HIV Today:
Examining the Latest Treatment Advances and Barriers to Success

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Disclosure

- **BMS Speakers Bureau**

Objectives

Pharmacist

- **Explain the latest recommendations in the management of HIV-infected patients.**
- **Identify current trends in epidemiology of HIV.**
- **Summarize potential drug-drug and drug-food interactions among commonly co-administered medications and antiretrovirals.**

Pharmacy Technicians

- **Identify the three major classes of antiretroviral drugs.**
- **List common side effects associated with antiretroviral medications.**
- **Explain the rationale for using cocktails of drugs (HAART) in the treatment of HIV.**

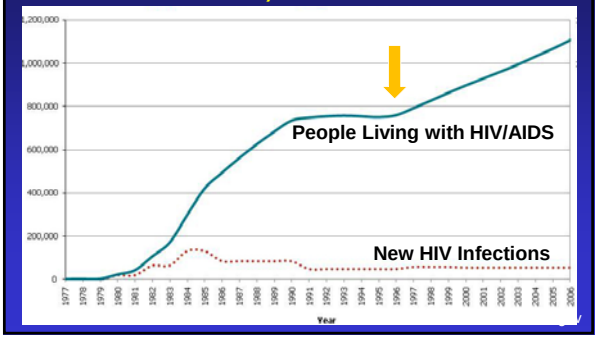
Outline

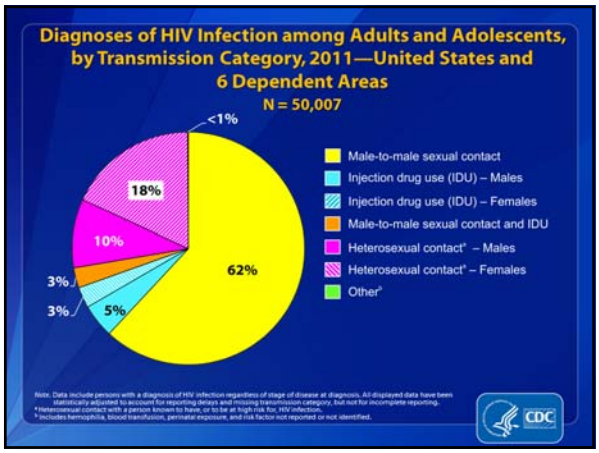
- Management of HIV-infected patients
  - Epidemiology
  - Guidelines
- Barriers to treatment success
  - Adherence
  - Side effects
  - Medication errors
  - Drug interactions
- Future Options and Strategies

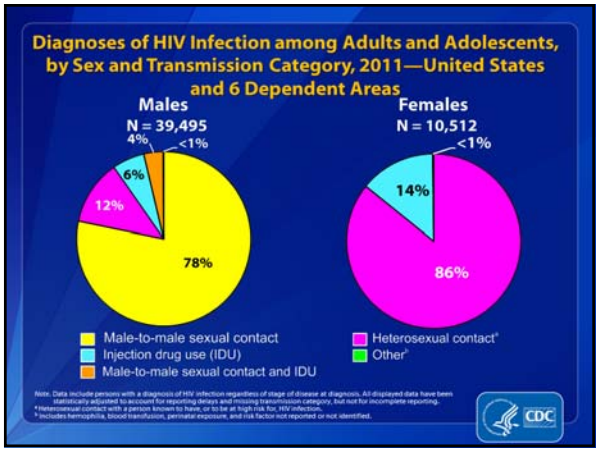
U.S. Epidemiology

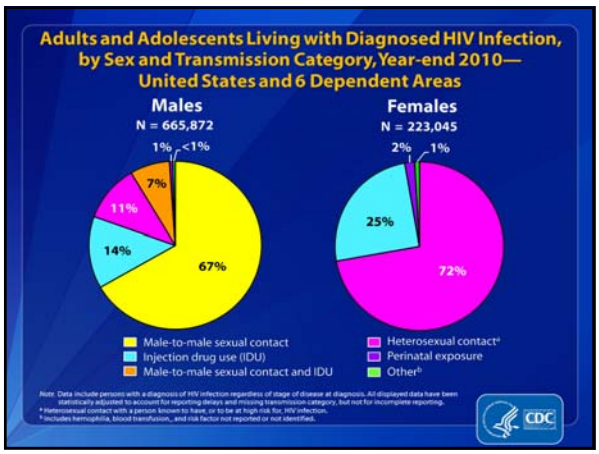
- **Estimated 1.1 million infected with HIV in US**
  - **State of NJ: 4th highest number of people living with HIV diagnosis (per 100,000 population)**
- **Combination antiretroviral therapy (ART) has become much improved of the past decade: less pills, better tolerated, more options**
- **Patients living longer with the disease**
  - **More coexisting diseases as patients age (hypertension, diabetes, etc.)**
- **Antiretroviral therapy started earlier than ever**
  - **Prevent morbidity/mortality from AIDS & non-AIDS diseases**

