Fundamentals of Antiretroviral Therapy

Southeast AIDS Education & Training Center
HIV Clinical Overview
12 May 2016

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AETC AIDS Education & Training Center Program Southeast

VANDERBILT UNIVERSITY School of Medicine

TN CFAR TENNESSEE CENTER FOR AIDS RESEARCH

Disclosures

- **Relevant Financial Disclosures**

  None

- **Non-FDA Approved Uses**

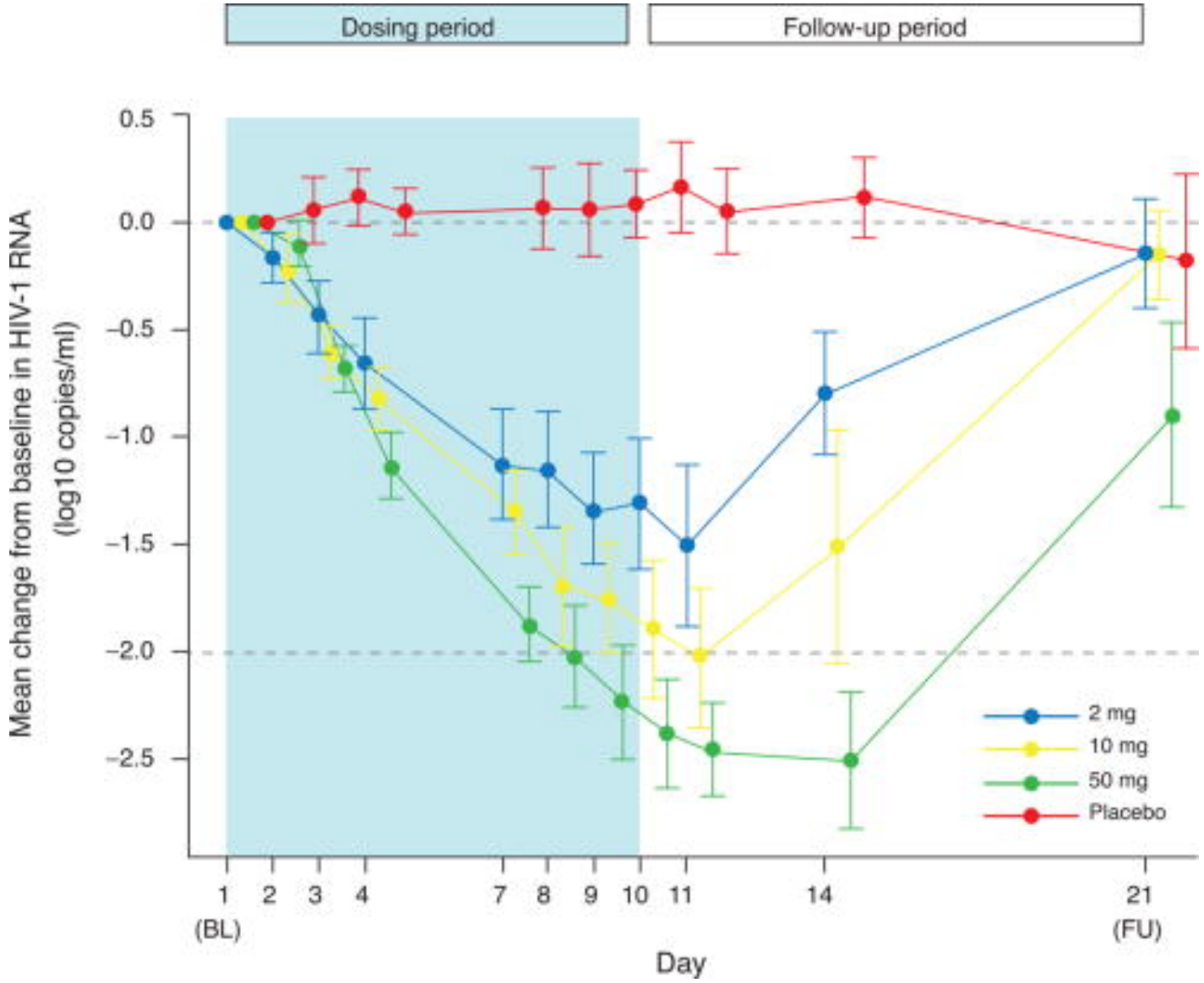
  None

Objectives

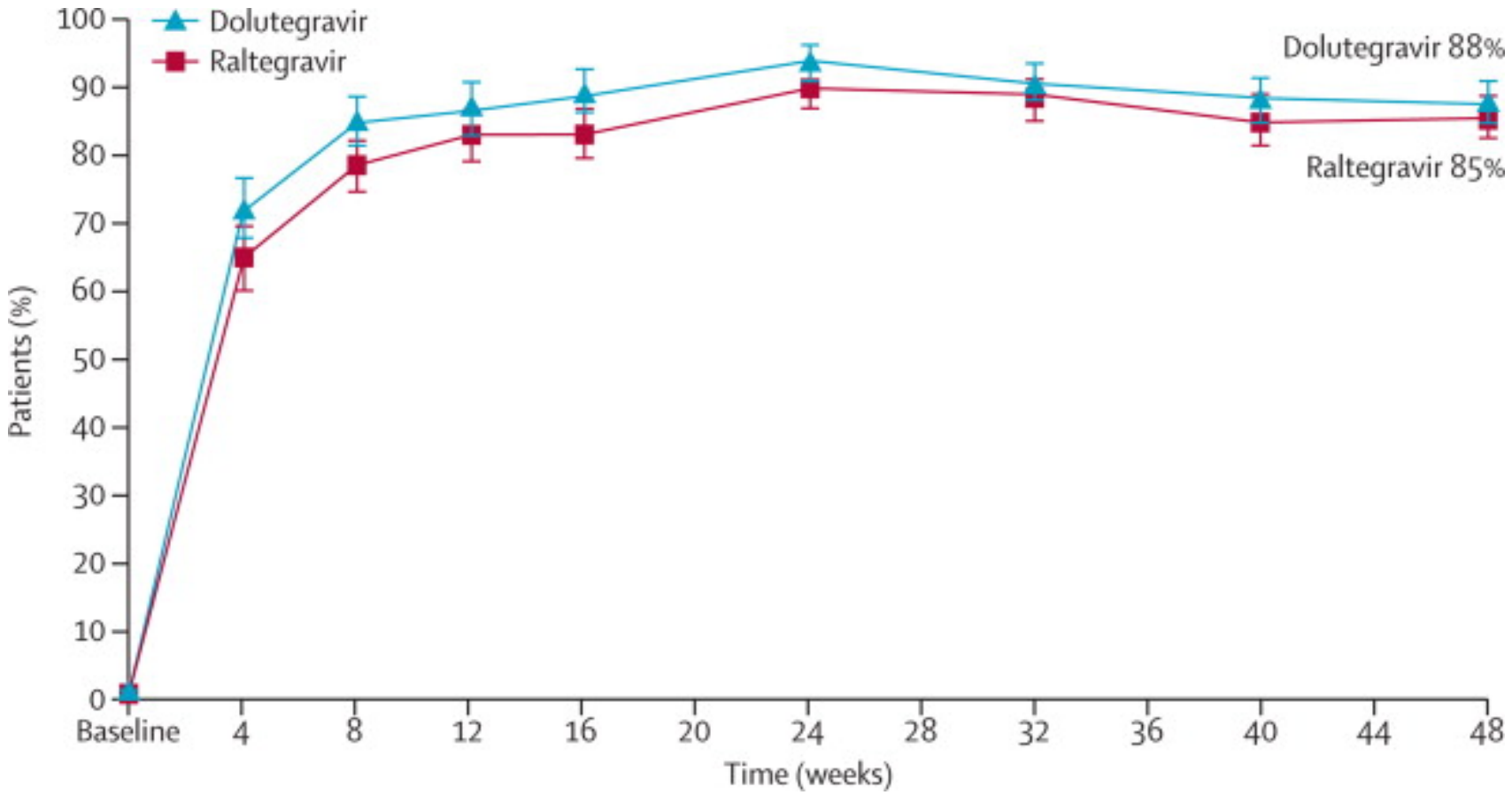
- Describe fundamentals of antiretroviral therapy (ART)
  - Identify HIV antiretroviral drugs by mechanism/class, names, and coformulations
  - Summarize current treatment guidelines for initiating ART (or at least know where to find them)

How do we characterize ART?

- **Potency**:
  - How effective suppressing HIV replication?
  - **log HIV RNA decline**, **% patients suppressed** at a certain time period, rapidity of decline, duration of response
  - PI, NNRTI, integrase inhibitors > potency than NRTI
  - Usually potency is more of an issue in salvage regimens



Min, et al. *AIDS*. 25(14):1737-1745, September 10, 2011.



Raffi, et al. *Lancet* 2013 (381): 735-43.

How do we characterize ART?

- **Adverse Events (AEs):**
  - Short- and long-term AEs
  - Co-morbidities play a role in long term AEs
  - May be related to drug-drug interactions

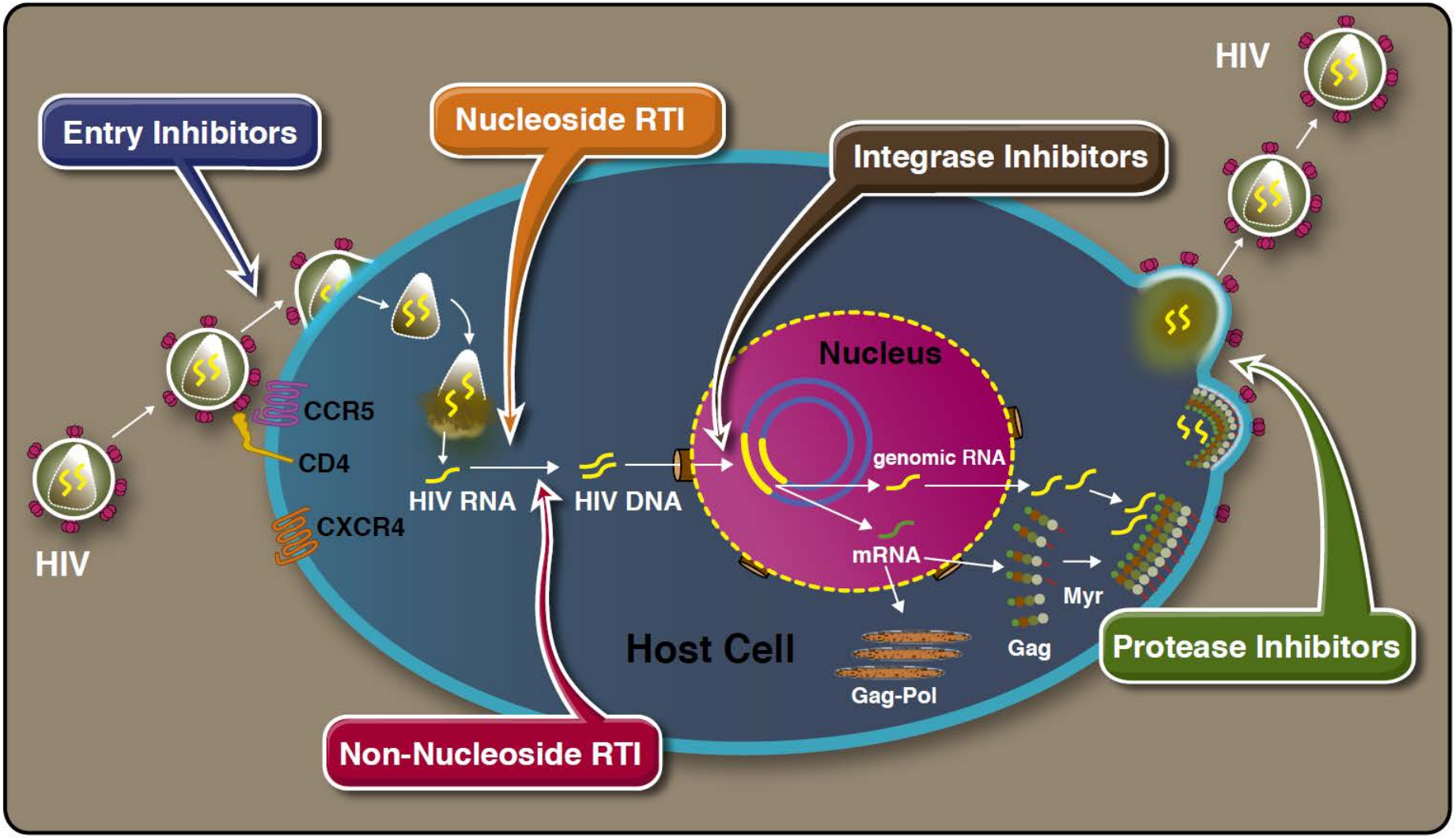
How do we characterize ART?

- **Tolerability:**
  - Short-term side effects
  - Dosing requirements, pill size & burden, route
  - Patient (pill size) or medication (AEs) related

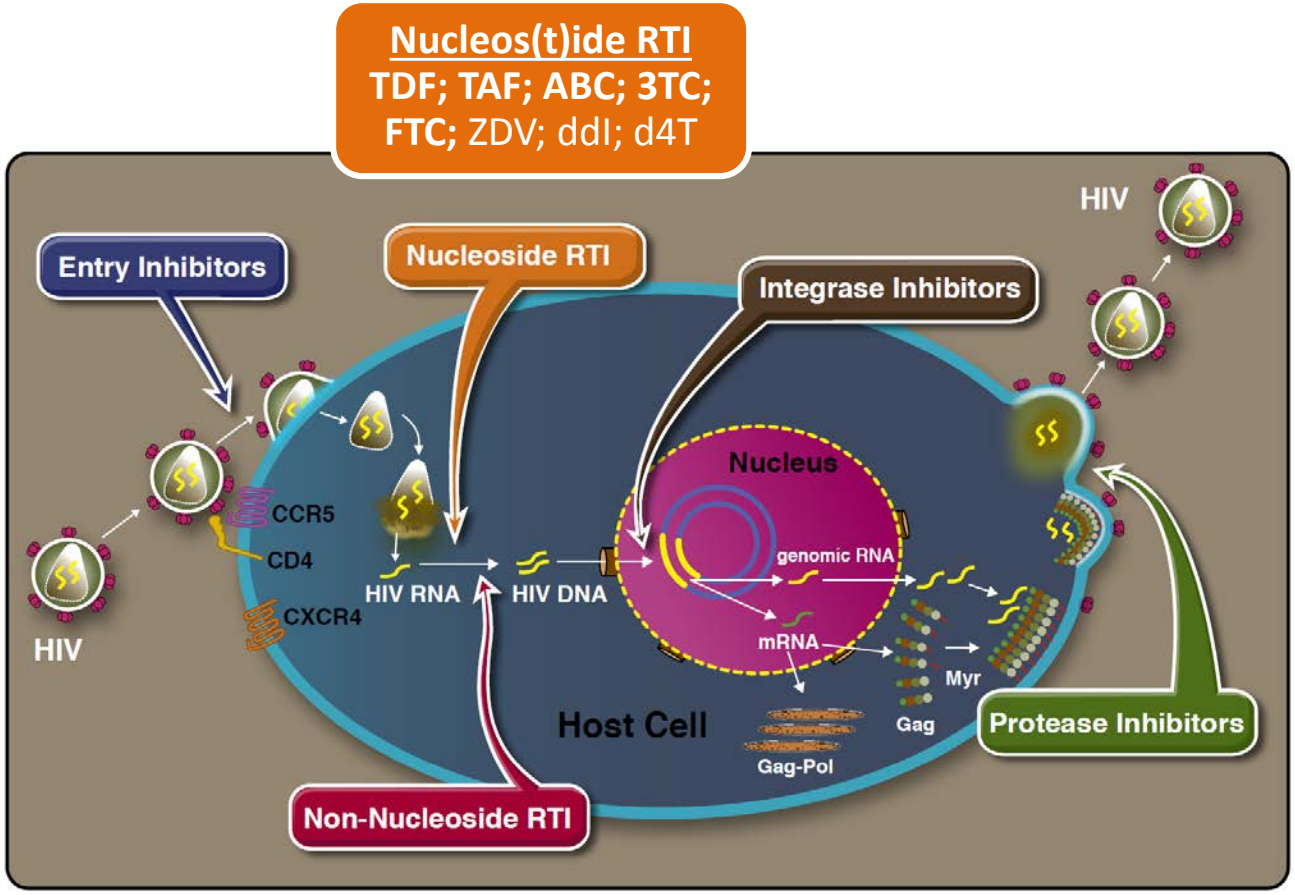
How do we characterize ART?

- **Resistance:**
  - Stay tuned…

Retrovirus Life Cycle



Retrovirus Life Cycle



Nucleos(t)ide Reverse Transcriptase Inhibitor (NRTI)

- **Lamivudine (Epivir® 3TC)**
- **Emtricitabine (Emtriva® FTC)**
- **Abacavir (Ziagen® ABC)**
- **Tenofovir diisoproxil fumarate (Viread® TDF)**
- **Tenfovir alafenamide (TAF- see coformulations)**

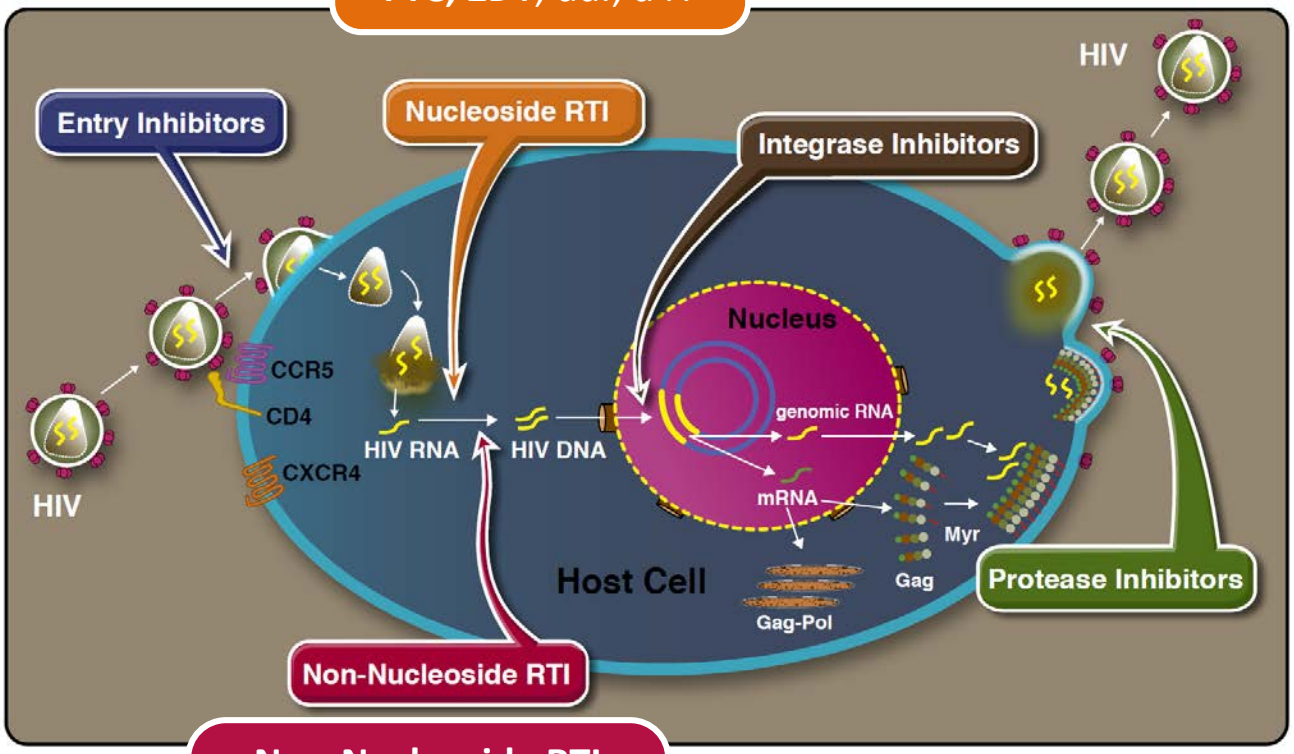
- Zidovudine (Retrovir® AZT)
- Didanosine (Videx EC® ddI)
- Stavudine (Zerit® d4T)

