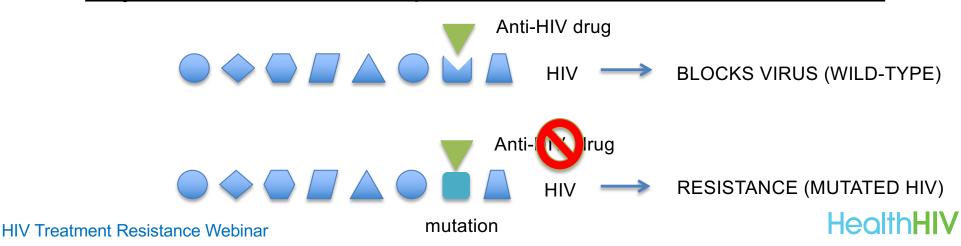
## What are the benefits of taking my HIV medicine every day as prescribed?

- Allows HIV medications to work as optimally as possible to reduce the amount of HIV in my body.
- Helps keep my immune system stronger and better able to fight infections and keep me healthy.
- Reduces the risk of me passing HIV to others.
- Helps prevent HIV from becoming resistant to my medications.



### What is HIV resistance to medications?

- Resistance means that the virus has mutated or changed so that certain HIV drugs are no longer effective.
  - Resistance is caused by mutations that occur in the virus ->
    these mutations can cause resistance to one antiretroviral drug
    or to many antiretroviral drugs
  - Anytime HIV is able to reproduce itself, mutations can occur



# 10 Important Things to Know About HIV Drug Resistance



2. "Wild-type HIV" is the Natural State of the Virus

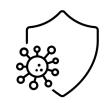


3. HIV Replicates Quickly but is Prone to Make Mistakes (Mutations)



# 10 Important Things to Know About HIV Drug Resistance

- 4. Mutations Can Increase to Deepen Drug Resistance
- Having a Resistant Strain of Virus Doesn't Mean That You Are Resistant (It's about the virus)

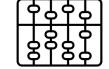


ក្សាក្តា 6. ភ្នំកុំស្ថិតិ បាន Viral Resistance Can be Passed to Others



# 10 Important Things to Know About HIV Drug Resistance

- 7. Resistance Testing Helps Guide the Selection of the Best Drugs for Your Virus
- 8. Poor Adherence Gives the Virus a Survival Edge



- 9. Resistance to One Drug Can Affect Multiple Drugs in the Same Class of Drugs
- 10. Resistance is Manageable, but it is Forever





## **Understanding Your Lab Test Results**



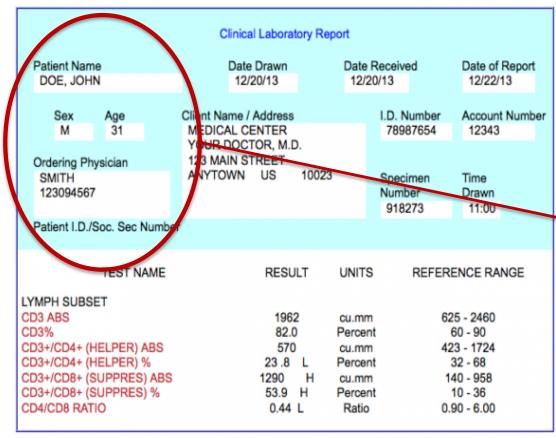
#### CD4+ T Cell Counts and HIV

- CD4+ T cells are central players in the human immune system and are specifically infected by HIV. A person with a healthy immune system has 500 to 1,600 CD4+ T cells in a cubic millimeter (mm³) or drop of blood. AIDS is diagnosed when the CD4+ T cells are lower than 200/mm³.
- AIDS-defining infections, also called opportunistic infections, typically occur in PWH with CD4+ T cells below 200/mm<sup>3</sup>.
   Viruses, bacteria, or fungi that don't usually make healthy people sick can cause these infections in someone with AIDS.