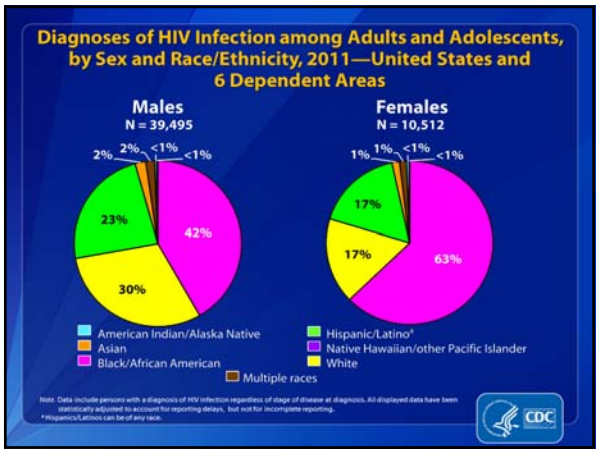
HIV Incidence and Prevalence, United States, 1977-2006

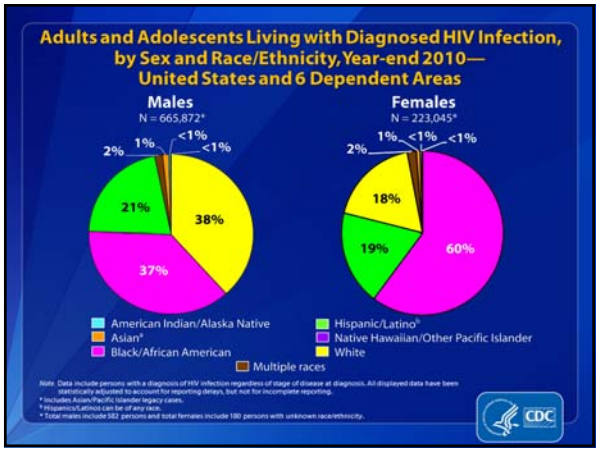


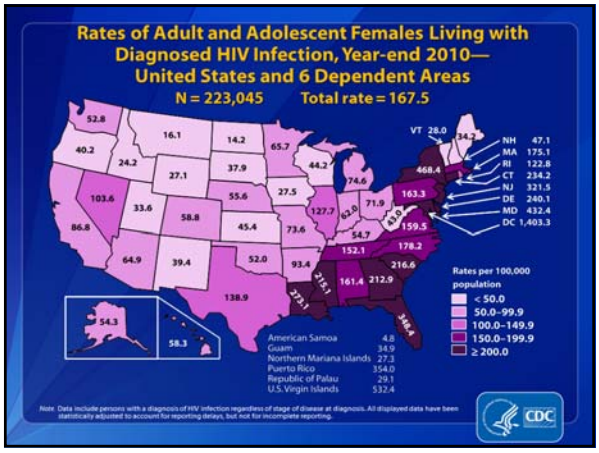

Diagnoses of HIV Infection among Adults and Adolescents, by Transmission Category, 2011—United States and 6 Dependent Areas
N = 50,007
<1%
18%
10%
3%
3%
5%
62%
Male-to-male sexual contact
Injection drug use (IDU) – Males
Injection drug use (IDU) – Females
Male-to-male sexual contact and IDU
Heterosexual contact[a] – Males
Heterosexual contact[a] – Females
Other[b]
CDC


Diagnoses of HIV Infection among Adults and Adolescents, by Sex and Transmission Category, 2011—United States and 6 Dependent Areas
Males
N = 39,495
4%
<1%
6%
12%
78%
Females
N = 10,512
<1%
14%
86%
Male-to-male sexual contact
Injection drug use (IDU)
Male-to-male sexual contact and IDU
Heterosexual contact[a]
Other[b]
CDC

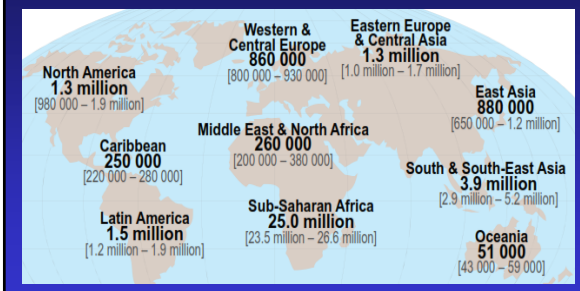

Adults and Adolescents Living with Diagnosed HIV Infection, by Sex and Transmission Category, Year-end 2010—United States and 6 Dependent Areas
Males
N = 665,872
1%
<1%
7%
11%
14%
67%
Females
N = 223,045
2%
1%
25%
72%
Male-to-male sexual contact
Injection drug use (IDU)
Male-to-male sexual contact and IDU
Heterosexual contact[a]
Perinatal exposure
Other[b]
CDC