NRTI Adverse Effects

- Class Effects
  - Nausea (mild)
  - Mitochondrial toxicity (historical interest?)
- ABC
  - Hypersensitivity
  - HLA-B*5701 mediated (NPV 100%)
- TDF
  - Renal toxicity
  - Tubulopathy; Fanconi's syndrome
  - TAF avoids this (↓[plasma] ↑[cellular])

Retrovirus Life Cycle

Nucleoside RTI
TDF; TAF; ABC; 3TC; FTC; ZDV; ddI; d4T



Non-Nucleoside RTI
EFV; NVP
etravirine (ETR)
rilpivirine (RPV)

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)

- **Efavirenz (Sustiva® EFV)**
- **Etravirine (Intelence® ETR)**
- **Rilpivirine (Edurant® RPV)**

- Nevirapine (Viramune® NVP)
- ~~Delavirdine (Rescriptor® DLV)~~

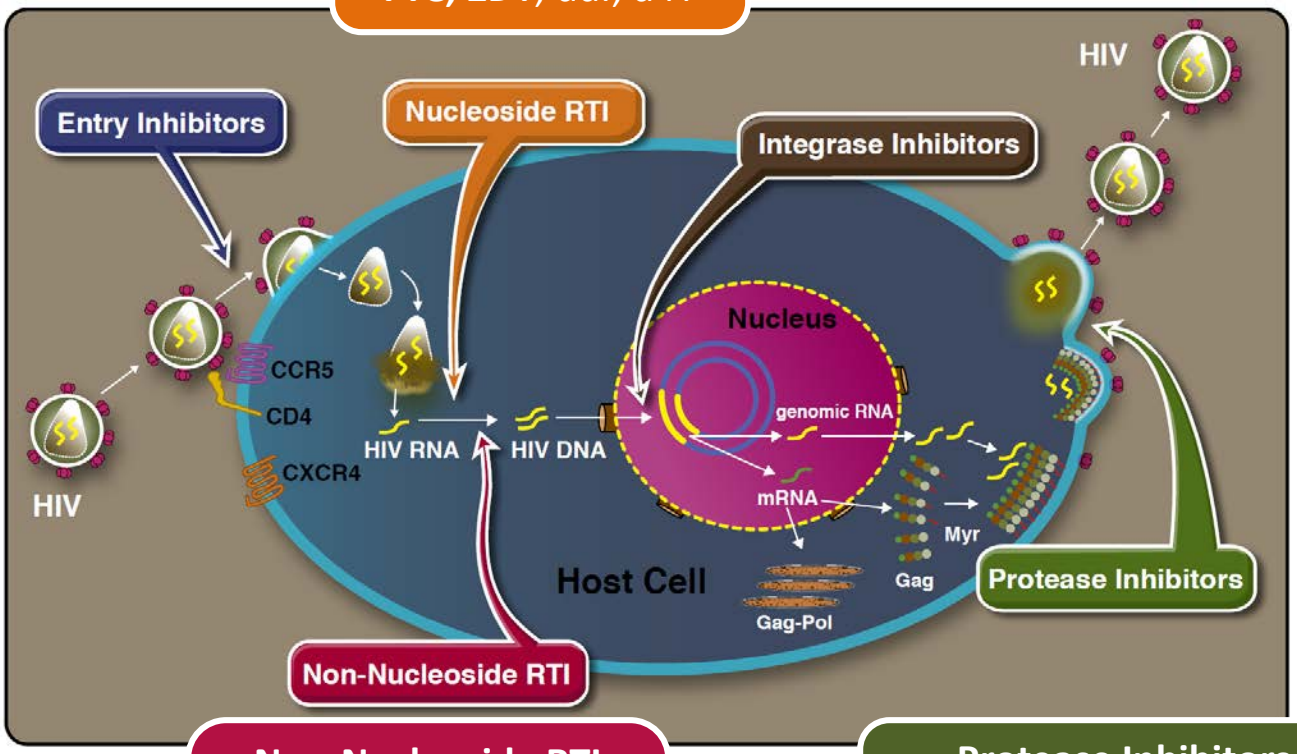
NNRTI Adverse Effects

- Class Effects
  - Rash (including Stevens-Johnson syndrome)
  - Hepatotoxicity
- EFV
  - Neuropsychiatric: abnormal dreams, dizziness, impaired concentration
  - Pregnancy risk
  - Dyslipidemia
  - Suicidality
- ETR & RPV
  - Rash (including SJS)

Low resistance threshold

Retrovirus Life Cycle

Nucleoside RTI
TDF; TAF; ABC; 3TC; FTC; ZDV; ddI; d4T



Non-Nucleoside RTI
EFV; NVP
etravirine (ETR)
rilpivirine (RPV)

Protease Inhibitors
ATV; DRV; LPVr; FPV; SQV; IDV; RTV; NFV; TPV

Protease Inhibitors (PI)

- **Darunavir (Prezista® DRV)**
- **Atazanavir (Reyataz® ATV)**
- **Ritonavir (Norvir® RTV, r) – boosting only**
- **[Cobicistat (Tybost® COBI, c) – boosting only]**
- **Fosamprenavir (Lexiva® FPV)**
- **Lopinavir + Ritonavir (Kaletra® LPVr)**

- Indinavir (Crixivan® IDV)
- Nelfinavir (Viracept® NFV)
- Saquinavir (Invirase® SQV)
- Tipranavir (Aptivus® TPV)
- ~~Amprenavir (Agenerase® APV)~~

PI Adverse Effects

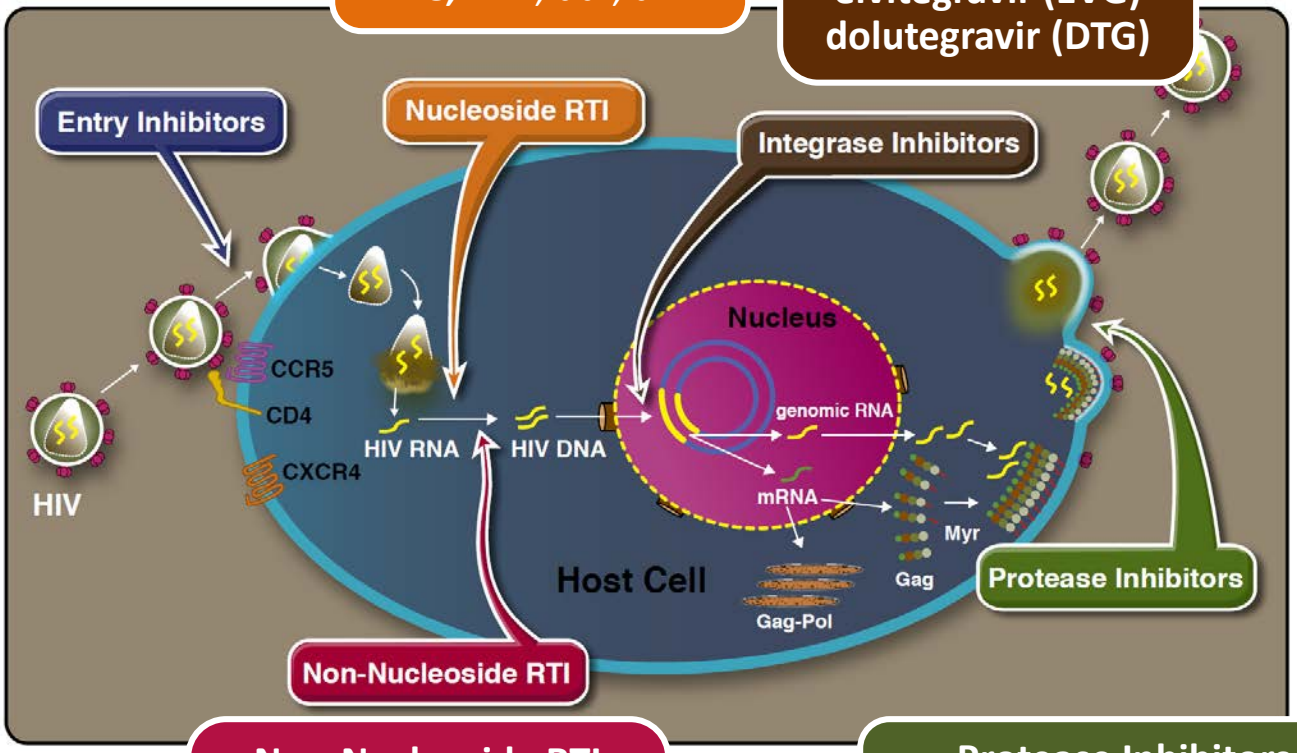
- Class Effects:
  - Diarrhea (most boosted PI, RTV dose is key)
  - Nausea
  - Metabolic
    - Fat deposition- lipodystrophy/lipohypertrophy
      - Abdomen, buffalo hump
    - Increased cholesterol and/or triglycerides
      - Less with ATV, DRV
    - Insulin resistance
  - Darunavir (and TPV, FPV) – sulfa-related rash
  - Hepatotoxicity: TPV and DRV > others?
  - Cobicistat: increased Cr
  - Atazanavir (and indinavir)
    - Increased bilirubin (possible jaundice)
    - Kidney stones

<u>High resistance threshold</u>

Retrovirus Life Cycle

Nucleoside RTI
TDF; TAF; ABC; 3TC; FTC; ZDV; ddI; d4T

Integrase Inhibitors
raltegravir (RAL)
elvitegravir (EVG)
dolutegravir (DTG)



Non-Nucleoside RTI
EFV; NVP
etravirine (ETR)
rilpivirine (RPV)

Protease Inhibitors
ATV; DRV; LPVr; FPV; SQV; IDV; RTV; NFV; TPV

Integrase Strand Transfer Inhibitors (INSTI)

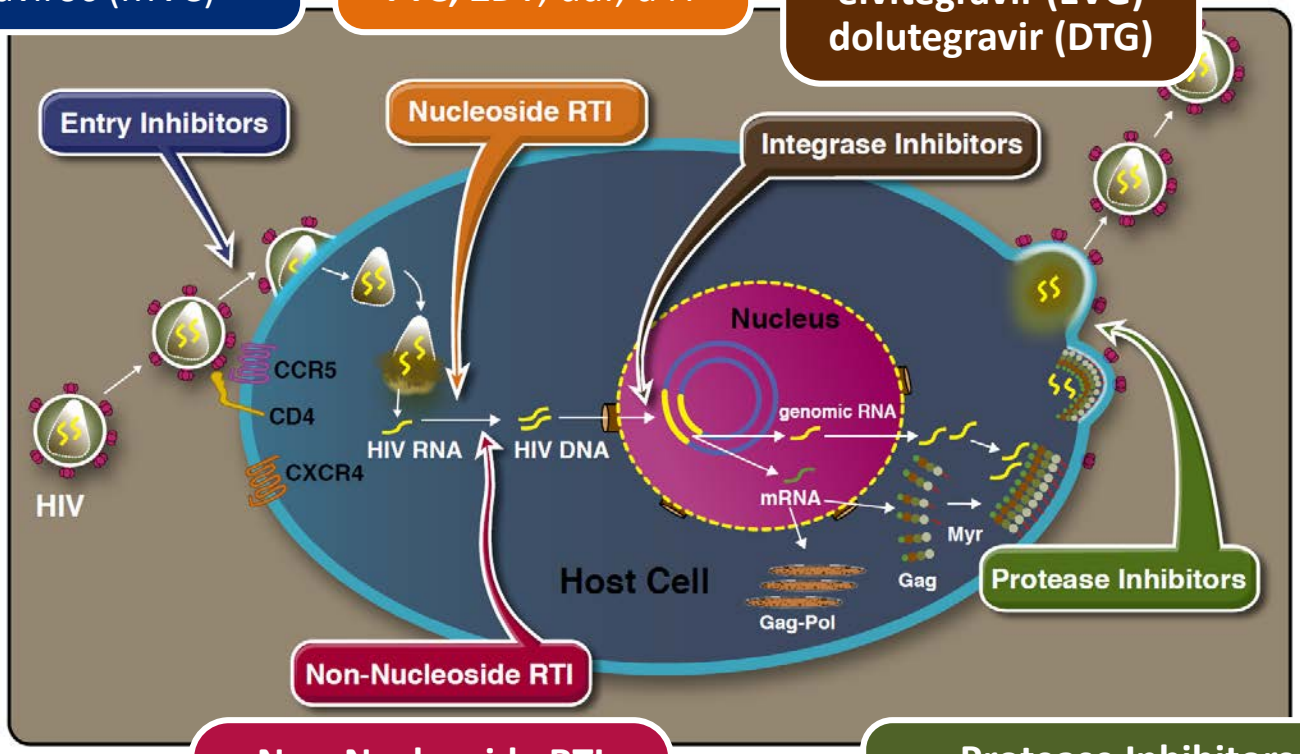
- **Raltegravir (Isentress® RAL)**
- **Elvitegravir (Vitekta® EVG) –** coformulated in Stribild® and Genvoya®
- **Dolutegravir (Tivicay® DTG) –** coformulated in Triumeq®

Retrovirus Life Cycle

Entry Inhibitors
enfuvirtide (ENF; T20)
maraviroc (MVC)

Nucleoside RTI
TDF; TAF; ABC; 3TC; FTC; ZDV; ddI; d4T

Integrase Inhibitors
raltegravir (RAL)
elvitegravir (EVG)
dolutegravir (DTG)



Non-Nucleoside RTI
EFV; NVP
etravirine (ETR)
rilpivirine (RPV)

Protease Inhibitors
ATV; DRV; LPVr; FPV; SQV; IDV; RTV; NFV; TPV

ART Co-formulations

- **Epzicom®** **ABC/3TC**
- **Truvada®** **TDF/FTC**
- **Descovy®** **TAF/FTC**
- **Atripla®** **EFV/TDF/FTC**
- **Complera®** **RPV/TDF/FTC**
- **Odefsey®** **RPV/TAF/FTC**
- **Stribild®** **EVGc/TDF/FTC**
- **Genvoya®** **EVGc/TAF/FTC**
- **Triumeq®** **DTG/ABC/3TC**
- **Prezcobix®** **DRVc**
- **Evotaz®** **ATVc**
- Combivir® AZT/3TC
- Trizivir® AZT/ABC/3TC

Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents

Developed by the HHS Panel on Antiretroviral Guidelines for Adults and Adolescents – A Working Group of the Office of AIDS Research Advisory Council (OARAC)

Panel on Antiretroviral Guidelines for Adults and Adolescents.
Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents.
Department of Health and Human Services.
Available at ***http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.***

DHHS evidence ratings

- **Recommendations**
  A. Strong
  B. Moderate
  C. Optional
- **Evidence**
  I. RCT
  II. Observational studies
  III. Expert opinion

When to start?

Initiation of Antiretroviral Therapy (Last updated January 28, 2016; last reviewed January 28, 2016)

Panel's Recommendations
• Antiretroviral therapy (ART) is recommended for all HIV-infected individuals, regardless of CD4 T lymphocyte cell count, to reduce the morbidity and mortality associated with HIV infection (**AI**).
• ART is also recommended for HIV-infected individuals to prevent HIV transmission (**AI**).
• When initiating ART, it is important to educate patients regarding the benefits and considerations regarding ART, and to address strategies to optimize adherence. On a case-by-case basis, ART may be deferred because of clinical and/or psychosocial factors, but therapy should be initiated as soon as possible.

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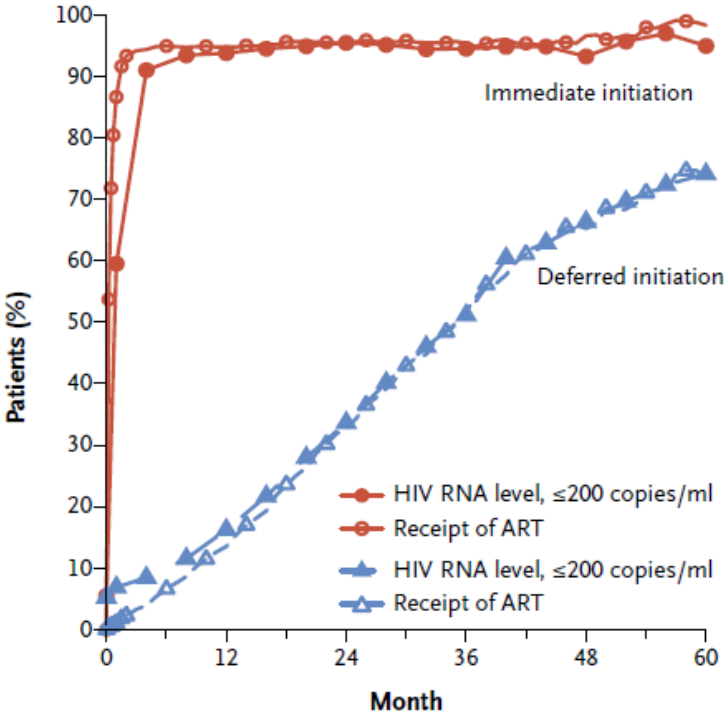
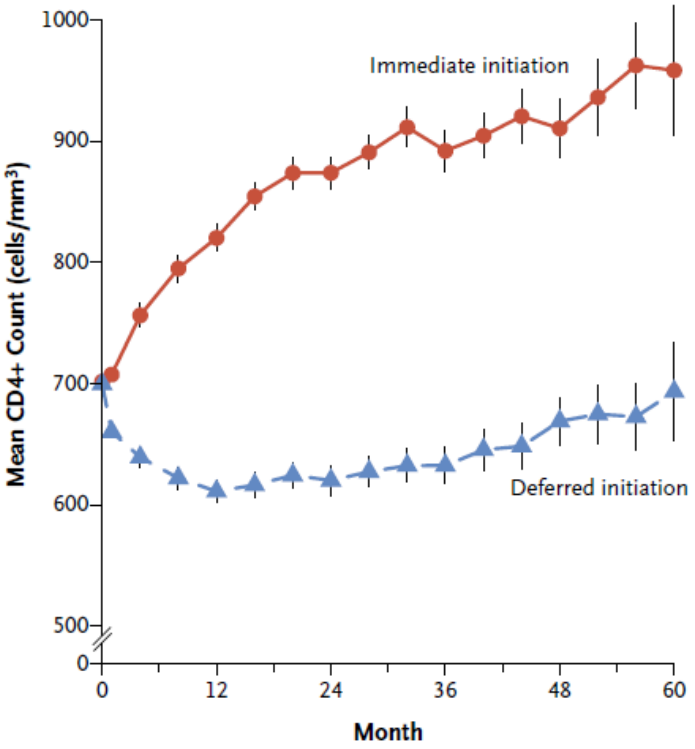
Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