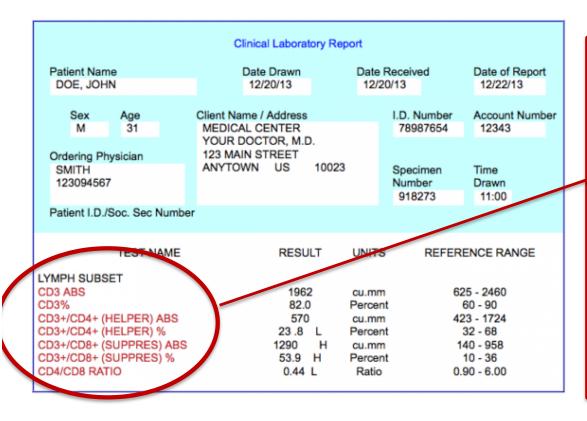
Clinical Laboratory Report									
Patient Name DOE, JOHN	Date Drawn 12/20/13	Date Recei 12/20/13	ived Date of Report 12/22/13						
Sex Age M 31	Client Name / Address MEDICAL CENTER		Number Account Number 12343						
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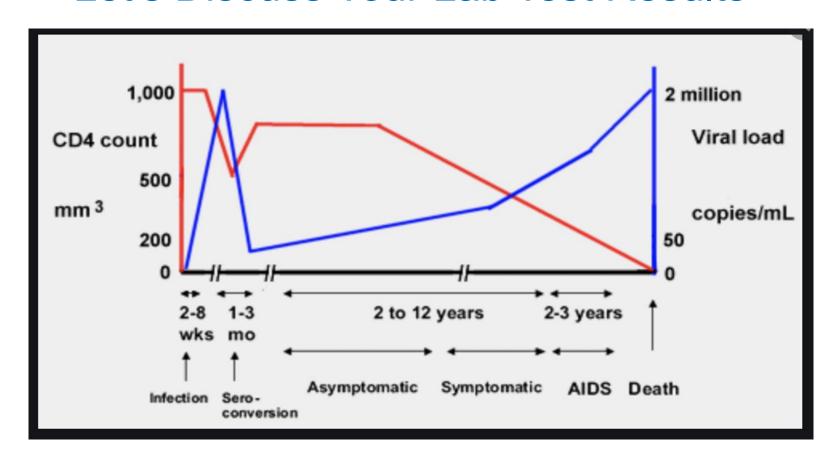
When reviewing your lab test report, be sure that the patient information matches your own, including the ordering physician information.



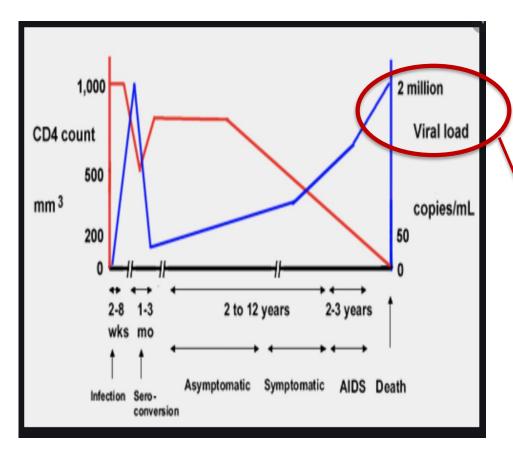


Be sure to look for the test results for the CD3+/CD4+ or "Helper" cells. They are reported both as a percentage (%) of all T cells and as an absolute number of cells. Check the Reference or "normal" range to best understand where your T cells are.









Viral load (aka HIV RNA) is the direct measurement of HIV in the blood. It's highest right after contracting HIV and then fluctuates as the immune system fights against it. Eventually, HIV destroys CD4+T cells and infections occur. Anti-HIV medication strongly controls the virus and protects and allows CD4+T cells to reconstitute or re-plenish themselves back to normal levels.

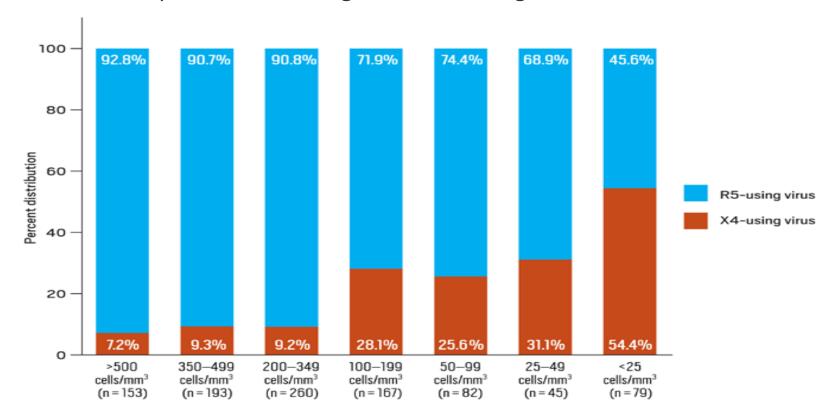


### Your Lab Test: Helpful Terminology Explained

- What is HLA-B\*5701?
  - A positive test result means you have the HLA-B\*5701 gene and have a higher risk of developing a potentially life-threatening reaction to abacavir. If your test result is positive, you should not take abacavir.
- What is Viral Tropism?
  - HIV can use two different entry pathways to infect human CD4+ T cells, the R5 or X4 route. Different strains of HIV use one pathway exclusively while some use both. Maraviroc is an anti-HIV drug that effectively blocks R5-type HIV, but not X4 HIV. A tropism test will define which pathway a virus uses.