Diagnoses of HIV Infection among Adults and Adolescents, by Sex and Race/Ethnicity, 2011—United States and 6 Dependent Areas
Males
N = 39,495
2%
2%
<1%
<1%
23%
42%
30%
Females
N = 10,512
1%
1%
<1%
<1%
17%
17%
63%
American Indian/Alaska Native
Asian
Black/African American
Multiple races
Hispanic/Latino*
Native Hawaiian/other Pacific Islander
White
Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
*Hispanics/Latinos can be of any race.
CDC


Adults and Adolescents Living with Diagnosed HIV Infection, by Sex and Race/Ethnicity, Year-end 2010— United States and 6 Dependent Areas
Males
N = 665,872*
2%
1%
<1%
<1%
21%
38%
37%
Females
N = 223,045*
2%
1%
<1%
<1%
18%
19%
60%
American Indian/Alaska Native
Asian*
Black/African American
Multiple races
Hispanic/Latino*
Native Hawaiian/Other Pacific Islander
White
Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
* Includes Asian/Pacific Islander legacy cases.
* Hispanics/Latinos can be of any race.
* Total males include 582 persons and total females include 100 persons with unknown race/ethnicity.
CDC


Rates of Adult and Adolescent Females Living with Diagnosed HIV Infection, Year-end 2010— United States and 6 Dependent Areas
N = 223,045 Total rate = 167.5
52.8
16.1
14.2
65.7
40.2
24.2
27.1
37.9
44.2
74.6
468.4
103.6
33.6
58.8
55.6
27.5
127.7
64.9
71.9
163.3
86.8
45.4
73.6
54.7
83.0
159.5
64.9
39.4
52.0
93.4
152.1
178.2
216.6
138.9
215.1
161.4
212.9
273.1
348.4
54.3
58.3
VT 28.0
34.2
NH 47.1
MA 175.1
RI 122.8
CT 234.2
NJ 321.5
DE 240.1
MD 432.4
DC 1,403.3
Rates per 100,000 population
< 50.0
50.0–99.9
100.0–149.9
150.0–199.9
≥ 200.0
American Samoa 4.8
Guam 34.9
Northern Mariana Islands 27.3
Puerto Rico 354.0
Republic of Palau 29.1
U.S. Virgin Islands 532.4
Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays, but not for incomplete reporting.
CDC

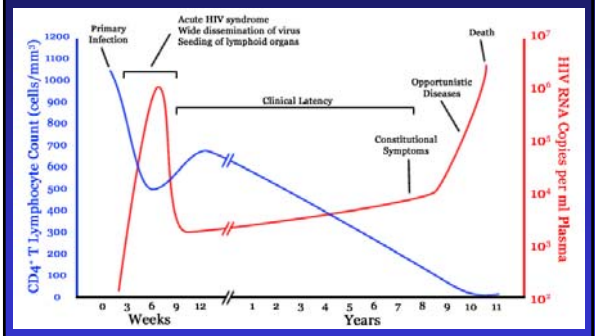
Adults and Children Living With HIV in 2012



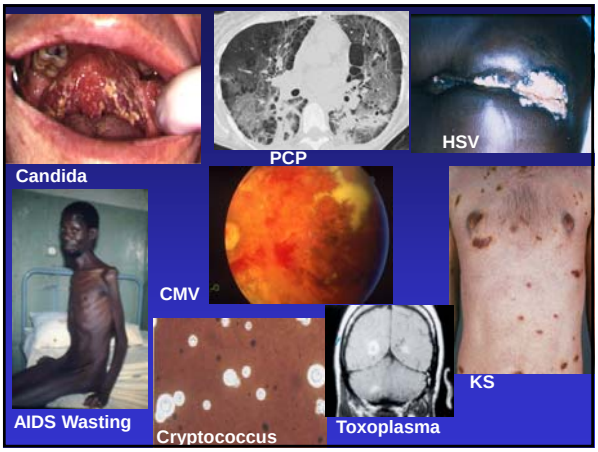
People Living with HIV: 35.3 million (32.2-38.8)

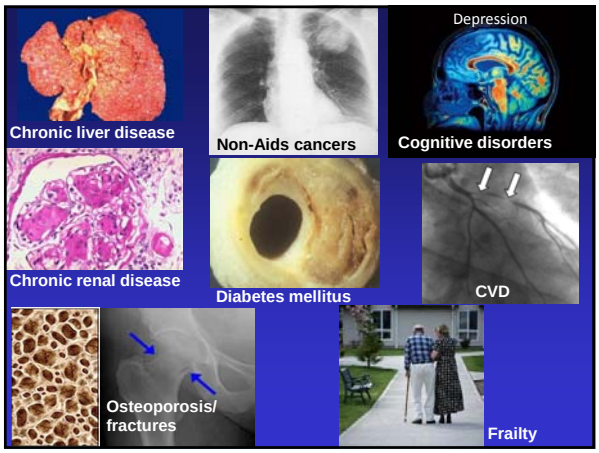
UNAIDS, 2013. Available at: http://www.unaids.org.