A ART Use and HIV RNA Level



B CD4+ Count

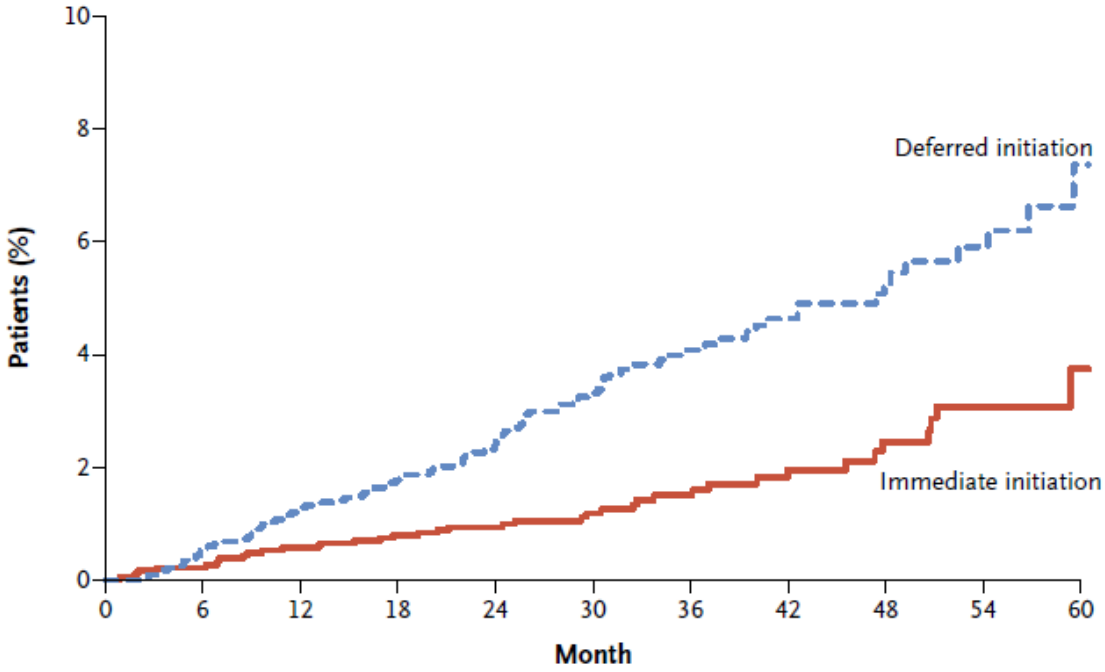


N Engl J Med 2015;373:795-807.
DOI: 10.1056/NEJMoa1506816

Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

A Time to First Primary Event



No. at Risk											
Immediate initiation	2326	2302	2279	2163	1801	1437	1031	757	541	336	110
Deferred initiation	2359	2326	2281	2135	1803	1417	1021	729	520	334	103
Estimated Percentage											
Immediate initiation		0.2	0.6	0.8	0.9	1.2	1.5	2.0	2.5	3.1	3.7
Deferred initiation		0.5	1.2	1.8	2.4	3.3	4.1	4.6	5.3	5.9	7.4

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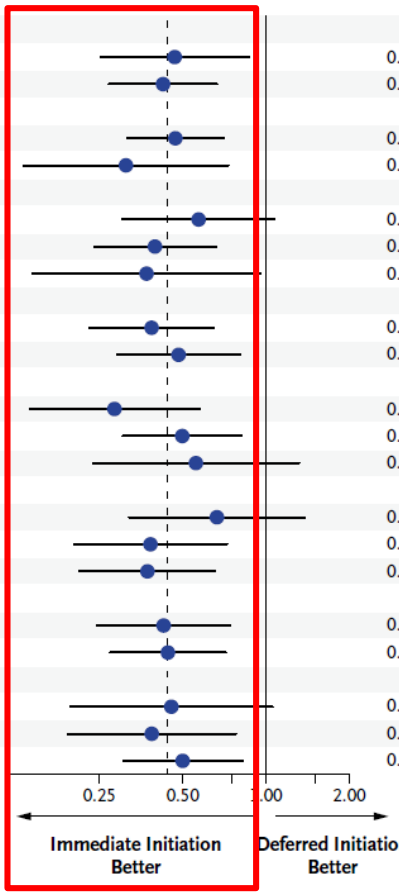
Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection

The INSIGHT START Study Group*

Subgroup	Percentage in Group	Immediate Initiation	Deferred Initiation	P Value for Interaction
		no. of patients with event (rate per 100 person-yr)		
Age				0.98
≤35 yr	48.8	15 (0.43)	31 (0.91)	0.47
>35 yr	51.2	27 (0.78)	65 (1.85)	0.42
Sex				0.38
Male	73.2	35 (0.66)	74 (1.40)	0.47
Female	26.8	7 (0.42)	22 (1.34)	0.31
Race				0.65
Black	30.1	15 (0.82)	28 (1.52)	0.57
White	44.5	21 (0.63)	53 (1.54)	0.40
Other	25.4	6 (0.34)	15 (0.91)	0.37
Geographic region				0.55
High income	46.0	20 (0.56)	51 (1.42)	0.39
Low or moderate income	54.0	22 (0.65)	45 (1.35)	0.48
Baseline CD4+				0.71
<600 cells/mm^3	31.5	10 (0.44)	35 (1.54)	0.28
600–800 cells/mm^3	48.6	24 (0.70)	46 (1.38)	0.50
>800 cells/mm^3	19.9	8 (0.63)	15 (1.14)	0.56
Baseline HIV RNA				0.25
<5000 copies/ml	31.8	12 (0.56)	18 (0.83)	0.66
5000–30,000 copies/ml	35.5	13 (0.53)	36 (1.41)	0.38
>30,000 copies/ml	32.5	17 (0.72)	42 (1.92)	0.37
Smoker				0.93
Yes	31.9	18 (0.78)	43 (1.81)	0.43
No	68.1	24 (0.52)	53 (1.16)	0.44
Framingham 10-yr CHD risk				0.56
<0.8	32.7	8 (0.35)	17 (0.77)	0.46
0.8–3.6	32.3	11 (0.48)	27 (1.23)	0.39
>3.6	33.5	23 (1.00)	50 (2.05)	0.50



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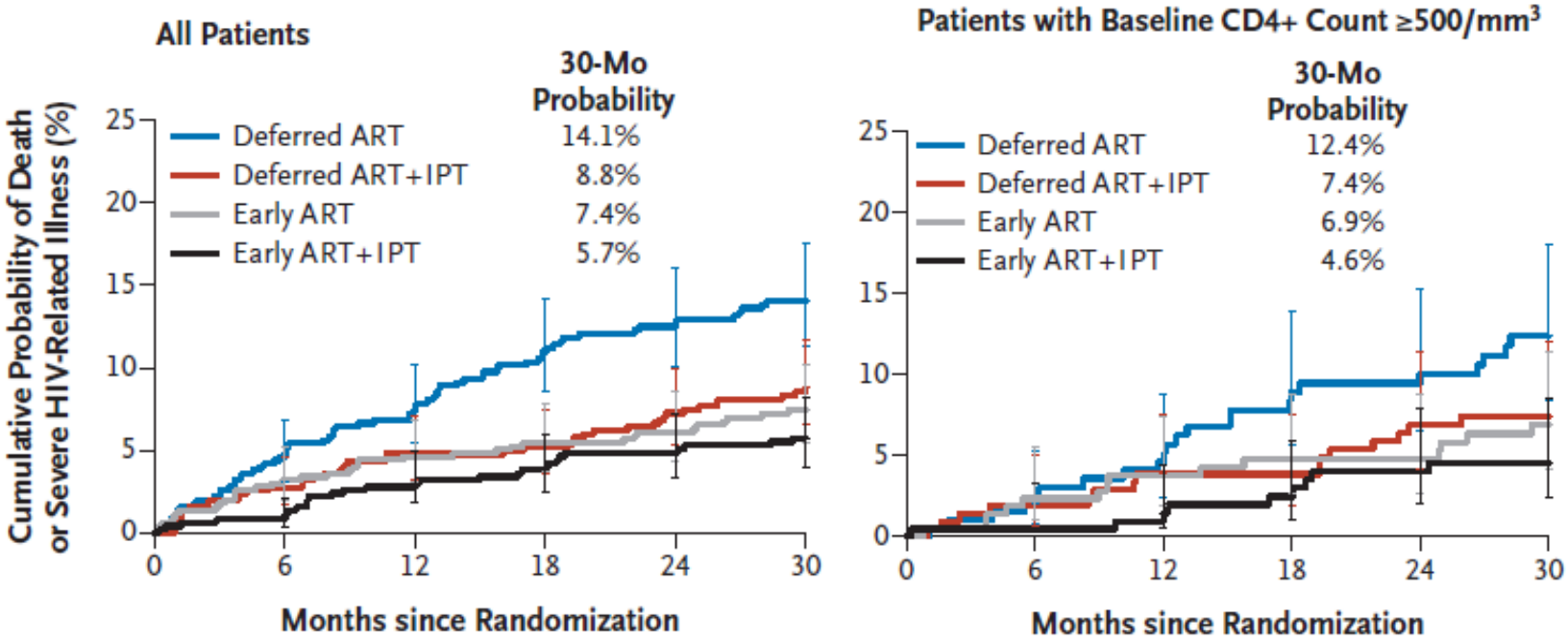
A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*

A Primary Outcome



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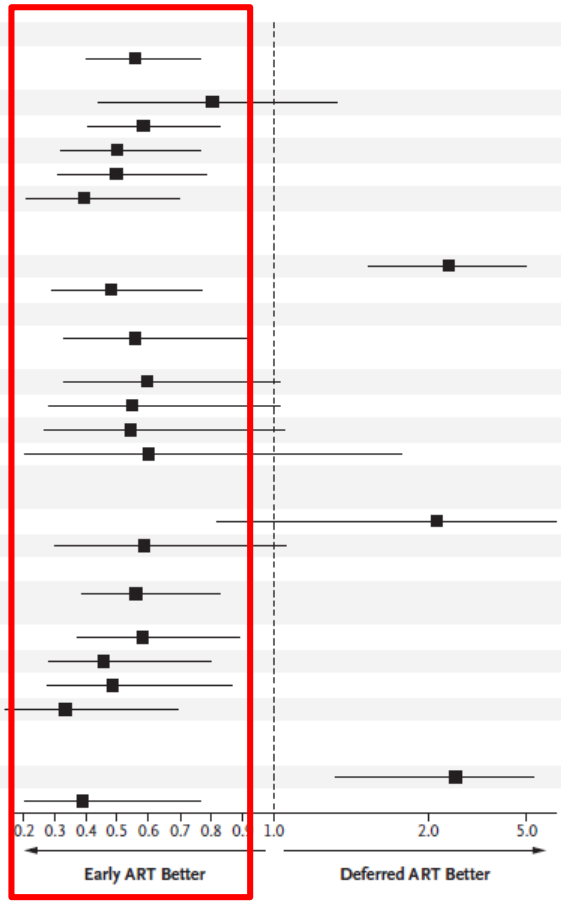
A Trial of Early Antiretrovirals and Isoniazid Preventive Therapy in Africa

The TEMPRANO ANRS 12136 Study Group*

Subgroup	Early ART (groups 3 and 4)			Deferred ART (groups 1 and 2)			Adjusted Hazard Ratio (95% CI)
	no. of patients	*person-yr*	*rate*	*no. of patients*	*person-yr*	*rate*	
All patients							
Death or severe HIV-related illness (primary outcome)	64	2313	2.8	111	2248	4.9	0.56 (0.41–0.76)
Death	21	2520	0.8	26	2502	1.0	0.80 (0.45–1.40)
Death or AIDS	50	2333	2.1	84	2288	3.7	0.58 (0.41–0.83)
AIDS	33	2333	1.4	65	2288	2.8	0.50 (0.33–0.76)
Tuberculosis	28	2337	1.2	55	2298	2.4	0.50 (0.32–0.79)
Invasive bacterial diseases	14	2358	0.6	36	2332	1.5	0.39 (0.21–0.71)
Other grade 3 or 4 adverse event (main secondary outcome)							
<6 mo after randomization	43	489	8.8	17	500	3.4	2.57 (1.47–4.51)
6–30 mo after randomization	27	1775	1.5	57	1798	3.2	0.48 (0.30–0.76)
Patients with baseline CD4+ count ≥500/mm^3							
Death or severe HIV-related illness (primary outcome)	23	966	2.4	38	919	4.1	0.56 (0.33–0.94)
Death or AIDS	19	972	1.9	30	930	3.2	0.59 (0.33–1.06)
AIDS	14	972	1.4	24	930	2.6	0.55 (0.28–1.06)
Tuberculosis	12	974	1.2	21	932	2.3	0.54 (0.26–1.09)
Invasive bacterial diseases	5	983	0.5	8	954	0.8	0.61 (0.20–1.88)
Other grade 3 or 4 adverse event (main secondary outcome)							
<6 mo after randomization	12	206	5.8	5	202	2.5	2.33 (0.82–6.61)
6–30 mo after randomization	15	742	2.0	25	727	3.4	0.58 (0.30–1.09)
Patients with baseline CD4+ count <500/mm^3							
Death or severe HIV-related illness (primary outcome)	41	1347	3.0	73	1329	5.5	0.56 (0.38–0.83)
Death or AIDS	31	1361	2.3	54	1359	4.0	0.58 (0.37–0.90)
AIDS	19	1361	1.4	41	1359	3.0	0.47 (0.27–0.81)
Tuberculosis	16	1363	1.2	34	1366	2.5	0.48 (0.27–0.87)
Invasive bacterial diseases	9	1375	0.7	28	1379	2.0	0.33 (0.15–0.69)
Other grade 3 or 4 adverse event (main secondary outcome)							
<6 mo after randomization	31	283	10.9	12	299	4.0	2.73 (1.40–5.31)
6–30 mo after randomization	12	1034	1.2	32	1071	3.0	0.39 (0.20–0.76)



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What to start?

What to Start: Initial Combination Regimens for the Antiretroviral-Naive Patient (Last updated January 28, 2016; last reviewed January 28, 2016)

Panel's Recommendations

- An antiretroviral regimen for a treatment-naive patient generally consists of two nucleoside reverse transcriptase inhibitors in combination with a third active antiretroviral drug from one of three drug classes: an integrase strand transfer inhibitor, a non-nucleoside reverse transcriptase inhibitor, or a protease inhibitor with a pharmacokinetic enhancer (cobicistat or ritonavir).
- The Panel classifies the following regimens as Recommended regimens for antiretroviral-naive patients:

  Integrase Strand Transfer Inhibitor-Based Regimens:

  - Dolutegravir/abacavir/lamivudine[a]—**only** for patients who are HLA-B*5701 negative (**AI**)
  - Dolutegravir plus tenofovir disoproxil fumarate/emtricitabine[a] (**AI**)
  - Elvitegravir/cobicistat/tenofovir alafenamide/emtricitabine—**only** for patients with pre-antiretroviral therapy CrCl ≥30 mL/min (**AI**)
  - Elvitegravir/cobicistat/tenofovir disoproxil fumarate/emtricitabine—**only** for patients with pre-antiretroviral therapy CrCl >70 mL/min (**AI**)
  - Raltegravir plus tenofovir/emtricitabine[a] (**AI**)

  Protease Inhibitor-Based Regimen:

  - Darunavir/ritonavir plus tenofovir disoproxil fumarate/emtricitabine[a] (**AI**)

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Department of Health and Human Services.
Available at http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.

DHHS evidence ratings & ART categories

- **Recommendations**
  A. Strong
  B. Moderate
  C. Optional
- **Evidence**
  I. RCT
  II. Observational studies
  III. Expert opinion

- **First-line ART regimen categories**
  - **Recommended**: RCTs show efficacy/durability; favorable tolerability/toxicity
  - **Alternative**: Effective & tolerable, but with potential disadvantages; may be preferred for some patients.

What to start?
Recommended first-line regimens

INSTI-based	**DTG**/ABC/3TC[1] **DTG** + TDF/FTC **EVGc**/TDF/FTC[2] **EVGc/TAF**/FTC[3] **RAL** + TDF/FTC	**AI**
PI-based	**DRVr** + TDF/FTC	AI

[1]If HLA-B57*01 NEGATIVE
[2]If CrCl ≥70 mL/min
[3]If CrCl ≥30 mL/min

Recommended first-line ART regimen components - INSTIs

	PROS	CONS
INSTI -DTG -EVGc -RAL	•Good virologic response •Well tolerated/few AEs •Few drug-drug interactions •Preserves PIs/NNRTIs •High resistance barrier (DTG) •DTG "superior" to EFV & DRVr	•BID dosing (RAL) •Low resistance barrier (RAL & EVG) •Less experience w/ class •Requires boosting (EVG) •Potential CYP3A drug-interactions with COBI •AEs: myopathy/rhabdo, skin reactions

Recommended first-line ART regimen components - PIs

	PROS	CONS
PI -DRVr	•QD dosing •High resistance barrier •Resistance uncommon w/ failure •Experience w/ class •Preserves IIs/NNRTIs	•↑ metabolic effects •GI intolerance •Drug-drug interactions (CYP3A) •↑ pill burden

What to start?
Alternative first-line regimens

NNRTI-based	**EFV**/TDF/FTC **RPV**/TDF/FTC[1]	BI
PI-based	**ATVr** + TDF/FTC **ATVc** + TDF/FTC[2] **DRVr** + ABC/3TC[3] **DRVc** + TDF/FTC[2] **DRVc** + ABC/3TC[2,3]	BI BI BII BII BIII

[1]If HIV RNA <100,000 cps/mL & CD4 cells >200/mm^3

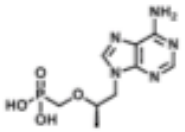
[2]If CrCl ≥70 mL/min

[3]If HLA-B57*01 NEGATIVE

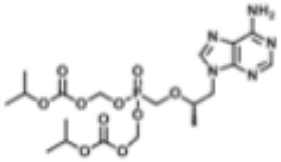
TAF – The newest NRTI

- **T**enofovir **A**la**F**enamide
  - Pro-drug of active TFV
  - More stable in plasma
  - Intracellular metabolism
  - Increased bioavailability with cobicistat

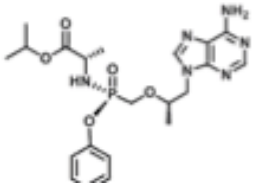
Tenofovir (TFV)

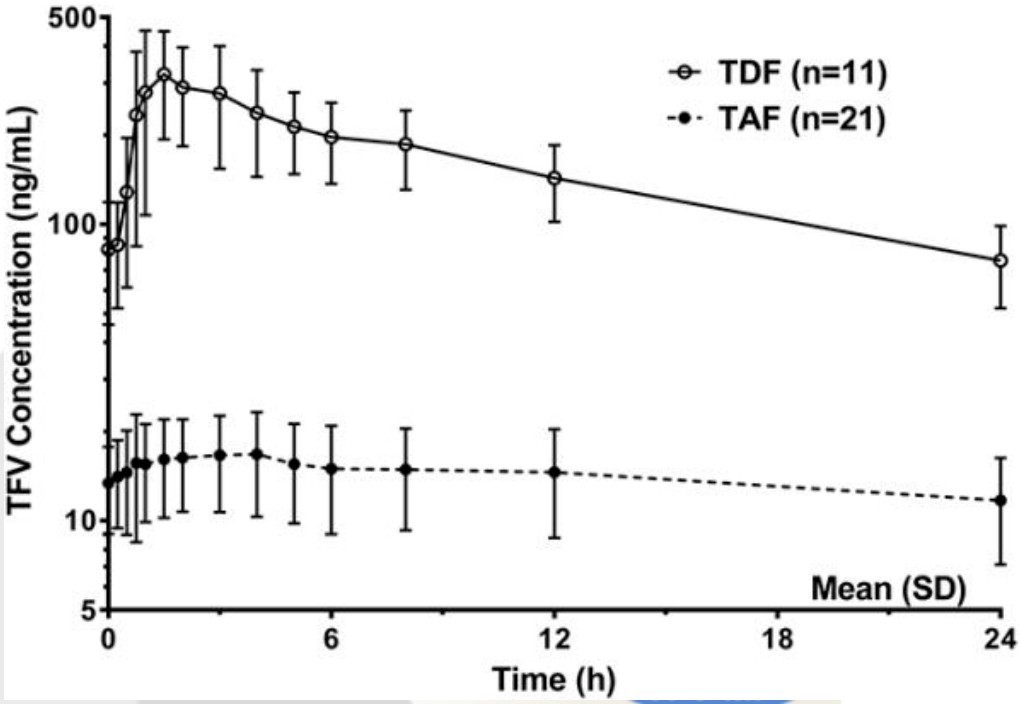


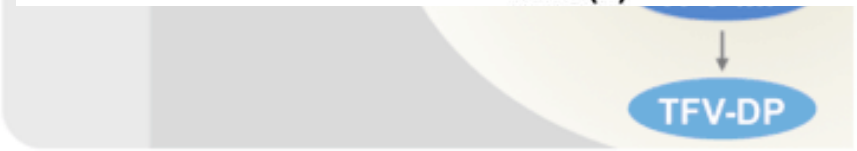
Tenofovir disoproxil fumarate (TDF)