"We need to ensure that people who start treatment can stay on effective treatment, to prevent the emergence of HIV drug resistance..."



Baseline CD4 cell count (n = total number of participants in category)



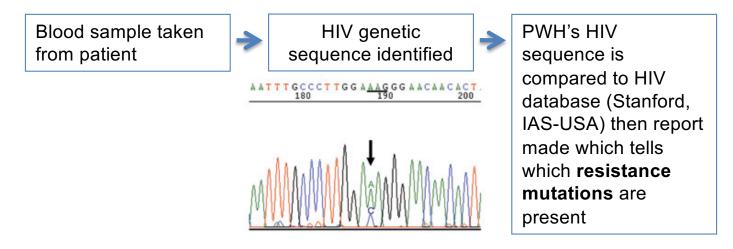
### When do we suspect resistance?

- 1. If a PWH has an increasing viral load while on ART then we suspect there may be resistance
  - This assumes the patient has been adherent in taking their HIV medications
- 2. All PWH should have viral resistance tests prior to starting ART for the first time
  - Transmitted resistance can occur about 5%-20% of the time



#### How do we test for resistance?

- HIV Genotype Test
  - This test determines the genetic sequence of the HIV in the PWH's blood which is then compared to a database to identify if mutations are present.





#### Component Results

Component HIV1 Genotype		Flag	R ()		Units	Status Final
Comment:					HIV Subty	_
Antiretrovira	ıl drugs	Resis Predi	tance cted	Mutatio		d
NRTIs ZDV (zidovudi ABC (abacavir ddI (didanosi 3TC (lamivudi FTC (emtricit d4T (stavudir TDF (tenofovi	ine or Retrov or Ziagen) ine or Videx) ine or Epivir tabine or Emt ne or Zerit) ir or Viread)	vir)	! ! ! NO! ! NO! ! NO! !YES! !YES! ! NO!	+M184V, +M184V,	V118I V118I	
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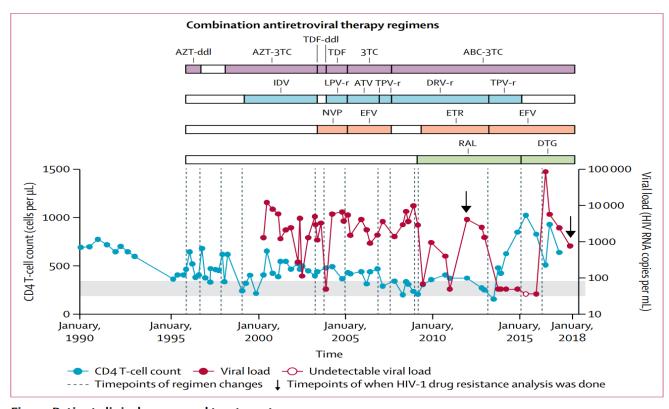
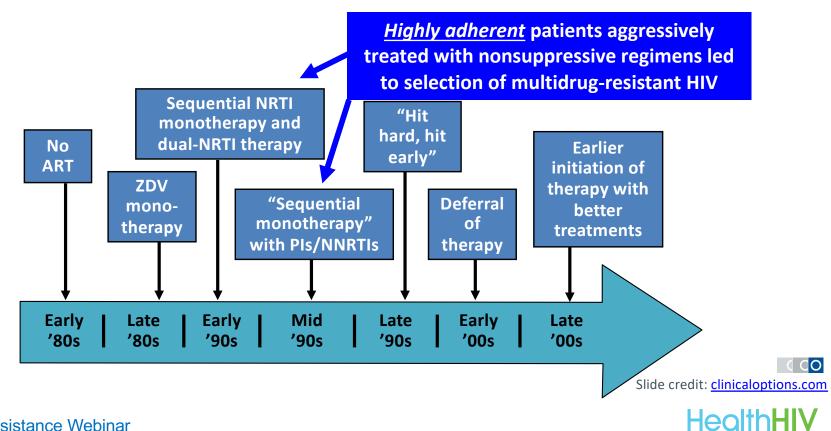