Natural Course of HIV Disease



http://www-micro.msb.le.ac.uk/3035/3035pics/Hivtimecourse.gif





Consequence of HIV Replication

- Prevention of AIDS-related illnesses still a major objective of treating HIV infection
- Collateral damage from HIV replication
  - Inflammation, oxidant stress, endothelial dysfunction, immune activation[1]
  - Exacerbates non-AIDS related conditions, such as cardiovascular, liver, and renal disease[2]

1. Boger et al. 17th International AIDS Conference, 2008: Abstract WEAB0105.
2. El-Sadr et al. *N Engl J Med.* 2006;355(5):2283-2296.

Association of CD4+ Cell Count Nadir With Clinical Outcomes

- Low CD4+ count nadir associated with
  - Increased rates of HIV-associated neurocognitive disorders[1]
  - Arterial stiffness contributing to CV risk[2]
  - Coronary heart disease[3]
  - Increased risk of fracture[4]

1. Ellis R et al. AIDS. 2011;25:1747-1751.
2. Ho J et al. AIDS. 2010 ;24:1897-1905.
3. Klein D et al. CROI 2011. Abstract 810.
4. Young B et al. *Clin Infect Dis*. 2011;52:1061-1068.

DHHS Guidelines, 2013: When to Start

- ART recommended for ALL HIV-infected patients; *strength* of recommendation varies according to CD4+ cell count

CD4+ Cell Count	Recommendation
▪ < 350 cells/mm³	▪ Start ART (AI)
▪ 350-500 cells/mm³	▪ Start ART (AII)
▪ > 500 cells/mm³	▪ Start ART (BIII)

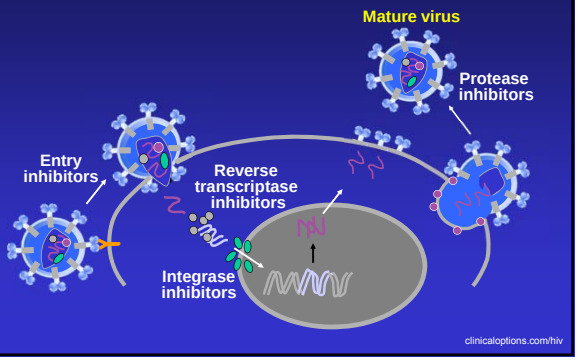
Clinical Conditions Favoring Initiation of Therapy Regardless of CD4+ Cell Count

- History of AIDS-defining illness (AI)
- Pregnancy (AI)
- HIV-associated nephropathy (AII)
- HBV coinfection (AII)
- Patients at risk of transmitting HIV to sexual partners (AI, heterosexuals; AIII, others)
- HCV coinfection* (BII)
- Patients > 50 years of age (BIII)

*Including those with high CD4+ cell count and/or with cirrhosis. Some pts with CD4+ counts > 500 cells/mm³ may elect to defer ART until after HCV therapy is completed.

http://aidsinfo.nih.gov

HIV Life Cycle & Inhibition



Current Antiretroviral Medications

NRTI (Nucleoside Reverse Transcriptase Inhibitors)
- Abacavir (Ziagen®)
- Didanosine (Videc EC®)
- Emtricitabine (Emtriva®)
- Lamivudine (Epivir®)
- Stavudine (Zerit®)
- Tenofovir (Viread®)
- Zidovudine (Retrovir®)

NNRTI (Non-Nucleoside Reverse Transcriptase Inhibitors)
- Delavirdine (Rescriptor®)
- Efavirenz (Sustiva®)
- Etravirine (Intelence®)
- Nevirapine (Viramune®)
- Rilpivirine (Edurant®)

PI (Protease Inhibitors)
- Atazanavir (Reyataz®)
- Darunavir (Prezista®)
- Fosamprenavir (Lexiva®)
- Indinavir (Crixivan®)
- Lopinavir/ritonavir (Kaletra®)
- Nelfinavir (Viracept®)
- Ritonavir (Norvir®)
- Saquinavir (Invirase®)
- Tipranavir (Aptivus®)

Entry Inh. / Integrase Inh.
- Maraviroc (Selzentry®)
- Enfuvirtide (Fuzeon®)
- Elvitegravir (co-form. Stribild®)
- Raltegravir (Isentress®)
- Dolutegravir (Tivicay®)

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- Stavudine (Zerit®)
- **Tenofovir (Viread®)**
- Zidovudine (Retrovir®)

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- **Elvitegravir (co-form. Stribild®)**
- **Raltegravir (Isentress®)**
- **Dolutegravir (Tivicay®)**

Combination Products


Combivir® (lamivudine/zidovudine)


Epzicom® (abacavir/lamivudine)


Truvada® (emtricitabine/tenofovir)


Trizivir® (zidovudine/lamivudine/abacavir)


Atripla® (efavirenz/emtricitabine/tenofovir)


Complera® (rilpivirine/emtricitabine/tenofovir)


Stribild™ (elvitegravir/cobicistat/emtricitabine/ tenofovir)