Tenofovir alafenamide (TAF)



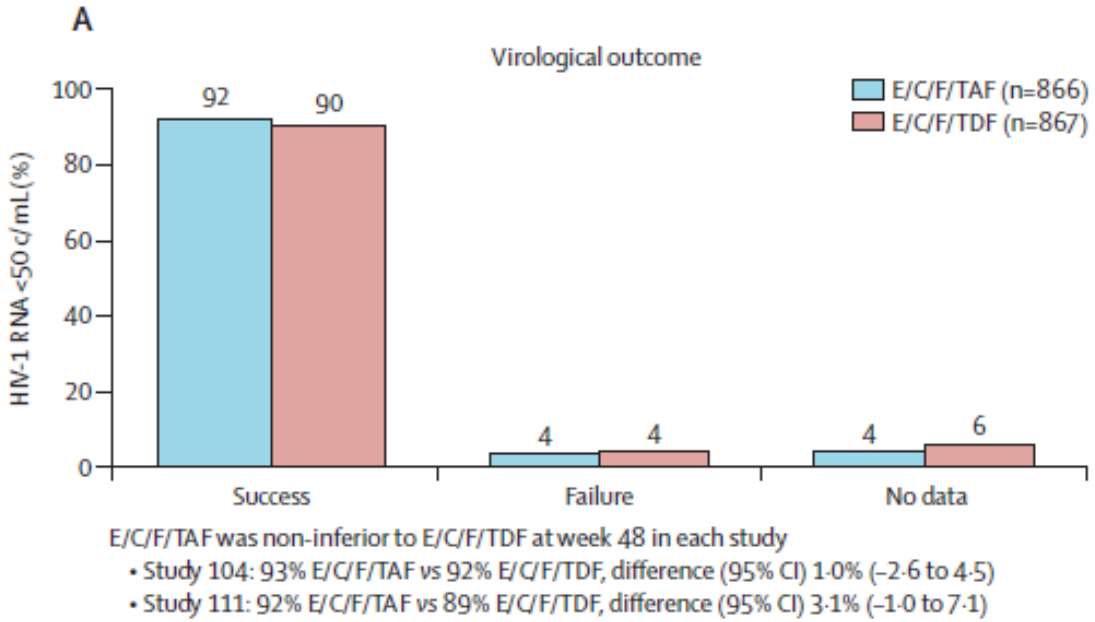




ugust 1, 2015.

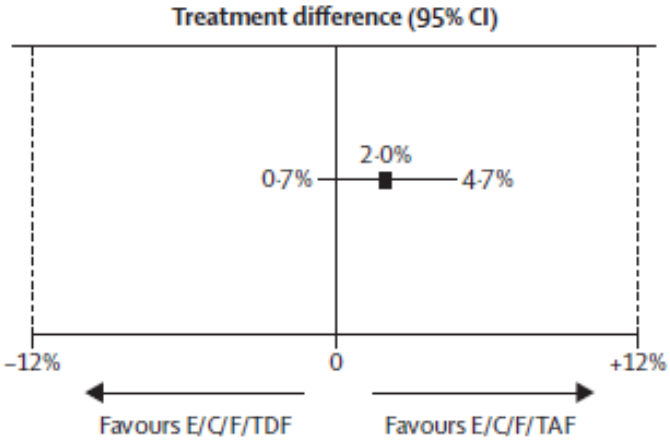
Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials

Virologic efficacy



E/C/F/TAF was non-inferior to E/C/F/TDF at week 48 in each study

- Study 104: 93% E/C/F/TAF *vs* 92% E/C/F/TDF, difference (95% CI) 1·0% (–2·6 to 4·5)
- Study 111: 92% E/C/F/TAF *vs* 89% E/C/F/TDF, difference (95% CI) 3·1% (–1·0 to 7·1)

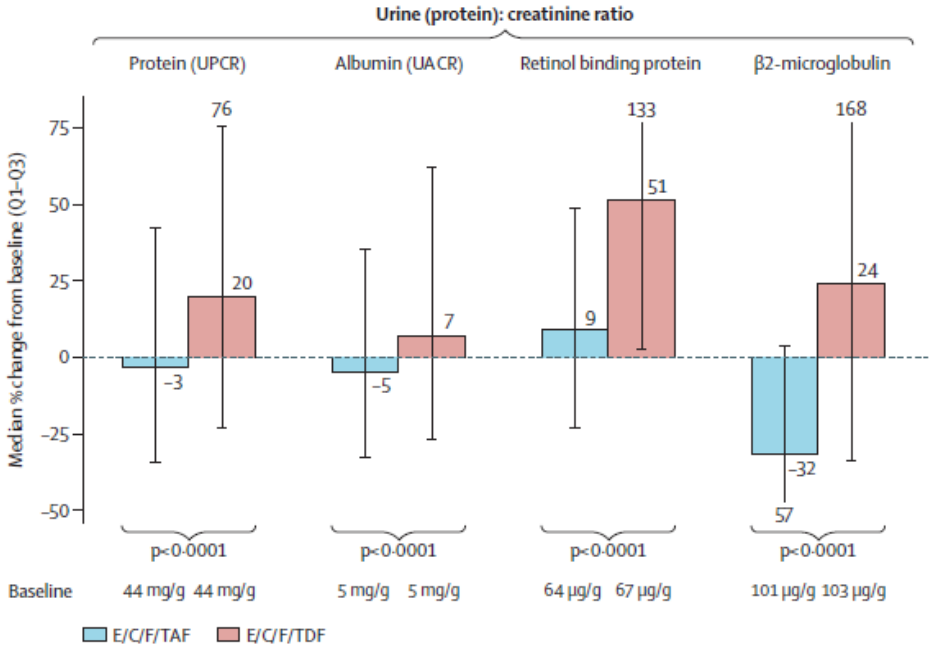


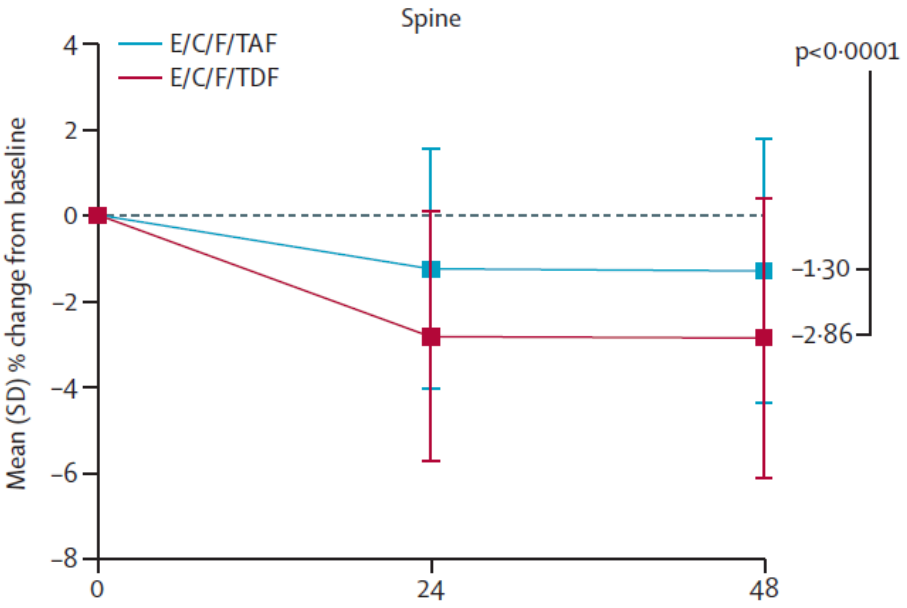
Lancet 2015; 385: 2606–15

Published Online
April 16, 2015
http://dx.doi.org/10.1016/
S0140-6736(15)60616-X

Tenofovir alafenamide versus tenofovir disoproxil fumarate, coformulated with elvitegravir, cobicistat, and emtricitabine, for initial treatment of HIV-1 infection: two randomised, double-blind, phase 3, non-inferiority trials

Renal & bone effects





Lancet 2015; 385: 2606–15
Published Online
April 16, 2015
http://dx.doi.org/10.1016/
S0140-6736(15)60616-X

TAF forms available

TAF/FTC/EVGc

TAF/FTC/RPV

TAF/FTC

What to start?

- **Questions to consider:**
  - **Baseline renal insufficiency?**
    - Avoid TDF – use ABC or TAF
    - Avoid cobicistat with TDF if CrCl ≤70 mL/min
    - Avoid cobicistat if CrCl ≤30 mL/min
  - **Importance of pill burden?**
    - Single pill?
    - QD vs. BID?
  - **GERD/acid suppression?**
    - Avoid ATV and RPV
  - **Sulfa allergy?**
    - Caution with DRV?
      - DRV allergy rare (<2%); more frequent with TMP-SMX allergy (OR>4)

Buijs, et al. *AIDS* 2015; 29: 785-91

  - **Drug interactions?**

Monitoring after ART initiation

Laboratory Test	Timepoint/Frequency of Testing					
	Entry into Care	ART Initiation[b] or Modification	2 to 8 Weeks After ART Initiation or Modification	Every 3 to 6 Months	Every 6 Months	Every 12 Months
HIV Serology	√ If HIV diagnosis has not been confirmed					
CD4 Count	√	√		√ During first 2 years of ART or if viremia develops while patient on ART or CD4 count <300 cells/ mm^3		√ After 2 years on ART with consistently suppressed viral load: *CD4 Count 300–500 cells/mm^3:* • Every 12 months *CD4 Count >500 cells/mm^3:* • CD4 monitoring is optional
HIV Viral Load	√	√	√[d]	√[e]	√[e]	
Resistance Testing	√	√[f]				
HLA-B*5701 Testing		√ If considering ABC				

http://aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf.

Drug-drug interactions: All PIs are CYP3A4 inhibitors

Contraindicated

- **Statins**
  - **Simvastatin**
  - **Lovastatin**
- **Fluticasone**
- **Rifampin**
- Amiodarone
- Triazolam
- Quindine

Major Interactions

- Phosphodiesterase Type 5 inhibitors
- Oral Contraceptives
- Azole Antifungals
- NNRTIs
- Methadone
- Anticonvulsants
- Rifabutin
- Midazolam

Summary

- **ART characteristics**
  - Potency
  - Adverse events
  - Tolerability
  - Resistance
- **Start ART as early as possible**
- **Use "recommended" regimens** unless there is a compelling reason not to
  - See **Table 7** in the DHHS Guidelines

Basics of HIV Resistance

Southeast AIDS Education & Training Center
HIV Clinical Overview
12 May 2016

Todd Hulgan, MD, MPH
Department of Medicine, Division of Infectious Diseases
Vanderbilt University School of Medicine
Tennessee Center for AIDS Research (TN-CFAR)
Tennessee Valley Veterans Healthcare System
todd.hulgan@vanderbilt.edu

AETC AIDS Education & Training Center Program Southeast

VANDERBILT UNIVERSITY School of Medicine

TN CFAR TENNESSEE CENTER FOR AIDS RESEARCH

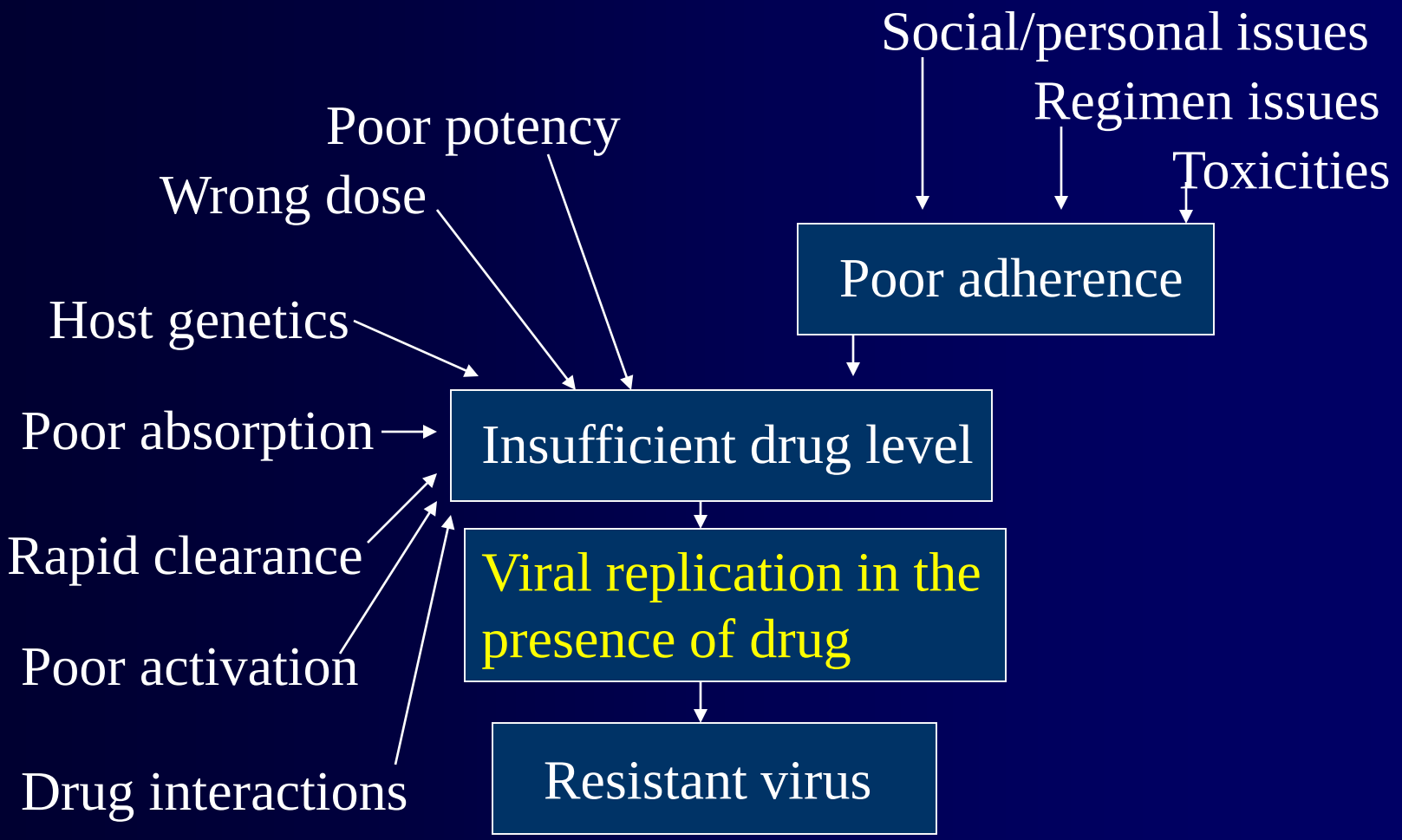
Objectives

- Define the basics of HIV resistance
  - **How**…does resistance develop?
  - **When**…is resistance testing recommended?
  - [**Viral fitness and reversion**]
  - **What**…should I use to test for resistance?
  - **Who**…are patients with resistance?
  - **Where**…do I go for more information?

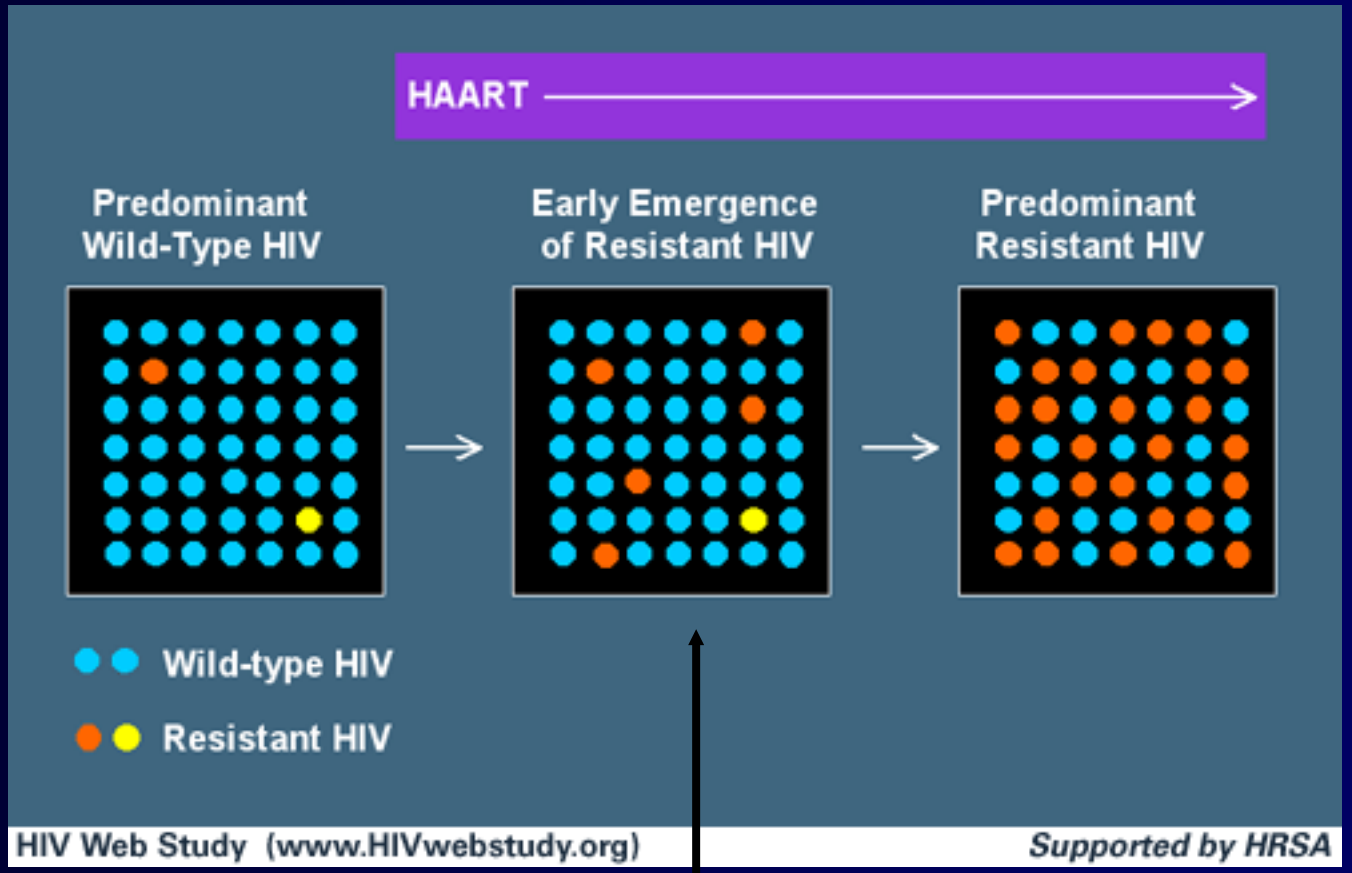
How do we characterize ART?