Figure: Patient clinical course and treatment

The different combination antiretroviral therapy regimens received by the patient over time are illustrated in the top panel as nucleoside reverse transcriptase inhibitors (purple), protease inhibitors (blue), non-nucleoside reverse transcriptase inhibitors (orange), and integrase strand transfer inhibitors (green). Undetectable HIV-1 viral load was defined as less than 50 RNA copies per mL or less than 37 RNA copies per mL, depending on the test used. The CD4T-cell count range of 200–350 cells per  $\mu$ L is highlighted (CD4T-cell counts of <200 cells per  $\mu$ L are considered to indicate AIDS). AZT=azidothymidine. ddl=didanosine. 3TC=lamivudine. TDF=tenofovir disoproxil fumarate. ABC=abacavir. IDV=indinavir. LPV=lopinavir. r=ritonavir. ATV=atazanavir. TPV=tipranavir. DRV=darunavir. NVP=nevirapine. EFV=efavirenz. ETR=etravirine. RAL=raltegravir. DTG=dolutegravir.



#### Who Are the People With Multidrug Resistant HIV?



# Heavily Treatment–Experienced People With HIV: Who are They?

- 2 primary populations of PWH<sup>[3-5]</sup>
  - 1) Older people with HIV treated in early days of ART with less potent regimens that had low resistance barriers
  - 2) Younger people who acquired HIV infection during or soon after birth, now adults
- Currently, maraviroc, ibalizumab, fostemsavir, and enfuvirtide are the best options<sup>[6-8]</sup>
- ART with new ways of working against HIV plays a critical role for these people with HIV: those with resistance to multiple drug classes and no/limited treatment options<sup>[1,2]</sup>

1. Struble. AIDS Lond Engl. 2005;19:747. 2. Richman. AIDS Lond Engl. 2004;18:1393. 3. Weinstock. J Infect Dis. 2004;189:2174. 4. Yazdanpanah. Clin Infect Dis. 2009;49:1441. 5. Tassiopoulos. Clin Infect Dis. 2020;71:133. 6. Emu. NEJM. 2018;379:645. 7. Reeves. J Virol. 2005;79:4991. 8. Kozal. NEJM. 2020;382:1232.

Slide credit: clinical options.com



# Trogarzo® (ibalizumab-uiyk)

- Trogarzo<sup>®</sup>, in combination with other antiretrovirals has been shown to be effective for the treatment of HIV in highly treatment-experienced PWH with multiple drug resistant HIV failing their current antiretroviral regimen.
- Trogarzo® is administered as an intravenous infusion every 2 weeks. It may be a more effective and easier HIV therapy for those struggling with oral medication adherence.
- Clinical trials with Trogarzo<sup>®</sup> showed that 63% of PWH had undetectable viral loads ~ 1 year after starting treatment.



# Trogarzo® Infusion

- The length of the initial infusion is generally 30 minutes with subsequent infusions of 15 min.
- This estimate only includes the time that it takes for the medication to go into your body; it will take additional time to prepare supplies and medications and to place the IV catheter.
- Side effects which led to discontinuing Trogarzo infusions occurred in 5 of 40 (13%) PWH over 25 weeks of treatment.



## **Healthcare Team**

- Often a team approach within your provider's practice is a strategy to help improve adherence during your care.
- Having a healthcare team can help strengthen your relationship with the resources you will need to focus on your health.
- Your team can also help to keep you aware of the resources in your community or nationwide.



# Use Your Healthcare Team for Support

- Keep a list of questions you have and bring those with you to all of your appointments
- Keep track of potential side effects and concerns and share those with your provider
- If something about your routine or needs change, please let your provider know so they may provide support



# Understanding HIV and Resistance

- Theratechnologies website HIVandResistance.com
- HIV organizations or clinics
  - Join email list
  - Access to valuable information and resources
- People with HIV
  - Understanding HIV and Resistance Brochure
  - HIV Discussion Guide





# **Today I have HIV**

A Patient's perspective on Resistance and Options

Scott Bertani, MPA
Director of Advocacy, HealthHIV



## February 1996: The Diagnosis – C3

### **Treatment Options come online**

Resistance was a luxury to be had in later, better days.