Triumeq® (abacavir/dolutegravir/lamivudine)

Combination Products


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Epzicom® (abacavir/lamivudine)


Truvada® (emtricitabine/tenofovir)


Trizivir® (zidovudine/lamivudine/abacavir)


Atripla® (efavirenz/emtricitabine/tenofovir)


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Stribild™ (elvitegravir/cobicistat/emtricitabine/ tenofovir)


Triumeq® (abacavir/dolutegravir/lamivudine)

Current Antiretroviral Medications

NRTI
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- Lamivudine (Epivir®)
- Stavudine (Zerit®)
- Tenofovir (Viread®)
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NNRTI
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PI
- Atazanavir (Reyataz®)
- Darunavir (Prezista®)
- Fosamprenavir (Lexiva®)
- Indinavir (Crixivan®)
- Lopinavir/ritonavir (Kaletra®)
- Nelfinavir (Viracept®)
- Ritonavir (Norvir®)
- Saquinavir (Invirase®)
- Tipranavir (Aptivus®)

Miscellaneous
- Maraviroc (Selzentry®)
- Enfuvirtide (Fuzeon®)
- Elvitegravir (Vitekta®)
- Raltegravir (Isentress®)
- Dolutegravir (Tivicay®)

Recommended for Treatment-Naïve Patients

Contains 2 NRTIs PLUS one other active agent

2-NRTIs		
tenofovir/emtricitabine (Truvada®)	NNRTI	efavirenz
		rilpivirine
abacavir/lamivudine† (Epzicom®)	PI	atazanavir + ritonavir
		darunavir + ritonavir
	Integrase Inhibitors	raltegravir
		elvitegravir
		dolutegravir

† If test negative for HLA-B*5701

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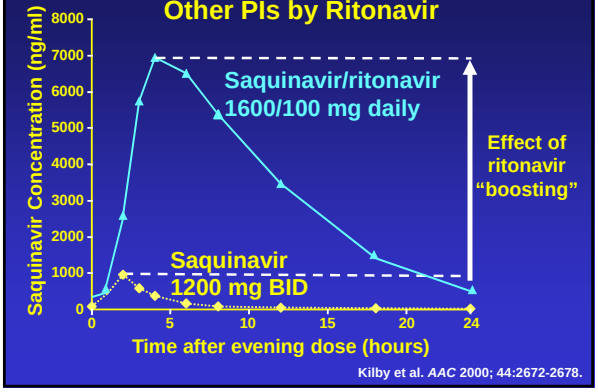
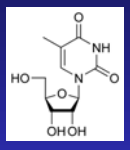
Pharmacokinetic Enhancement of Other PIs by Ritonavir

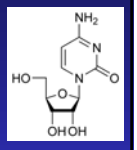


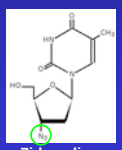
Kilby et al. *AAC* 2000; 44:2672-2678.

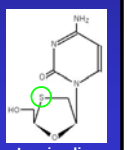
Nucleoside Reverse Transcriptase Inhibitors (NRTIs)

- Thymidine
  - Stavudine (Zerit®)
  - Zidovudine (Retrovir®)
- Cytosine
  - Emtricitabine (Emtriva®)
  - Lamivudine (Epivir®)
- Guanosine
  - Abacavir (Ziagen®)
- Adenosine
  - Didanosine (Videx®)
  - Tenofovir DF* (Viread®)


Thymidine


Cytosine


Zidovudine


Lamivudine

NRTIs

- Established backbone of combination therapy
- Minimal drug interactions
- Renal dose adjustment needed (except abacavir)
- Hepatitis B virus activity: lamivudine, emtricitabine, tenofovir
- Adverse effects
  - Mitochondrial tox. (didanosine > stavudine > zidovudine >> others)
    - Lactic acidosis ± hepatic steatosis, lipoatrophy
  - Zidovudine: bone marrow suppression
  - Stavudine & didanosine: peripheral neuropathy, pancreatitis
  - Didanosine: food and drug interactions
  - Abacavir: hypersensitivity reaction
  - Tenofovir: renal impairment, GI intolerance

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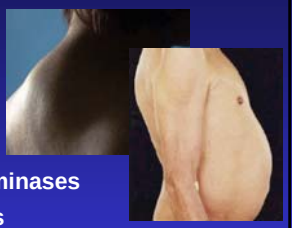
Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

- Historically easier regimens than other classes
- Not associated with significant long-term adverse effects
- Low genetic barrier
- Drug interactions - all 3A4 substrates & inducers/inhibitors
- Nevirapine (Viramune®)
  - Hepatotoxicity (esp. if $CD4^+$ >250 c/mL in women or >400 c/mL in men)
  - Rash (life-threatening events occur 1-4% of the time)
- Efavirenz (Sustiva®)
  - CNS effects (dizziness, vivid dreams, loss of concentration)
  - Pregnancy Category D
- Etravirine (Intelence®)
  - Effective in patients with NNRTI mutations
- Rilpivirine (Edurant®)
  - Less CNS effects than efavirenz
  - Pregnancy Category B