- **Resistance:**
  - Development of genetic mutations in viral DNA that make that strain less sensitive to a drug
  - Drugs have different *thresholds* to resistance.
    - High threshold = several steps need to take place for a viral strain to become resistant
    - Medications with a “low threshold” should be combined with potent active agents in a regimen

How does resistance develop?



How does resistance develop?

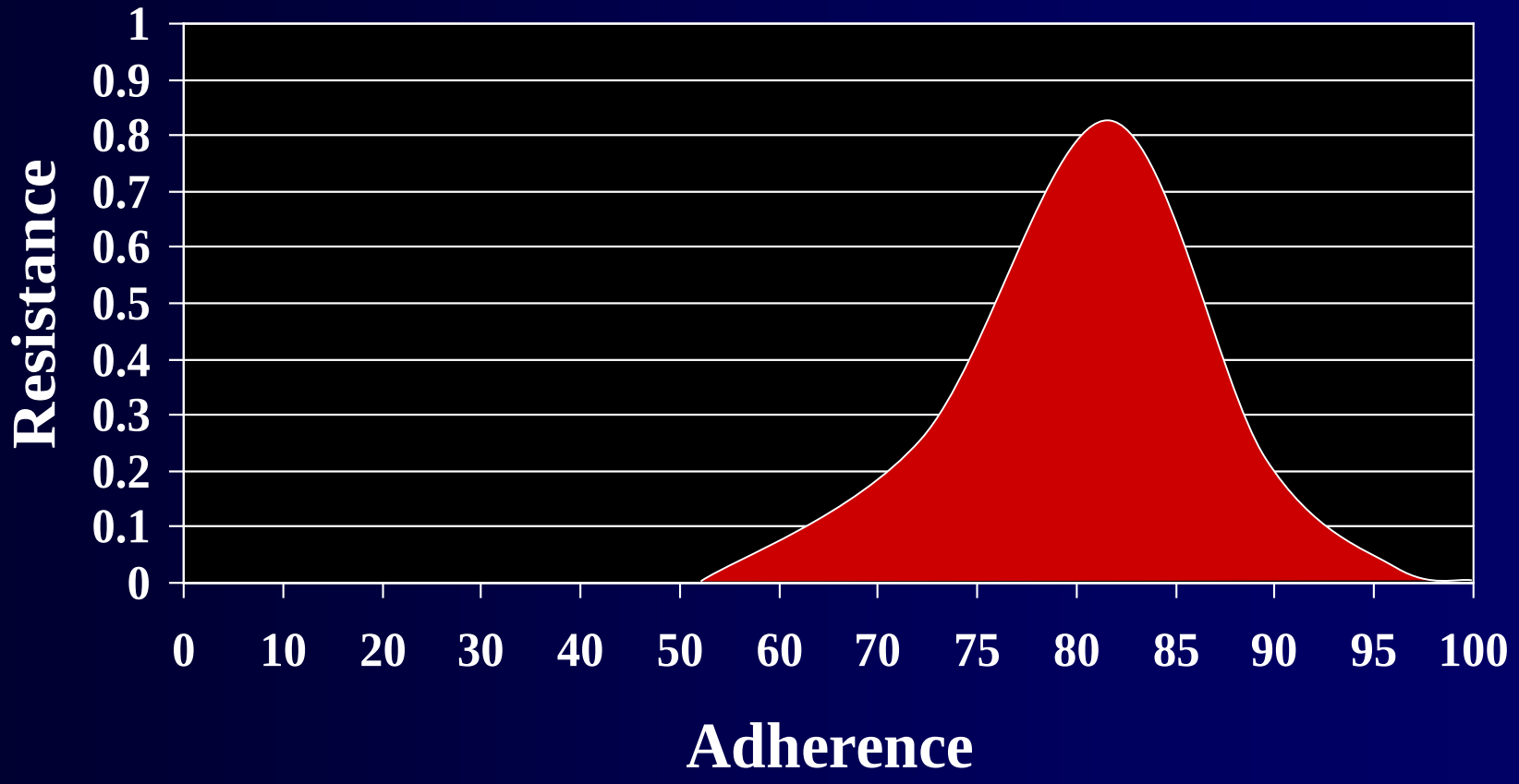


Continuation of a failing ART regimen after early resistance has developed selects for expansion of resistance

True or False?

The patients with the lowest levels of adherence are the most likely to develop resistance to their ARVs

What is the relationship between adherence and resistance?



Testing for Drug Resistance

- Before initiation of ART:
  - **Transmitted resistance in 6-16%** of HIV-infected patients
  - In absence of therapy, resistance mutations may decline over time and become undetectable by current assays, but may persist and cause treatment failure when ART is started
  - Identification of resistance mutations may optimize treatment outcomes
  - **Resistance testing (genotype) recommended for all at entry to care**
  - Recommended for all pregnant women
- Patients with virologic failure:
  - Perform **while patient is taking ART, or ≤4 weeks after discontinuing therapy**
  - Interpret in combination with history of ARV exposure and ARV adherence

Treatment-Experienced Patients: Virologic Failure, Definitions

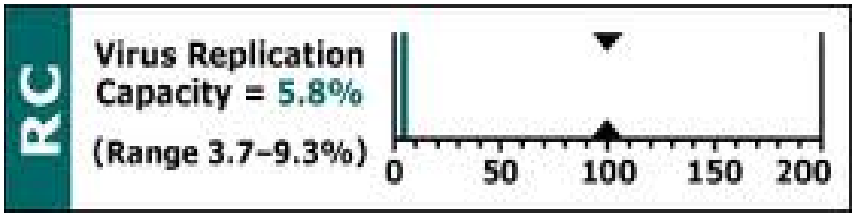
- **Virologic failure:**
  - **Inability to achieve or maintain HIV RNA <200 copies/mL**
- Incomplete virologic response:
  - Confirmed HIV RNA ≥200 copies/mL after 24 weeks on ART
- Virologic rebound:
  - Confirmed HIV RNA ≥200 copies/mL after virologic suppression
- Virologic blip:
  - An isolated detectable HIV RNA level that is followed by a return to virologic suppression
- Virologic suppression:
  - Confirmed HIV RNA below LLOD (eg, <50 copies/mL)

Treatment-Experienced Patients: Management of Virologic Failure

- Carefully assess causes of virologic failure; management will vary according to cause
- Check HIV RNA, CD4 count, ART history, prior and current ARV resistance test results
  - **Resistance test should be done while patient is taking the failing regimen, or within 4 weeks of treatment discontinuation**
  - **If >4 weeks since ARV discontinuation, resistance testing may still provide useful information, though it may not detect previously selected mutations**

HIV fitness

- Fitness can be measured:
  - In the lab:
    - Replicative capacity
  - In the patient
    - Current viral load



- It can explain some phenomena:
  - Meds that shouldn't be active having an impact:
    - 3TC/FTC, other NRTIs
  - Duration of resistance mutations

Reversion to Predominant Wild-Type Virus After Discontinuing ART

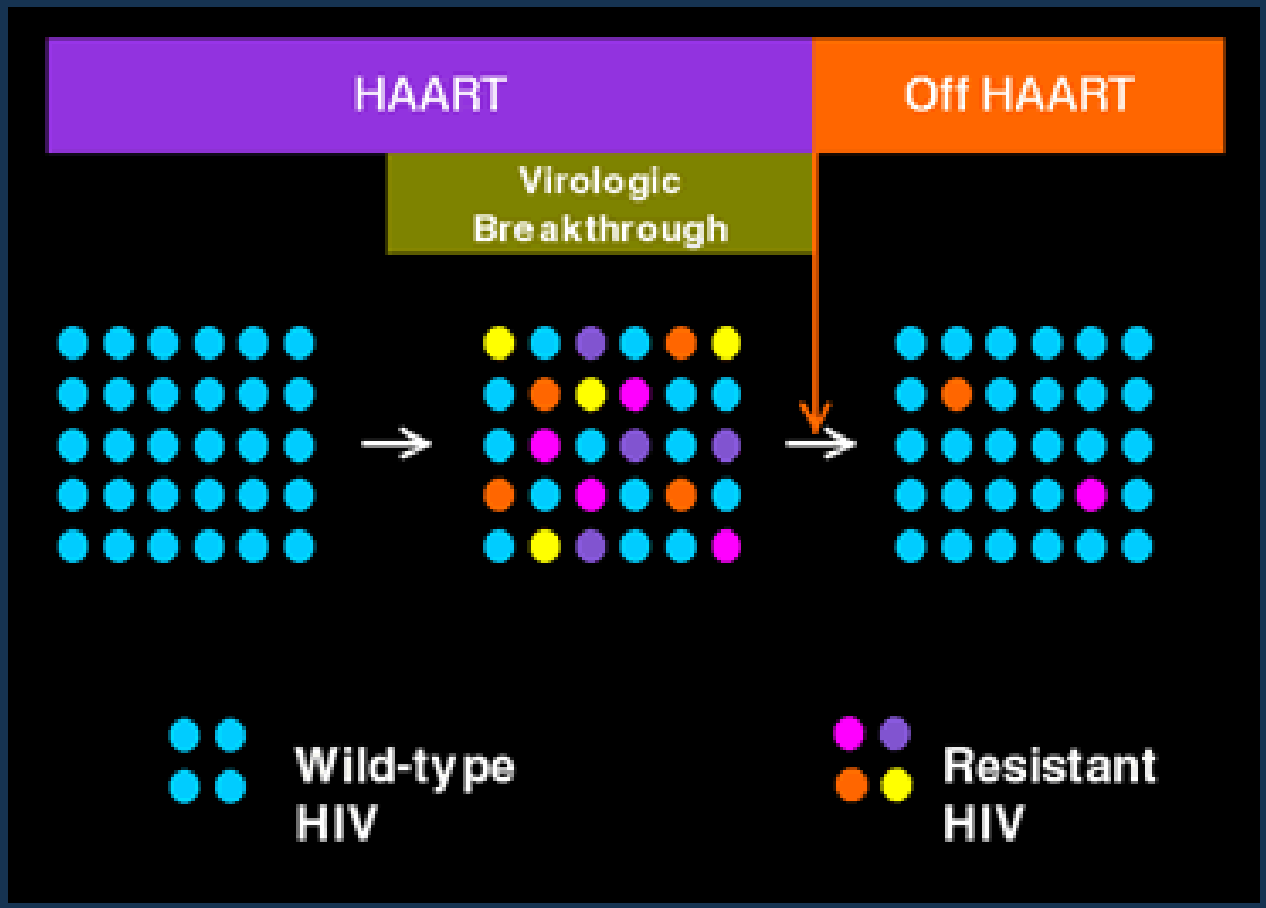


Illustration by David Spach, MD

Drug Resistance Testing: Recommendations

RECOMMENDED	COMMENT
Acute HIV infection, regardless of whether treatment is to be started	To determine if resistant virus was transmitted; guide treatment decisions. If treatment is deferred, consider repeat testing at time of ART initiation. Genotype preferred.
Chronic HIV infection, at entry into care	Transmitted drug-resistant virus is common in some areas; is more likely to be detected earlier in the course of HIV infection. If treatment is deferred, consider repeat testing at time of ART initiation. Genotype preferred to phenotype. Consider integrase genotypic resistance assay if integrase inhibitor resistance is a concern.

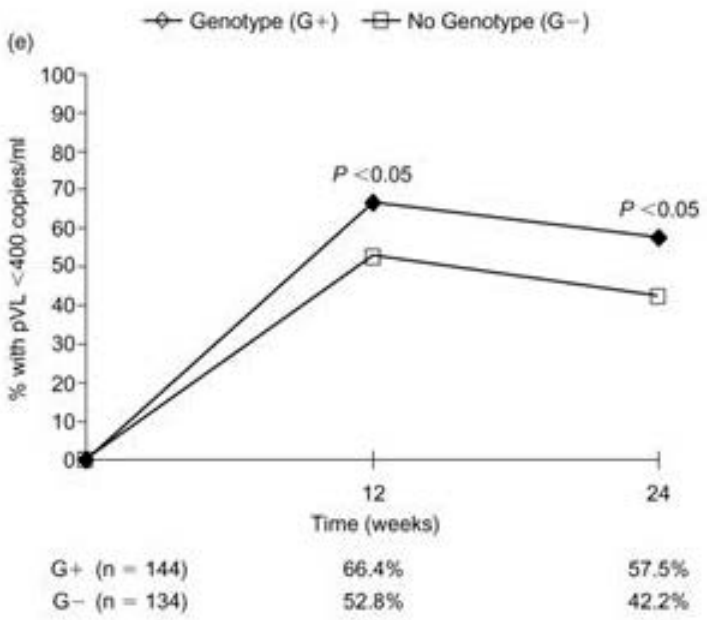
Drug Resistance Testing: Recommendations (2)

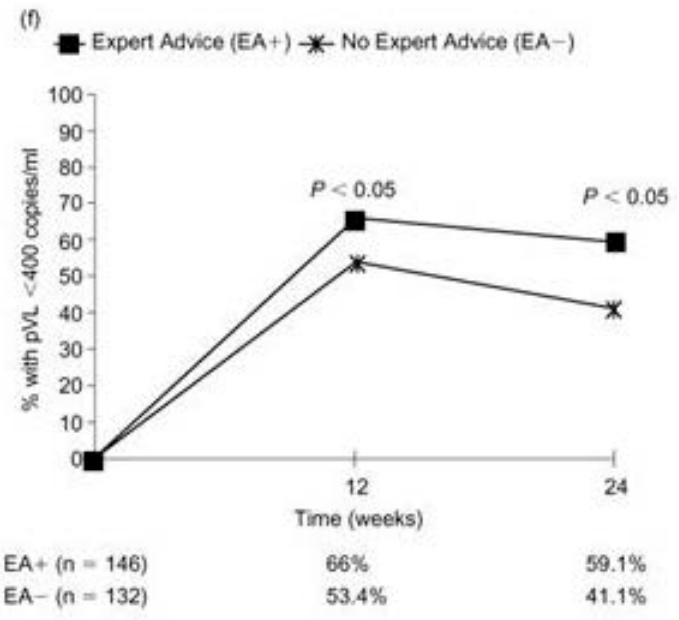
RECOMMENDED	COMMENT
Virologic failure during ART	To assist in selecting active drugs for a new regimen. Genotype preferred if patient on 1st or 2nd regimen; add phenotype if known or suspected complex drug resistance pattern. If virologic failure on integrase inhibitor or fusion inhibitor, consider specific genotypic testing for resistance to these to determine whether to continue them. (Coreceptor tropism assay if considering use of CCR5 antagonist; consider if virologic failure on CCR5 antagonist.)
Suboptimal suppression of viral load after starting ART	To assist in selecting active drugs for a new regimen.

Drug Resistance Testing: Recommendations (4)

NOT USUALLY RECOMMENDED	COMMENT
After discontinuation (>4 weeks) of ARVs	Resistance mutations may become minor species in the absence of selective drug pressure.
Plasma HIV RNA <500 copies/mL	Resistance assays cannot be performed consistently if HIV RNA is low.