#### A history of (HAART) options for (the) treatment (naïve):

- NRTIs or Nukes: Targeting the action of an HIV protein called reverse transcriptase.
- Protease: Block the activity of the protease enzyme, which HIV uses to break up large polyproteins into the smaller pieces, resulting in more immature viral particles.
- NNRTIs or Non-Nukes: Also target Reverse Transcriptase, but in a different way to NRTIs by binding directly to it, blocking the Reverse Transcription process.

#### Followed later by:

- Integrase Inhibitors: Target a protein in HIV called integrase which is essential for viral replication
- Entry Inhibitors: Stop HIV from entering human cells. CCR5 inhibitors and fusion inhibitors
- Chemokine Coreceptor antagonist: CCR5 antagonist and CXCR4 antagonist

#### Trogarzo a Post-attachment Inhibitor:

- Post-attachment inhibitors bind to the CD4 receptor on T-cells. They prevent the HIV gp120 protein from changing its shape to engage with co-receptors after it engages with the CD4 receptor.
- More than 30 Antiretroviral Medications in 6 Drug Classes
- 16 Pills: Morning, Noon & Night:
  - Learning Adherence (rituals)



#### **Mutations**

I promise to monitor my mute button while on Zoom calls



## What if we copied this instead?

I promisedto monitor my mute button on Zoom conf calls.



#### **Mutations**

### Can occur randomly

Have an effect on the wild-type virus

Drug-resistant strains

## Aren't always our fault

Adherence challenges are real



## How bad is Drug Resistance for People like You and Me?

#### **Options**

Genotypic Resistance Testing: Reverse transcriptase (RT), Protease (PR), and Integrase (IN) genes

Viral Load Testing

Clinical Care Maintenance

Daily Adherence

#### Selective Pressure on the Wild: Fold Factor

Phenotypic Resistance Testing: Calculates growth rate compared to the rate of your Wild Type virus



## How do people develop drug resistance?

#### **Acquired HIV Drug Resistance**

Sometimes the drugs themselves, or a combination of how a person's body reacts to the drug can cause it

Clinical Care Maintenance

Daily Adherence

#### **Transmitted HIV Drug Resistance.**

That occurs when a person with HIV who's never been on treatment acquires a strain of HIV that is already resistant to one or more HIV drugs.



#### How do you know if you've developed resistance?

#### Viral Load Blip? Or?

#### Generally speaking, watch out for 3 things:

- 1. If your viral load goes above 1,000 copies/mL, drug resistance testing's recommended.
- 2. If your viral load goes above 500 copies/mL, but remains below 1,000 copies/mL, drug resistance testing might not be whereas successful, remember, but worth considering. OR
- 3. If your treatment regimen is not lowering your viral load as quickly as it should be, then drug resistance testing is again recommended.



# Six Quick Takeaways:

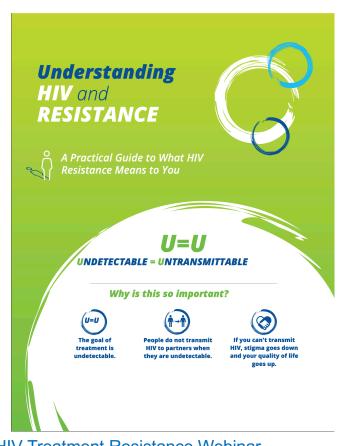
- 1. Learn everything you can about your treatment options. Like I did in the early days.
- **2. Work with your provider** to choose the best possible regimen after resistance testing.
- **3. Treatment Adherence** is where it's at. *No more than one missed dose a month.*
- **4. Talk with your doctor and communicate honestly and routinely**. We've fought hard in making sure our Sexual Orientation Gender Identify Biological preference info is included.
- **5. Monitor your health**—labs, metabolic panels, STI testing, mental health, substance use, etc.
- 6. Be good to yourself and others.



# Q&A



# **Understanding HIV and Resistance:** A Practical Guide to What HIV Resistance Means to You



- What happens if HIV is not well controlled?
- Why do my HIV medications change?
- What is HIV resistance?
- Questions to ask your doctor.