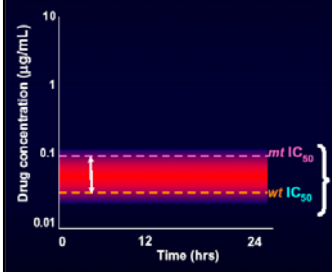
http://aidsinfo.nih.gov

Protease Inhibitors

- Class adverse effects
  - Metabolic complications
    - Hyperlipidemia
    - Insulin resistance
    - Lipodystrophy
- GI intolerance
- Elevated serum transaminases
- Specific adverse effects
  - Sulfonamide (rash): fosamprenavir, tipranavir, darunavir
  - Hyperbilirubinemia, nephrolithiasis: atazanavir, indinavir
  - Tipranavir – rash, hyperlipidemia, liver toxicity
  - Saquinavir – QTc prolongation



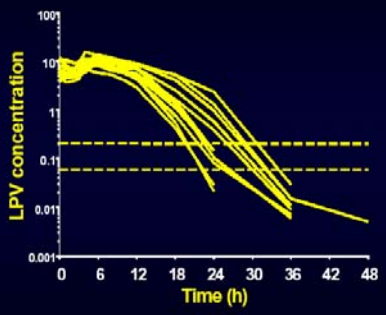
Barriers to boosted PI resistance



Narrow level of drug-exposure at which resistant virus is more fit than wild-type virus

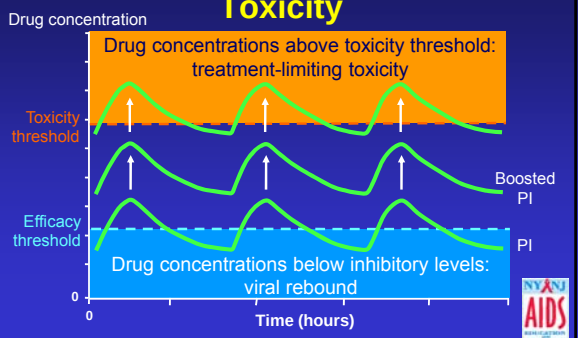
Adapted from Bertz R et al., *5th Int'l Workshop Clin Pharm in HIV*, Rome, April 2004 # 6.1

Primary resistance to LPV is rare *in vivo*



Kempf D et al, JID, 2004

Boosted PI Therapy: Hitting Toxicity



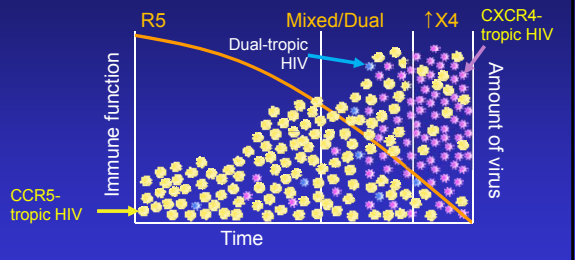
Integrase Strand Transfer Inhibitors

- Raltegravir (Isentress®)
  - BID dosing
  - May ↑ creatine kinase (CK); myopathy and rhabdomyolysis have been reported
  - Metabolized by glucuronidation (UGT-1A1)
- Elvitegravir(Vitekta®)
  - 3A4 substrate; requires boosting
- Dolutegravir (Tivicay®)
  - Once daily dosing for tx naïve; boosting not needed
  - Less risk of resistance if treatment fails
  - Remains active in most patients with integrase resistance

Other Antiretrovirals

- Enfuvirtide (Fuzeon®)
  - Fusion inhibitor
  - Subcutaneous injection → injection site reactions (98%)
- Maraviroc (Selzentry®)
  - CCR5 antagonist
  - Requires tropism assay (costly)
  - Dosing range variable (150 mg – 600 mg BID)
  - Drug interactions (3A4 substrate)

HIV Tropism and Disease Progression



Courtesy GSK interactive CD "Exploring an allosteric world: CCR5 entry inhibitors and HIV"

clinicaloptions.com/hiv

Recommended for Treatment-Naïve Patients

Contains 2 NRTIs PLUS one other active agent

2-NRTIs		
tenofovir/emtricitabine (Truvada®)	NNRTI	efavirenz
		rilpivirine
abacavir/lamivudine† (Epzicom®)	PI	atazanavir + ritonavir
		darunavir + ritonavir
	Integrase Inhibitors	raltegravir
		elvitegravir
		dolutegravir