Clinical utility of HIV-1 genotyping and expert advice: the Havana trial



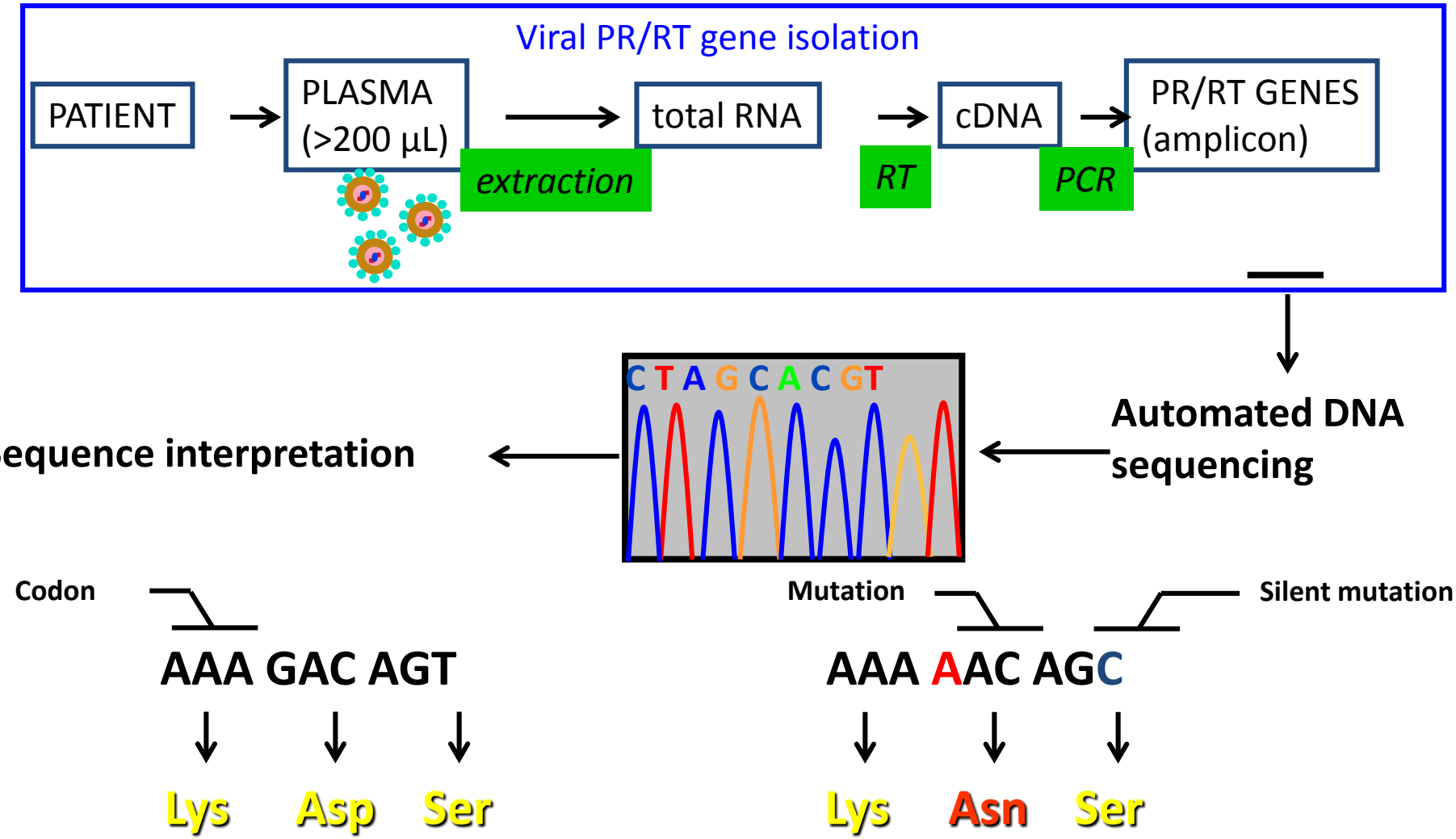


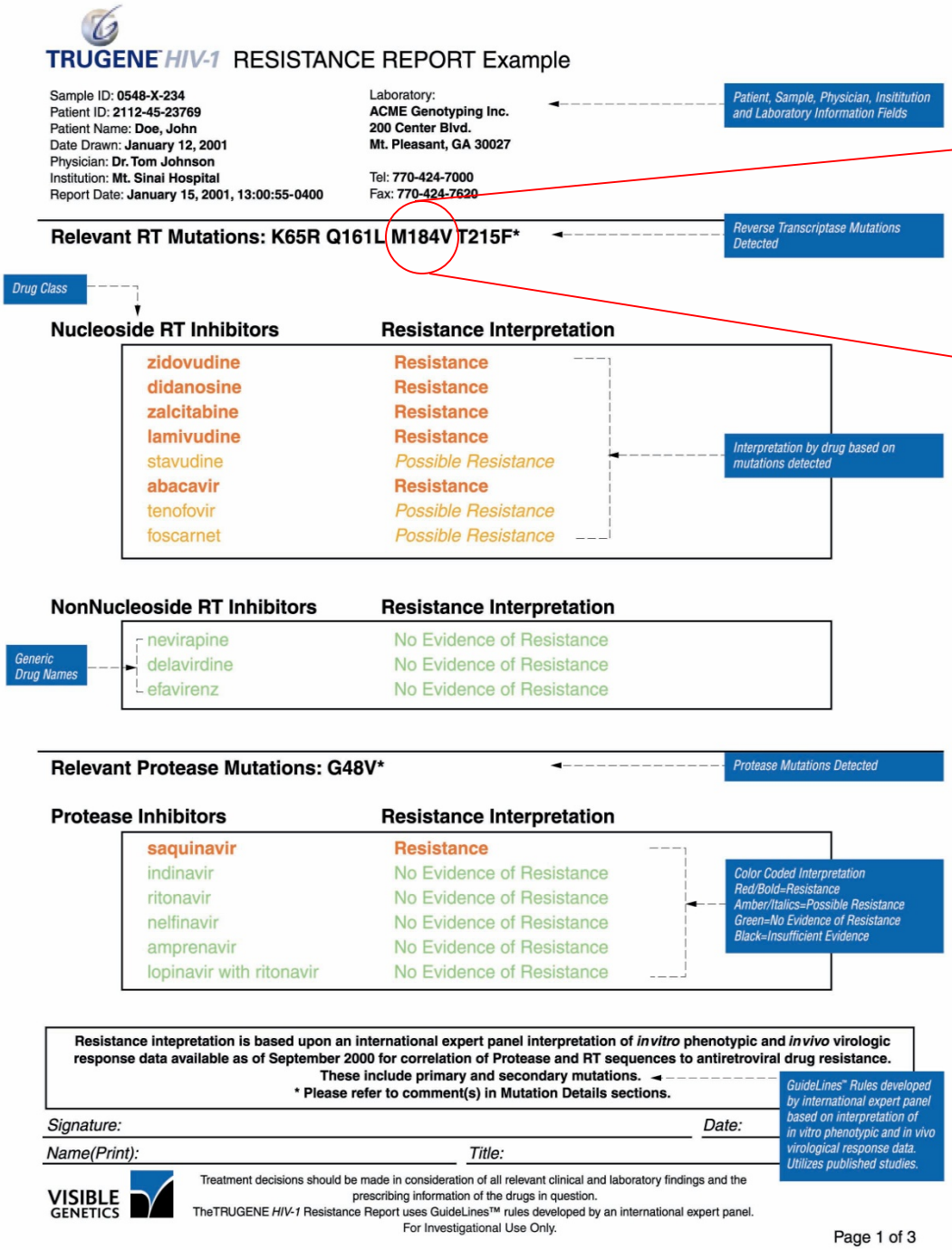
Tural, et al. *AIDS*. 16(2):209-218, January 25, 2002.

What should I use to test for resistance?

1. Genotype
2. Phenotype
3. Virtual phenotype
4. Co-receptor tropism (Trofile®)

Genotype Assay





M184V

M = Methionine
184 = the codon #
V = Valine

A mutation at codon #184 in the gene Reverse Transcriptase codes for a Valine residue where normally a Methionine residue is found.

ViroSeq™ HIV-1 Antiretroviral Drug Resistance Report

Patient ID		Testing Laboratory	Vanderbilt University Med Ctr
Patient Name Last			
Patient Name First MI		Lab Director	Jim Chappell, MDPhD
Accession Number		Department ID	Molecular Infectious Disease Lab
Patient Gender		Mailstop	N/A
Patient Birthdate & Age		Street Address1	1211 Medical Center Drive
Report Generated By		Street Address2	TVC 4606
Report Date & Time		City	Nashville
Ordering Physician		State/Province	TN
Institution		Postal Code	37232
Date Drawn		Country	USA
Assay Operator		Telephone/Fax	Ph: (615) 936-6435 Fax: (615) 343-8420
Field1		E-mail	N/A
Field2		Web Site	www.labvu.com

Drug Class	Drug		Evidence of Resistance
NRTI	EPIVIR®	(lamivudine, 3TC)	None
	EMTRIVA®	(emtricitabine, FTC)	None
	RETROVIR®	*(zidovudine, AZT)*	*Possible Resistance***
	VIDEX®	*(didanosine, ddI)*	*Possible Resistance****
	ZERIT®	*(stavudine, d4T)*	*Possible Resistance****
	ZIAGEN®	*(abacavir, ABC)*	*Possible Resistance****
	VIREAD®	*(tenofovir, TDF)*	*Possible Resistance****
NNRTI	RESCRIPTOR®	(delavirdine, DLV)	Resistance
	SUSTIVA®	(efavirenz, EFV)	Resistance
	VIRAMUNE®	(nevirapine, NVP)	Resistance
	INTELENCE™	(etravirine, ETR)	None
PI +	AGENERASE®	(amprenavir, APV)	None
	LEXIVA®	(fosamprenavir, FOS)	None
	CRIXIVAN®	(indinavir, IDV)	None
	FORTOVASE® / INVIRASE®	(saquinavir, SQV)	None
	KALETRA®	(lopinavir + ritonavir, LPV)	None
	PREZISTA®	(darunavir, DRV)	None
	VIRACEPT®	(nelfinavir, NFV)	None
	REYATAZ®	(atazanavir, ATV)	None
	APTIVUS®	(tipranavir, TPV)	None

Drug Class	Drug Resistance Mutations Identified
NRTI	M41L, T215E
NNRTI	K103N
PI	L10I

* **NOTE**: At least one mutation used to determine Evidence of Resistance for this drug has not been fully validated.
** **NOTE**: At least one mutation used to determine Evidence of Resistance for this drug has not been clinically verified.
*** **NOTE**: For at least one mutation used to evaluate Evidence of Resistance for this drug, both notes above apply.
\+ Evidence of Resistance for Protease Inhibitors estimates response to ritonavir-boosted regimens. Refer to section titled "Notes on Evidence of Resistance".

Review & Release of Results

Signature / Date: Name(Print) / Title:

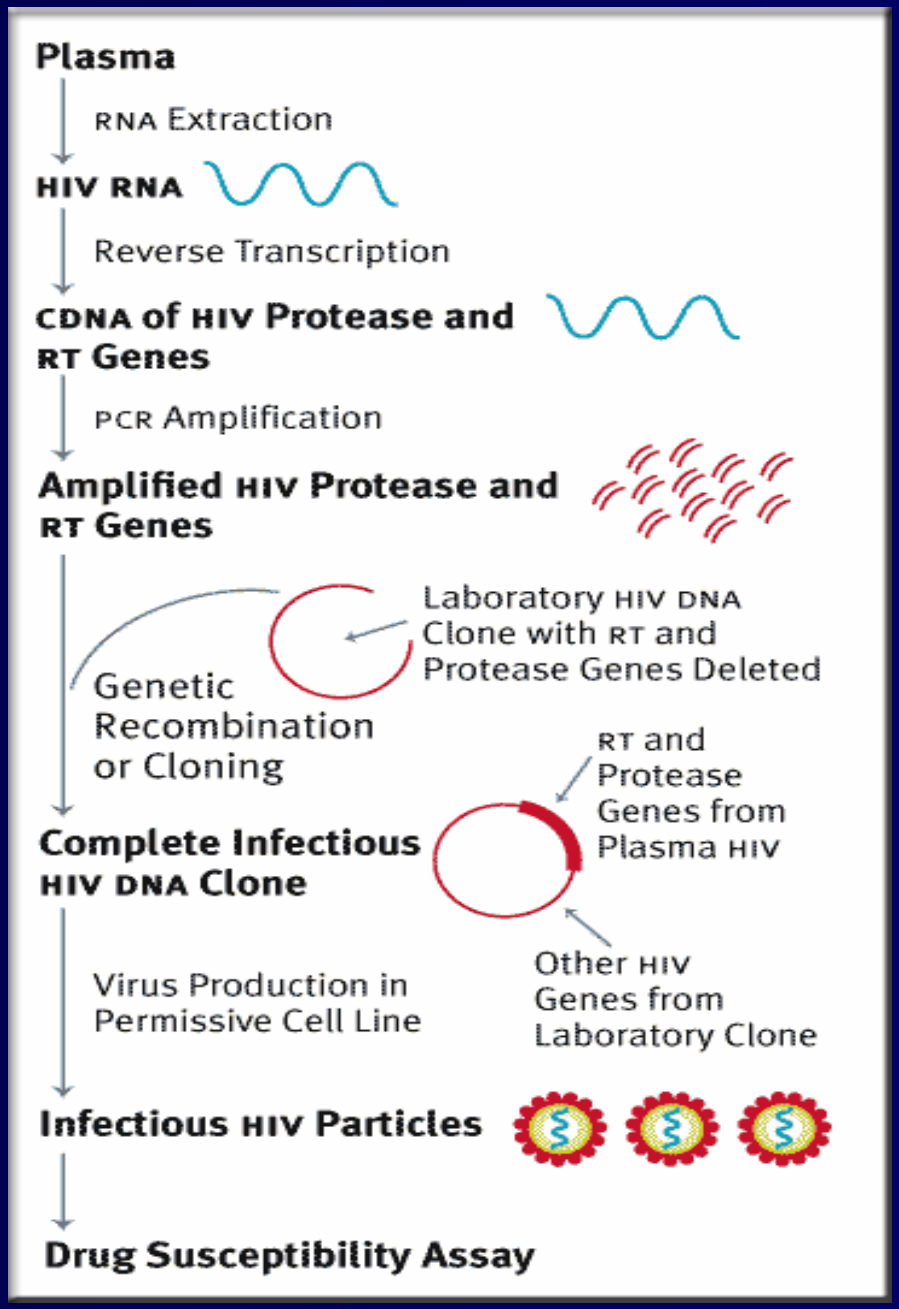
Notes:

FOR IN VITRO DIAGNOSTIC USE

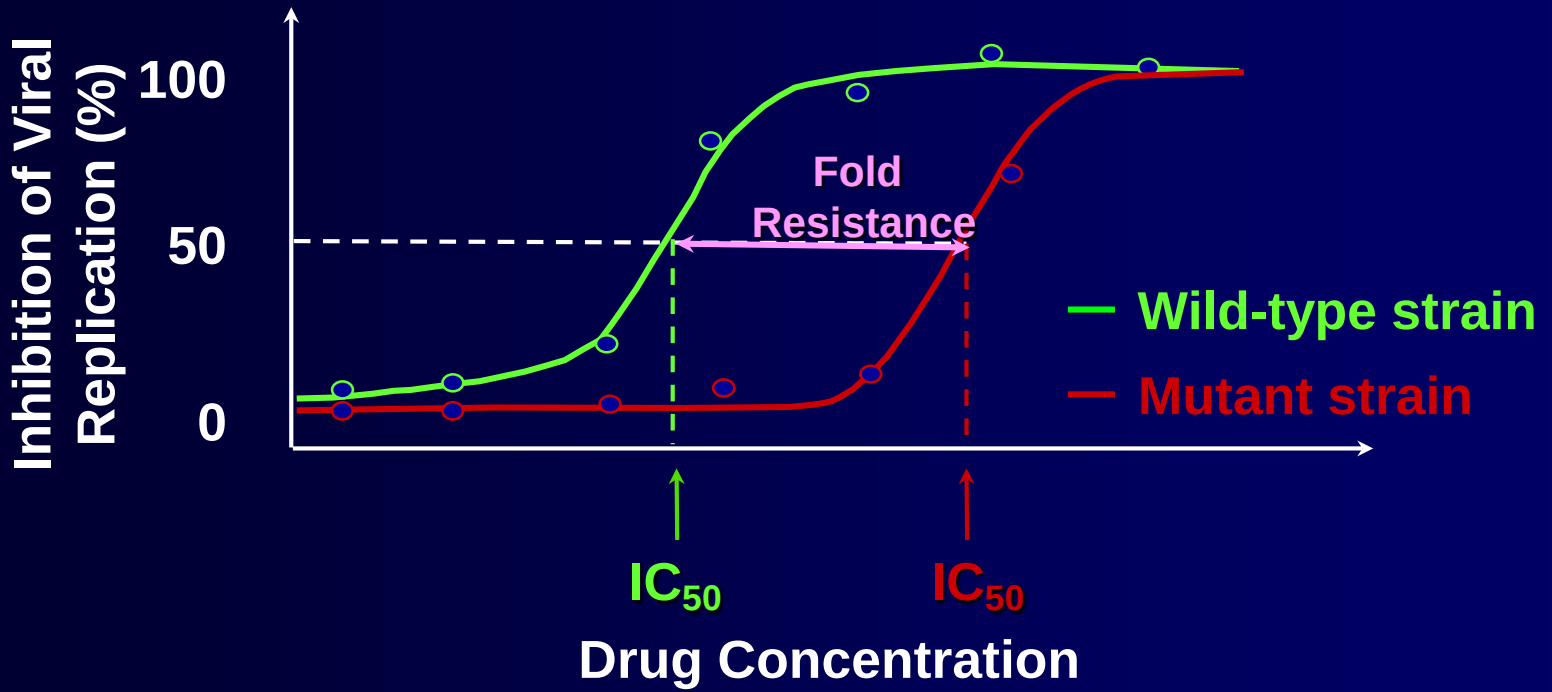
Project ID: Projects/Completed/69527

Phenotypic Resistance Testing

- Tests viability of a synthetic version of the patient's HIV in the presence of antiretroviral agents
- Similar to traditional bacterial antibiotic susceptibility assays
- Results reported as fold-change in susceptibility to antiretroviral agents

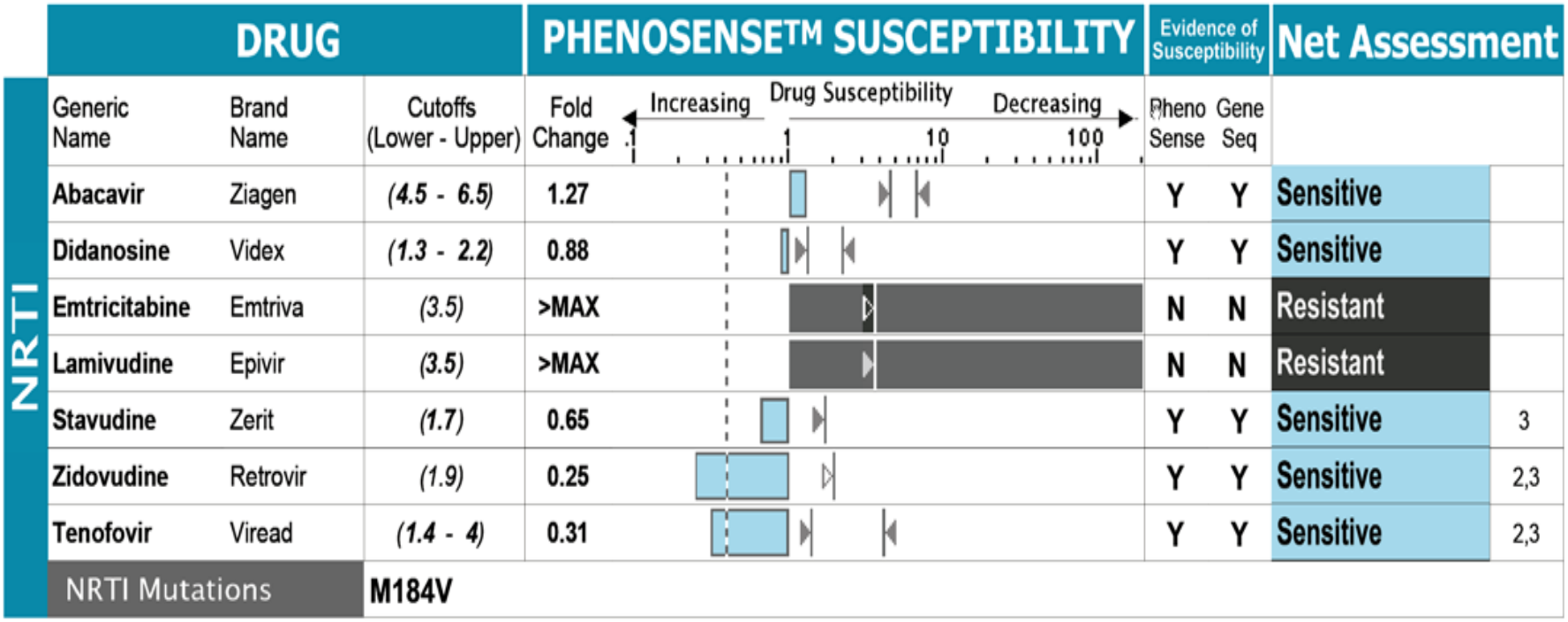


Phenotype Resistance Testing



Reviewed in Wilson. *AIDS Read* 2000;10:469.

Phenotype



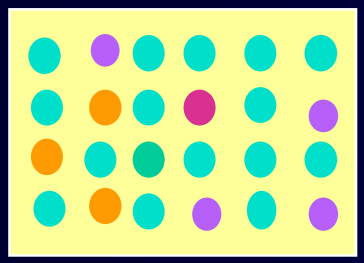
	DRUG			PHENOSENSE™ SUSCEPTIBILITY		Evidence of Susceptibility		Net Assessment	
	Generic Name	Brand Name	Cutoffs (Lower - Upper)	Fold Change	Increasing Drug Susceptibility Decreasing (.1 / 1 / 10 / 100)	Pheno Sense	Gene Seq		
NRTI	**Abacavir**	Ziagen	*(4.5 - 6.5)*	**1.27**		**Y**	**Y**	**Sensitive**	
NRTI	**Didanosine**	Videx	*(1.3 - 2.2)*	**0.88**		**Y**	**Y**	**Sensitive**	
NRTI	**Emtricitabine**	Emtriva	*(3.5)*	**>MAX**		**N**	**N**	**Resistant**	
NRTI	**Lamivudine**	Epivir	*(3.5)*	**>MAX**		**N**	**N**	**Resistant**	
NRTI	**Stavudine**	Zerit	*(1.7)*	**0.65**		**Y**	**Y**	**Sensitive**	3
NRTI	**Zidovudine**	Retrovir	*(1.9)*	**0.25**		**Y**	**Y**	**Sensitive**	2,3
NRTI	**Tenofovir**	Viread	*(1.4 - 4)*	**0.31**		**Y**	**Y**	**Sensitive**	2,3
NRTI	NRTI Mutations		**M184V**						

Genotypic vs. Phenotypic Resistance Tests

	Genotypic	Phenotypic
Basis of test	Detects drug resistance mutations present in relevant viral genes	Measures the ability of a virus to grow in different antiretroviral drug concentrations
Interpretation	Requires knowledge of mutations selected by individual antiretrovirals and potential for cross-resistance conferred by certain mutations	Visual interpretation by bars indicating susceptibility to individual agents
Sensitivity	Enhanced sensitivity for detecting mixtures of wild-type and resistant virus	Results reflect susceptibility of dominant viral species
Availability of results	1-2 wks	2-3 wks
Relative cost	Lower cost than phenotypic assays	Higher cost than genotypic assays

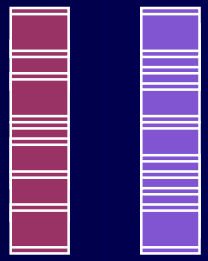
http://aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf.