HIVandResistance.com

**HIV Treatment Resistance Webinar** 



#### **HIV Discussion Guide**

#### **HIV** Discussion Guide 1. Do you know when your last viral load and CD4 count were? ☐ Yes or ☐ No If yes, what was the approximate date? 8. Do you know why you changed your HIV medications? 🗌 Yes or 🗌 No 2. Was your viral load undetectable? ☐Yes or ☐No If yes, then why did you change your HIV medications? If your viral load was not undetectable, what was your viral load? 3. What was your last CD4 count? 4. What are the names of your HIV medications? 9. Do you have any other health care concerns (Behavioral health, Substance abuse, Diabetes, COVID-19, Hypertension, Hepatitis)? Yes or No If yes, what are your concerns? 5. Are you having challenges taking your medication? Yes or No If yes, describe these challenges: If your viral load is not undetectable, 6. Are you following the instructions your SCHEDULE AN APPOINTMENT WITH YOUR healthcare provider gave you on how HEALTHCARE PROVIDER TO DISCUSS WHY. to take your HIV medications? Yes or No Ask your healthcare provider why your viral If no, what is different about how you load is detectable and if there are treatment take your HIV medications? options that can get your virus undetectable. Ask your healthcare provider if you need resistance testing. · Refer to the Understanding HIV and Resistance Brochure. 7. Have you changed your HIV medications in the past? Yes or No For more information go to If yes, how many times have you HIVandResistance.com changed your HIV medications? . THERA

Find out if your virus is at risk of becoming resistant to your medication.

Fill out and download this discussion guide to help you talk to your provider.

www.HIVandResistance.com



## HealthHIV Consumer Guide

CONSUMER GUIDE TO IMPROVIDE AND PRO

IMPROVING HIV CARE COORDINATION AND PROMOTING RESILIENCE



#### **COVID-19 AND CONTINUING HIV CARE**

During the COVID-19 pandemic, it is important that people with HIV continue their treatment Click here for information on staying connected to care:

https://aidsinfo.nih.gov/guidelines/html/8/covid-19-and-persons-with-hiv-interim-guidance-/554/interim-guidance-for-covid-19-and-persons-with-hiv



- People with HIV who have a detectable viral load may be at greater risk for serious illness due to COVID-19, so it is essential to continue care such as antiretroviral therapy (ART) medication.<sup>12</sup>
- People with HIV who become hospitalized should continue their ART during hospital ization. Take all antiretroviral (ARV) medications with you to the hospital, as many ARVs may not be available through the hospital's in-patient pharmacy.
- People with HIV on an ART regimen that includes Ibalizumab (Trogarzo<sup>III</sup>) IV infusions every 2 weeks should contact their providers or THERA patient support<sup>II</sup> for assistance 1-833-23-THERA (1-833-234-4372) to plan for confined treatment without interruption.<sup>1</sup>
- People with HIV at greater risk for serious illness due to COVID-19 are also those who:

  have other chronic conditions, such as cancer, diabetes, obesity, or respiratory conditions
  - are age 65+ years
- For those with more than one medical condition, it is important to coordinate care.<sup>12</sup>
- Some doctor's appointments, clinic visits, or lab tests may be postponed, particularly for those with well-controlled HIV.<sup>1</sup>
- Those with poorly controlled HIV can benefit from continuing or resuming care.
- People with HIV who stopped ART medication can benefit by starting again.
- It's important to keep at least a 30-day supply of medication on hand, and if possible, a 90-day supply.<sup>12</sup>
- No HIV medications (ART) are proven to prevent or treat COVID-19, therefore, it's not necessary to switch medications.<sup>12</sup>
- COVID-19 freatment and vaccine research studies are underway, and people with HIV may want to enroll.
   More information is available here: https://clinicaltrials.gov/
- https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/hiv.html?CDC\_AA\_refVal=https%3A%2F%2F www.cdc.gov%2Fcoronavirus%2F2019-ncov%2Fspecific-groups%2Fhiv.html
- 3. https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-at-higher-risk.html





IMPROVING HIV CARE COORDINATION
AND PROMOTING RESILIENCE

- HIV Clinical Considerations
- Telehealth
- AIDS Service Organizations and Community-Based Organizations
- Housing and Access to Healthcare
- Self-Care and Healthy Outlook: Aging People and People of Color
- Faith-Based Approaches for Social Connection

Download from:

https://tinyurl.com/yxlbrdy7



# This webinar is generously supported through an educational grant from:



www.Theratech.com



## For More Information & Technical Assistance



www.HealthHIV.org



www.HealthHCV.org



www.HealthLGBT.org



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202.232.6749



Info@HealthHIV.org



## For Questions Contact

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<a href="Michael@HealthHIV.org">Michael@HealthHIV.org</a>