† **If test negative for HLA-B*5701**

http://aidsinfo.nih.gov

Principles of Antiretroviral Therapy

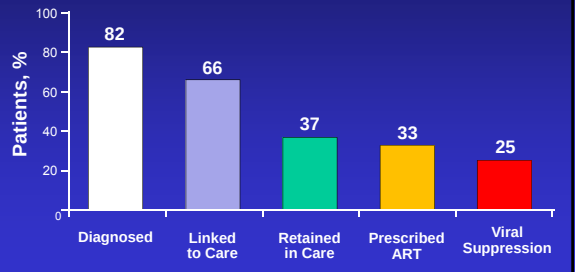
- HIV RNA (viral load)
  - Wk 24: < 50 copies/mL (undetectable)
- CD4 cell count
  - Increase of ~150 cells/mL in first year
- Failure
  - Virologic: incomplete or lack of HIV RNA response (> 400 c/mL)
  - Immunologic: $CD4^+$ ↑ < 25-50 cells/mL in first year
  - Clinical progression: occurrence/recurrence of HIV-related event

http://aidsinfo.nih.gov

If current treatment is so effective, then why is the eradication of HIV not yet a reality?

CDC: Differences in Continuum of Care in HIV-Infected Patients

- CDC study shows that only ~ 25% of US patients with HIV have suppressed HIV-1 RNA



Hall HI et al. AIDS 2012. Abstract FRLBX05.

CDC Guidelines for Screening and Testing: Adults and Adolescents

- All persons 13-64 years of age
- All patients initiating treatment for TB
- All patients seeking treatment for STDs
- Repeat screening annually for those known to be at high risk
- Encourage testing before initiating a new sexual relationship

cdc.gov

Current Challenges in Fighting HIV: US

- Patient level
  - Barriers to care
    - Not linked to care
    - Mistrust of medical community
    - Access to care issues
    - Stigmas (perceived and/or real)
    - Fragile support systems
    - Difficulty in communicating with physicians
    - Health literacy
  - Adherence
  - Side effects
  - Medication errors

Adherence

- High adherence rates associated with virologic suppression, low rates of resistance, and improved survival
- 2nd best predictor of progression to AIDS & death
- Consequences of nonadherence not always equal
- Adherence is a dynamic state

www.aidsetc.org

Predictors of Inadequate Adherence

- Regimen complexity and pill burden
- Low literacy level
- Active drug use or alcoholism
- Stigma
- Mental illness (especially depression)
- Cognitive impairment
- Lack of patient education
- Medication adverse effects
- Treatment fatigue

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Predictors of Inadequate Adherence

- Age, race, sex, educational level, socioeconomic status, and a past history of alcoholism or drug use do NOT reliably predict suboptimal adherence
- Higher socioeconomic status and education levels and lack of history of drug use do NOT reliably predict optimal adherence

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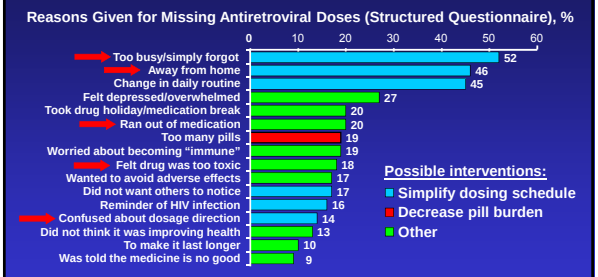
Why Do Patients Miss Doses?



Gifford AL et al. J Acquire Immune Defic Syndr. 2000;23:386-395.

clinicaloptions.com

Managing Adverse Effects

- About 25% of patients stop therapy within the first year on HAART because of side effects[1]
- Toxicity still a challenge in the management of HIV-infected patients
  - Long- and short-term safety
- Identification of drug-specific adverse effects may be difficult
- Appropriate measures may not always be clear

Their management must be individualized

1. D'Arminio Monforte A, et al. *AIDS* 2000; 14:499-507.

Common Adverse Effects

- Gastrointestinal
  - Diarrhea
  - Nausea/vomiting
- Dermatologic
- Neurologic Symptoms
  - Dizziness
  - Headache
  - Fatigue

Incidence of Medication Errors

- Incidence difficult to determine
  - Underreported
  - Unidentified
- Hospital setting
  - 25.8% of patients on ART had an error[1]
  - 86% of patients on ART had ≥ 1 drug-related issues[2]
  - 52% ART had an error at 48 hrs of admission[3]
- Retail setting

1. Rastegar DA et al. *CID* 2006;43:933-8.
2. Mok S et al. *AJHP* 2008;65:55-9.
3. Corrigan MA et al. *Ann Pharmacother* 2010;44:222-3.