The Virtual Phenotype



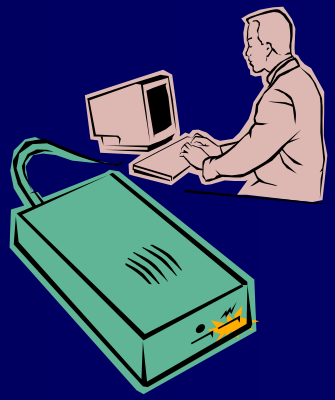
HIV

Genotype



RT Protease

Access Data



Genotype & Phenotype Data

Virtual Phenotype

Wild-type HIV

Resistant HIV

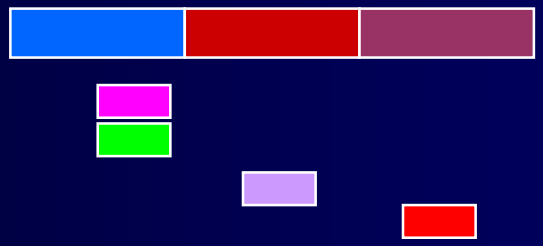
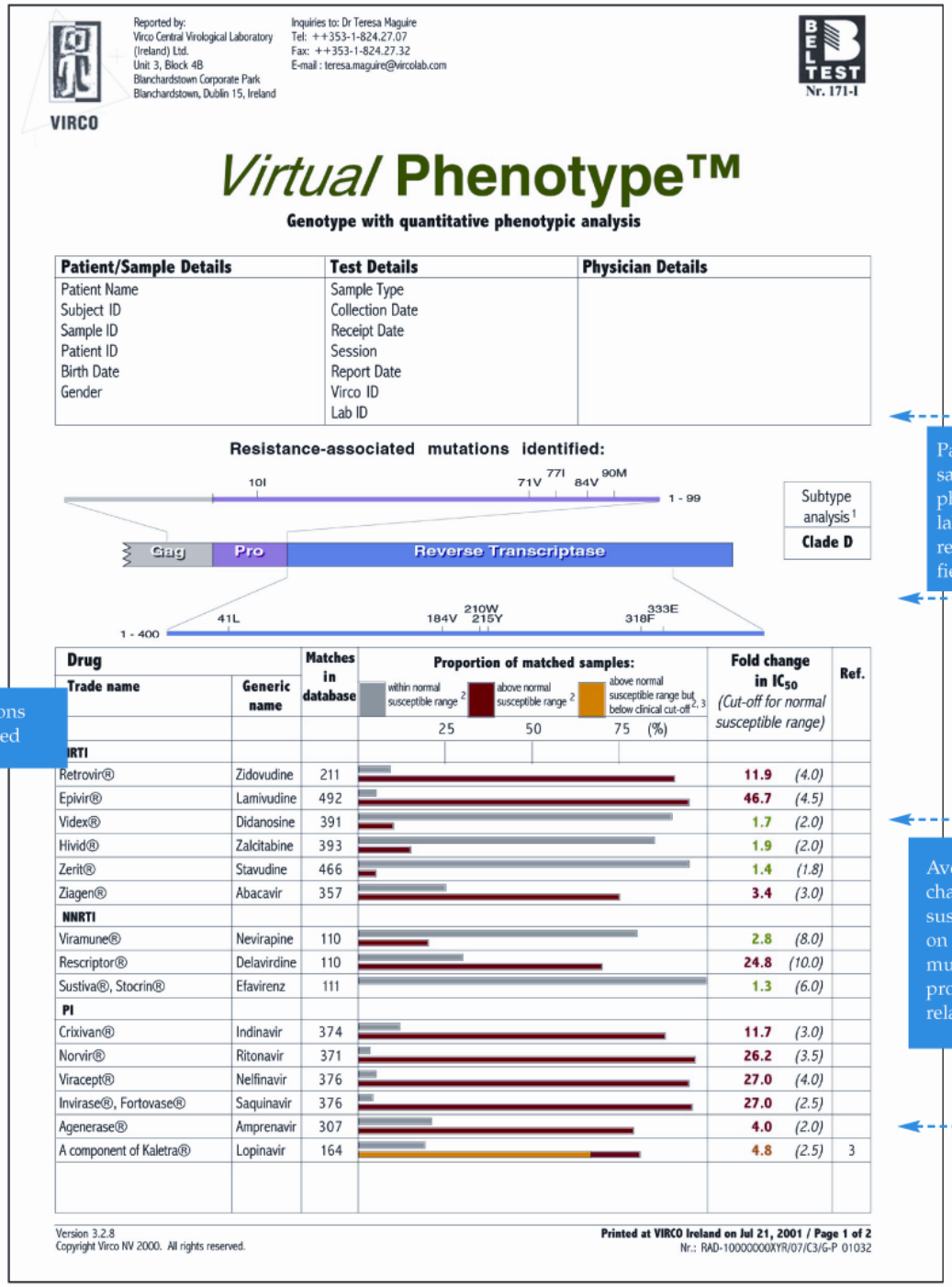


Illustration by David Spach, MD

The Virtual Phenotype Sample report



Reported by:
Virco Central Virological Laboratory
(Ireland) Ltd.
Unit 3, Block 4B
Blanchardstown Corporate Park
Blanchardstown, Dublin 15, Ireland

Inquiries to: Dr Teresa Maguire
Tel: ++353-1-824.27.07
Fax: ++353-1-824.27.32
E-mail : teresa.maguire@vircolab.com

VIRCO

BELTEST Nr. 171-I

Virtual Phenotype™

Genotype with quantitative phenotypic analysis

Patient/Sample Details	Test Details	Physician Details
Patient Name	Sample Type	
Subject ID	Collection Date	
Sample ID	Receipt Date	
Patient ID	Session	
Birth Date	Report Date	
Gender	Virco ID	
	Lab ID	

Resistance-associated mutations identified:

Subtype analysis[1]: **Clade D**

Drug: Trade name	Drug: Generic name	Matches in database	Proportion of matched samples: (within normal susceptible range[2] / above normal susceptible range[2] / above normal susceptible range but below clinical cut-off[2, 3]) 25 50 75 (%)	Fold change in IC_{50} (Cut-off for normal susceptible range)	Ref.
NRTI					
Retrovir®	Zidovudine	211		11.9 (4.0)	
Epivir®	Lamivudine	492		46.7 (4.5)	
Videx®	Didanosine	391		1.7 (2.0)	
Hivid®	Zalcitabine	393		1.9 (2.0)	
Zerit®	Stavudine	466		1.4 (1.8)	
Ziagen®	Abacavir	357		3.4 (3.0)	
NNRTI					
Viramune®	Nevirapine	110		2.8 (8.0)	
Rescriptor®	Delavirdine	110		24.8 (10.0)	
Sustiva®, Stocrin®	Efavirenz	111		1.3 (6.0)	
PI					
Crixivan®	Indinavir	374		11.7 (3.0)	
Norvir®	Ritonavir	371		26.2 (3.5)	
Viracept®	Nelfinavir	376		27.0 (4.0)	
Invirase®, Fortovase®	Saquinavir	376		27.0 (2.5)	
Agenerase®	Amprenavir	307		4.0 (2.0)	
A component of Kaletra®	Lopinavir	164		4.8 (2.5)	3

Version 3.2.8

Printed at VIRCO Ireland on Jul 21, 2001 / Page 1 of 2
Nr.: RAD-10000000XYR/07/C3/G-P 01032

Patient, sample, physician, and laboratory reference fields

Mutations identified

Average fold change in susceptibility based on comparison of mutations to a proprietary relational database

trofile™
CO-RECEPTOR TROPISM ASSAY

Monogram BIOSCIENCES
LabCorp Specialty Testing Group

Samuel H. Pepkowitz, MD, Medical Director
345 Oyster Point Blvd
South San Francisco, CA 94080 - Tel: (800) 777-0177

Patient Initials:	DOB	Patient ID/Medical Record #	Gender	Monogram Accession #
Date Collected	Date Received	Date Reported	Mode	Report Status
Investigator			Specimen ID	
Comments:			**HIV-1 Envelope Subtype: B**	

Tropotype Result

R5 D/M X4

Virus uses CCR5 co-receptors to enter the CD4+ cell.

R5

Activity of CCR5 antagonist anticipated?

- [x] YES
- [ ] NO

ABOUT TROPISM

TROFILE™ — A HIGHLY SENSITIVE TROPISM ASSAY

Trofile is a cell-based approach to determine a patient's HIV co-receptor tropism (or "Tropotype™"). Trofile uses the complete gp160 coding region of the HIV-1 envelope protein ensuring that all of the determinants of tropism are tested. CLIA* validation experiments demonstrate that Trofile is 100% sensitive at detecting 0.3% CXCR4-using minor variants.

TROFILE VIRAL CLASSIFICATION

Co-receptor tropism is defined as an interaction of a virus with a specific co-receptor on the target cell. To gain entry into CD4+ cells, HIV must bind to the cell surface CD4 receptor and to one of two co-receptors, CCR5 or CXCR4.

CCR5 Tropic (R5) HIV-1
Virus uses CCR5 to enter CD4+ cells.

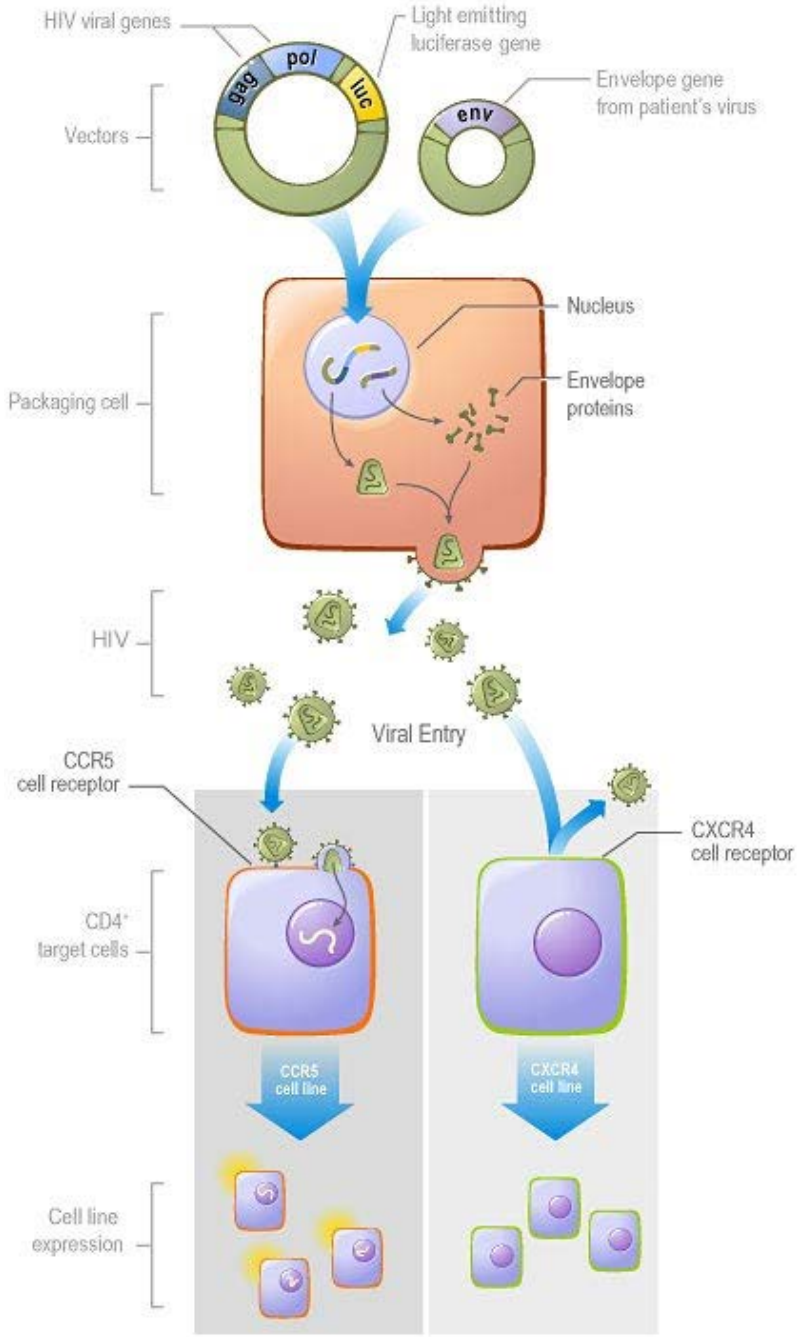
CXCR4 Tropic (X4) HIV-1
Virus uses CXCR4 to enter CD4+ cells.

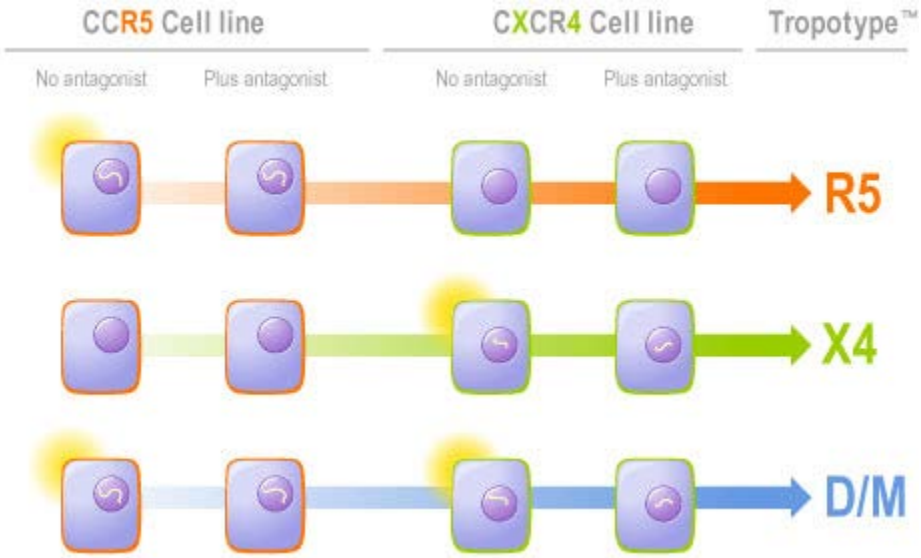
DUAL/MIXED Tropic (D/M) HIV-1
Dual-tropic viruses can use either CCR5 or CXCR4 to enter CD4+ cells. Mixed-tropic populations contain viruses with two or more tropisms.

Non-reportable
Co-receptor tropism could not be determined by the Trofile assay. Common causes of a non-reportable result are viral load <1,000 copies/mL, reduced viral fitness, or compromised sample collection/handling.

CCR5 CO-RECEPTOR ANTAGONISTS

This class of drugs binds to CCR5 and blocks CCR5-mediated HIV entry into host cells. Trofile is used to determine whether a CCR5 antagonist may be an appropriate drug for a patient. Several clinical trials of CCR5 antagonists have demonstrated the positive and negative predictive value of Trofile in clinical settings.





http://www.trofileassay.com/index.html

IAS–USA Drug Resistance Mutations Group

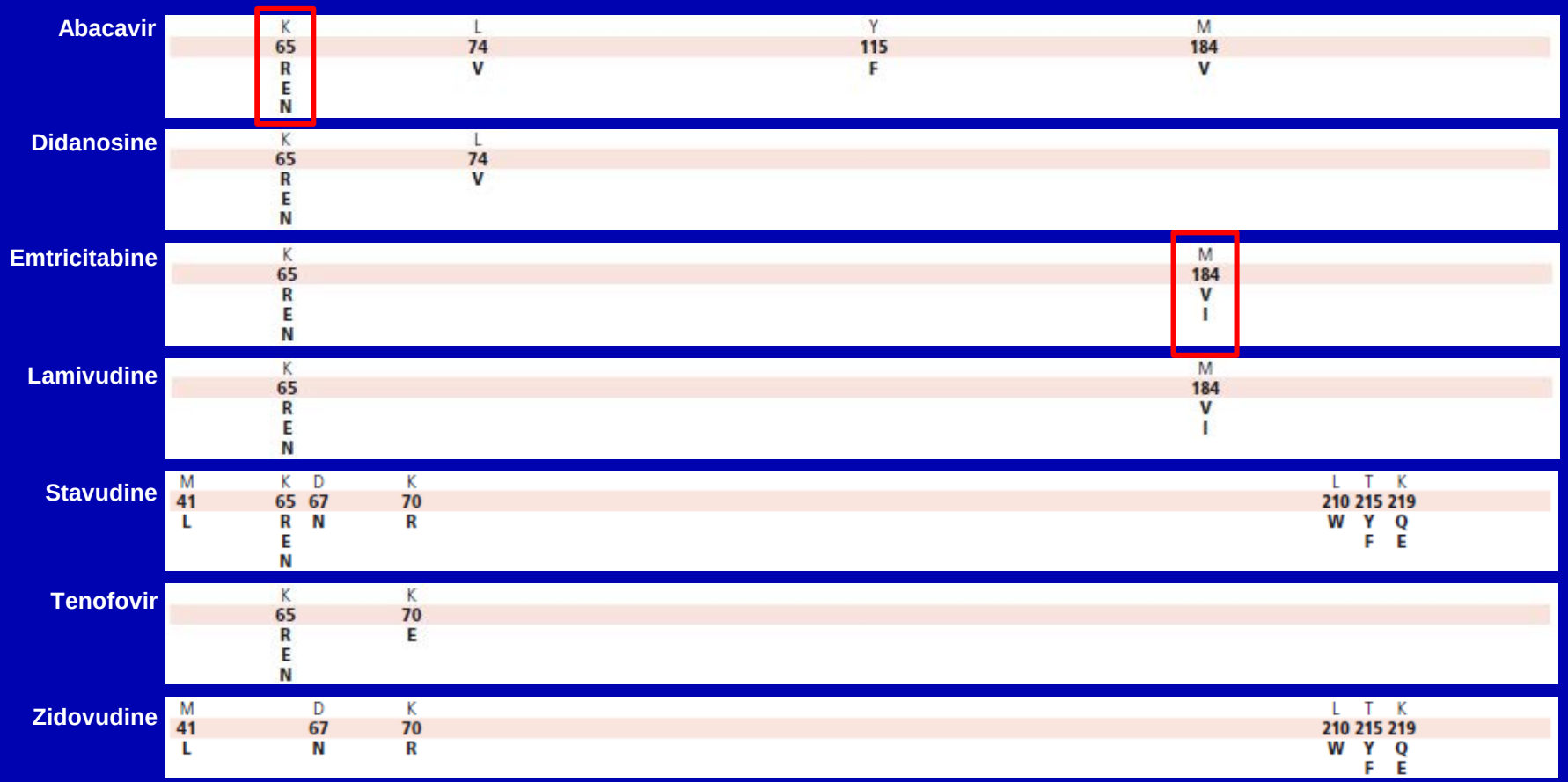
2015 Update of the Drug Resistance Mutations in HIV-1

Annemarie M. Wensing, MD, PhD; Vincent Calvez, MD, PhD; Huldrych F. Günthard, MD; Victoria A. Johnson, MD; Roger Paredes, MD, PhD; Deenan Pillay, MD, PhD; Robert W. Shafer, MD; and Douglas D. Richman, MD

***Top Antivir Med.* 23(4):132-141. Updates available at www.iasusa.org.**

IAS–USA is a not-for-profit, HIV clinical specialist–education organization.
It is entirely different from and not affiliated with the International AIDS Society.

Mutations in the Reverse Transcriptase Gene Associated With Resistance to Reverse Transcriptase Inhibitors (cont'd)



Wensing et al. *Top Antivir Med*. 2015;23(4):132-141.
Updates, user notes, and references available at www.iasusa.org.

Mutations in the Reverse Transcriptase Gene Associated With Resistance to Reverse Transcriptase Inhibitors (cont'd)

Nonnucleoside Analogue Reverse Transcriptase Inhibitors (NNRTIs)

Efavirenz

L	K	K	V	V	Y	Y	G	P	M
100	**101**	**103**	**106**	**108**	**181**	**188**	**190**	**225**	**230**
I	**P**	**N**	**M**	**I**	**C**	**L**	**S**	**H**	**L**
		S			**I**		**A**		

Etravirine

V	A	L	K		V		E	V	Y		G		M
90	98	**100**	**101**		106		138	179	**181**		190		230
I	G	**I***	E		I		A	D	**C***		S		L
			H				G	F	**I***		A		
			P*				K	T	**V***				
							Q						

Nevirapine

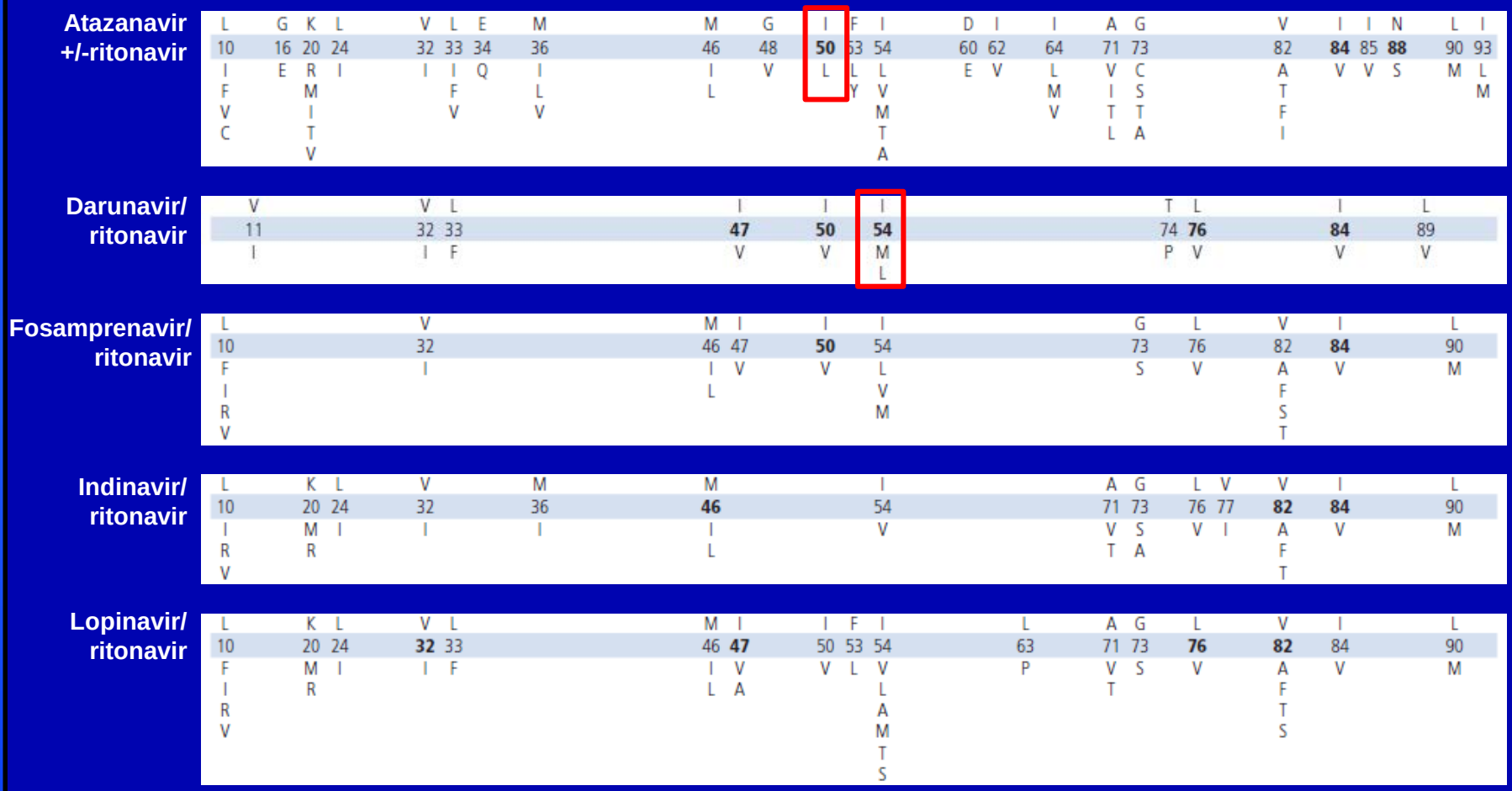
L	K	K	V	V	Y	Y	G	M
100	**101**	**103**	**106**	**108**	**181**	**188**	**190**	**230**
I	**P**	**N**	**A**	**I**	**C**	**C**	**A**	**L**
		S	**M**		**I**	**L**		
						H		

Rilpivirine

L	K	E	V	Y	Y	H	F	M
100	**101**	**138**	**179**	**181**	**188**	**221**	**227**	**230**
I	**E**	**A**	**L**	**C**	**L**	**Y**	**C**	**I**
	P	**G**		**I**				**L**
		K		**V**				
		Q						
		R						

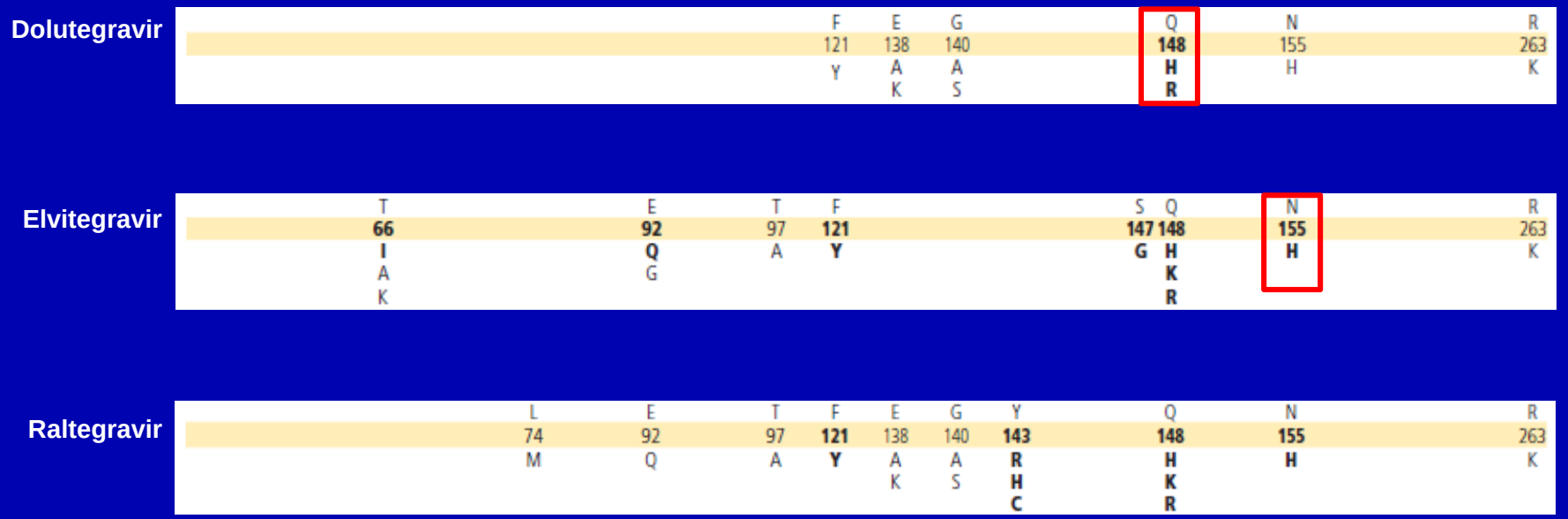
Wensing et al. *Top Antivir Med*. 2015;23(4):132-141.
Updates, user notes, and references available at www.iasusa.org.

Mutations in the Protease Gene Associated With Resistance to Protease Inhibitors



Wensing et al. *Top Antivir Med*. 2015;23(4):132-141.
Updates, user notes, and references available at www.iasusa.org.

Mutations in the Integrase Gene Associated With Resistance to Integrase Strand Transfer Inhibitors



Wensing et al. *Top Antivir Med*. 2015;23(4):132-141.
Updates, user notes, and references available at www.iasusa.org.

ART resistance pearls

- **M184V** – Common NRTI mutation; “goes away” quickly
  - Changes viral fitness
- **K103N** – Common NNRTI mutation; “stays around” longer
  - Most common transmitted resistance
- NNRTI resistance can occur after a single dose, and after stopping a co-formulated combination
- Resistance “barrier”: PIs > IIs > NRTIs ≥ NNRTIs
- First-line PI failure *without resistance* can occur – Why?
- Order integrase resistance test separately
- Concept of viral “fitness” and “reversion”

Summary

- **HIV resistance** should be considered at all points of care

- Check resistance using a **genotype**
  - At initial visit (if not already controlled on ART)
  - Before ART start
  - At virologic failure

- Use **external resources** and **local expertise**

A Brief Review of PrEP & nPEP

Southeast AIDS Education & Training Center
HIV Clinical Overview
12 May 2016

Todd Hulgan, MD, MPH
Department of Medicine, Division of Infectious Diseases
Vanderbilt University School of Medicine
Tennessee Center for AIDS Research (TN-CFAR)
Tennessee Valley Veterans Healthcare System
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AETC AIDS Education & Training Center Program Southeast

VANDERBILT UNIVERSITY School of Medicine

TN CFAR TENNESSEE CENTER FOR AIDS RESEARCH

Objectives

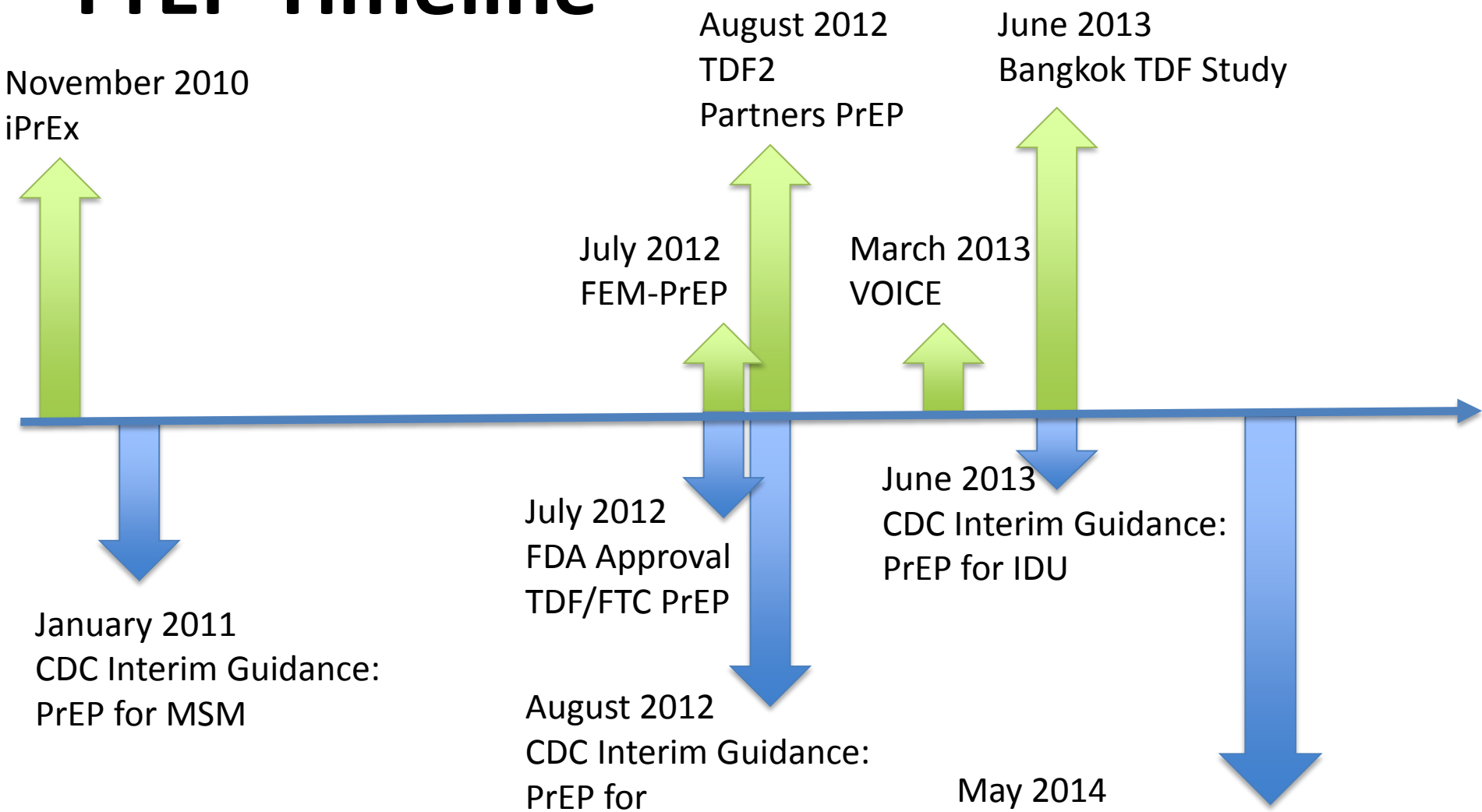
- Recognize US guidelines for **pre-exposure prophylaxis (PrEP)** and **non-occupational post-exposure prophylaxis (nPEP)**

PrEP: **Pr**e-**E**xposure **P**rophylaxis

- How does it work?
  - Uninfected person takes ART
  - May prevent replication of virus & infection

- Daily dosing of (and adherence to) TDF/FTC

PrEP Timeline



PrEP Studies

- iPrEX- mostly MSM, TDF/FTC once-daily reduced the risk of HIV infection by 42% overall
  - 92% among participants with blood drug levels indicating regular use
- Partners PrEP and TDF2- heterosexual couples in Africa, TDF/FTC or TDF alone reduced the risk of HIV acquisition by about 65%-75%
- Bangkok Tenofovir Study- IDU, daily TDF alone reduced HIV acquisition among IVDU ~50%

Grant et al. *N Engl J Med*. 2010;363(27):2587
Baeten et al. *N Engl J Med*. 2012;367(5):399
Thigpen *N Engl J Med*. 2012;367(5):42
Choopanya *Lancet*. 2013;381(9883):2083

US Public Health Service

PREEXPOSURE PROPHYLAXIS FOR THE PREVENTION OF HIV INFECTION IN THE UNITED STATES - 2014

A CLINICAL PRACTICE GUIDELINE

http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

Table 1: Summary of Guidance for PrEP Use

	Men Who Have Sex with Men	Heterosexual Women and Men	Injection Drug Users
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-prevalence area or network	HIV-positive injecting partner Sharing injection equipment Recent drug treatment (but currently injecting)
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 6 months, test for bacterial STIs		
	Do oral/rectal STI testing	Assess pregnancy intent Pregnancy test every 3 months	Access to clean needles/syringes and drug treatment services

STI: sexually transmitted infection

http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

PrEP: Candidates

Substantial risk of acquiring HIV infection

- **Men who have sex with men (MSM)**
  - HIV-positive sexual partner
  - Recent bacterial STI
  - High number of sex partners
  - History of inconsistent/no condom use
  - Commercial sex work

http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

PrEP: Candidates

Substantial risk of acquiring HIV infection

- **Transgender individuals**
  - Engaging in high-risk sexual behaviors

http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

PrEP: Candidates

Substantial risk of acquiring HIV infection

- **Heterosexual women and men**
  - HIV-positive sexual partner
  - Recent bacterial STI
  - High number of sex partners
  - History of inconsistent/no condom use
  - Commercial sex work
  - High-prevalence area or network

http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

PrEP: Candidates

Substantial risk of acquiring HIV infection

- **Injection drug users (IDU)**
  - HIV-positive injecting partner
  - Sharing injection equipment
  - Recent drug treatment (but currently injecting)

http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

PrEP: Clinical Eligibility

- Documented negative HIV test
- No signs/symptoms of acute HIV infection
- Normal renal function
- No contraindicated medications
- Documented hepatitis B infection & vaccination status

http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

PrEP: HIV Testing

- Are signs/symptoms of acute HIV present now or in prior 4 weeks?
  - Option 1: retest antibody in one month
  - Option 2: HIV antibody/antigen assay
  - Option 3: HIV-1 viral load

http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

Acute HIV Infection

Symptoms

- Fever
- Fatigue
- Myalgia
- Skin rash
- Headache
- Pharyngitis
- Cervical Lymphadenopathy
- Arthralgia
- Night sweats
- Diarrhea

Daar ES, Pilcher CD, Hecht FM. *Curr Opin HIV AIDS*. 2008;3(1):10-15.

Providing PrEP

Every visit:
Assess adherence
Risk reduction counseling
Provide condoms

Before starting PrEP:

- Clinical eligibility
- Educate
  - Side effects
  - Limitations
  - Daily adherence
  - Symptoms of seroconversion
  - Monitoring schedule
  - Safety
  - Criteria for discontinuation
- Partner information
- Social history: housing, substance use, mental health, domestic violence

www.hivguidelines.org

Providing PrEP

Every visit:
Assess adherence
Risk reduction counseling
Provide condoms

After confirmation of clinical eligibility:

- Prescribe no more than 90-day supply of PrEP
  - Truvada 1 tablet PO daily

    (TDF 300mg + FTC 200mg)
  - Insurance prior approval?
  - Truvada for PrEP Medication Assistance Program

http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

Discontinuing PrEP

- Positive HIV result
- Acute HIV signs or symptoms
- Non-adherence
- Renal disease
- Changed life situation: lower HIV risk

http://www.cdc.gov/hiv/pdf/guidelines/PrEPguidelines2014.pdf

Updated Guidelines for Antiretroviral Postexposure Prophylaxis After Sexual, Injection Drug Use, or Other Nonoccupational Exposure to HIV— United States, 2016

from the
Centers for Disease Control and Prevention,
U.S. Department of Health and Human Services

http://www.cdc.gov/hiv/guidelines/preventing.html

nPEP

Non-occupational Post-exposure Prophylaxis

- High risk exposure
- ≤72 hours after exposure
- Laboratory evaluation
- 28 day course
- Preferred: **TDF/FTC** + **RAL** or **DTG**
- Follow-up testing

http://www.cdc.gov/hiv/guidelines/preventing.html

- Resources for **ART interactions**:
  - http://aidsetc.org/aidsetc?page=cg-702_drug-drug_interactions
  - http://hivinsite.ucsf.edu/interactions
  - http://www.hiv-druginteractions.org/
  - http://aidsinfo.nih.gov/contentfiles/lvguidelines/adultandadolescentgl.pdf

- Resources for **ART resistance interpretation**:
  - https://www.iasusa.org/content/drug-resistance-mutations-in-HIV
  - http://hivdb.stanford.edu/
  - http://www.aidsetc.org/ppt/p02-et/et-01-00/nw_arv-resist-testing.ppt

- Resources for **PrEP & nPEP**
  - http://www.cdc.gov/hiv/guidelines/preventing.html
  - http://nccc.ucsf.edu/clinician-consultation/pep-post-exposure-prophylaxis/

- **Thanks!**
- Acknowledgements:
  - AETC National Resource Center http://www.aidsetc.org/
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  - CCO http://www.clinicaloptions.com/HIV.aspx
  - IAS-USA https://www.iasusa.org/
  - Providers at the Vanderbilt Comprehensive Care Clinic ART Conference
    - Steve Raffanti, MD
    - Anna Person, MD