Common Medication Errors

- Inappropriate dose
- Incorrect frequency
- Therapeutic duplication
- Wrong drug
- Incomplete antiretroviral regimen
- Drug interactions
- Inappropriate opportunistic infection prophylaxis

Reasons Errors Occur

- Lack of familiarity with dosing, adverse effects, and drug-drug interactions
- Drug information and best practices in HIV management always evolving
  - Resources/references not all equal
- Pharmacists need to remain updated
  - Continuing education, FDA alerts, email updates, scripts
- Patients
  - Different levels of knowledge/understanding

Inappropriate Dose/Frequency

- Daily instead of BID
- Wrong tablet dose
  - Intelence® 200 mg PO BID
  - 100 mg tablets available
- PI boosting
  - No ritonavir (boost) given:
  - Boosting freq. ≠ to other PI freq:

Raltegravir 1 tab daily 

Etravirine 100 mg tab BID 

Atazanavir 300 mg daily 

Darunavir 600 mg BID 
Ritonavir 1 tab daily

OR

Darunavir 800 mg daily 
Ritonavir 1 tab BID 

- In chronic kidney disease, no dose adjustment of NRTIs
  - All NRTIs (except abacavir) are renally eliminated
  - Adjustments differ between NRTIs, thus coformulations may need to be split into individual agents

Therapeutic Duplication

- **Caution with coformulations**

Order #1. Kaletra® (lopinavir/ritonavir) 2 tabs PO BID

Order #2. Norvir® (ritonavir) 100 mg 1 tab PO BID

Wrong Drug

- Do not accept prescriptions with potentially confusing abbreviations
  - ddI, d4T, NFV, NVP, ATV, AZT
- Close names - poor handwriting
  - Ritonavir or Retrovir
  - Nevirapine or Nelfinavir
  - Viramune® or Viracept® or Viread®
  - Intelence® or Isentress®
  - Complera® or Combivir®

Incomplete Antiretroviral Regimen

- Monotherapy not recommended
  - Except zidovudine in pregnancy
  - Boosted PI monotherapy being evaluated (study setting only)
- Dual NRTI therapy not recommended
- Need ≥ 2 fully active agents for ART success
- Ensure ritonavir (Norvir®) prescribed when indicated for boosting
  - Low-dose ritonavir doesn't count as active agent
  - Remember, following MUST be boosted:
    - Darunavir (Prezista®), Saquinavir (Invirase®), Tipranavir (Aptivus®)
  - Must boost: Reyataz® (300 mg cap), Lexiva® (if 2 tabs/day)

Drug Interactions (DIs)

- Most ARVs have the potential to interact with other ARVs and with other medications
  - The interaction may be complex and difficult to predict
  - Recommendations vary: dose adjustment of one or both agents, "use with caution" (due to lack of data or options) or contraindicated
  - Often a clinical decision: risk vs. benefit
- ALWAYS check for interactions before dispensing
- Most interactions center around drug metabolism and elimination, but there are some interactions that affect absorption

DIs: Drug Metabolism & Elimination

- PIs
  - CYP3A4 substrates and inhibitors
  - Ritonavir is the most potent 3A4 inhibitor
- NNRTIs
  - CYP3A4 substrates
  - Efavirenz, etravirine, and nevirapine induce 3A4 metabolism
- Most PIs and above NNRTIs can also exert inhibition and/or induction on other systems, such as drug transporters (P-gp), P450 enzymes, and/or phase II metabolism (glucuronidation)
- Some ARVs are 3A4 substrates, but not inhibitors or inducers
  - Rilpivirine, elvitegravir, maraviroc
  - Caution or dose adjustments often needed with other agents

DIs: Drug Metabolism & Elimination

- There are numerous potential interactions between PIs and NNRTIs with coadministered drugs
  - Remember that most (9 out of 10 rule) drugs levels will be either ↑ by PIs (inhibitors) or ↓ by NNRTIs (inducers)
    - If coadministered with a PI: dose may need to be lowered or the drug should be avoided altogether (contraindicated)
    - If coadministered with a NNRTI: may need dose adjustment or the drug should be avoided altogether (i.e. oral contraception)
  - However, there are always exceptions to the rule

DIs: Notable Interactions

- Statins
  - Simvastatin, lovastatin – contraindicated w/ PIs
  - Atorvastatin, rosuvastatin – caution w/ PIs; use low dose
  - Pravastatin – not 3A4 substrate; however, pravastation levels can be elevated by darunavir (use with caution)
- Rifamycins (enzyme inducers)
  - Rifampin should NOT be coadministered with a PI; okay with efavirenz (may need dose adjustment)
  - Rifabutin is a major 3A4 substrate, but only a weak inducer
    - Can be used with either NNRTIs or PIs, but must dose adjust
- Methadone
  - Concentration lowered by NNRTI & PI therapy; may require dose increase (or decrease if NNRTI or PI changed or stopped)

DIs: Notable Interactions

- Benzodiazepines
  - Midazolam (contraindicated w/ PIs); L.O.T. benzos okay
- Warfarin
  - Substrate of CYP3A4, 2C9/19 & 1A2
  - Metabolism can be induced or inhibited by NNRTI & PI therapy; monitor INR closely
- Calcium channel blockers
  - Caution with PIs with diltiazem or dihydropyridine coadminis.
- Corticosteroids
  - Systemic methylprednisolone, prednisolone, and triamcinolone levels expected to be increased by PIs – coadmin. with caution
  - Inhaled & intranasal fluticasone can lead to systemic accumulation – use with caution, avoid if possible or use altern.

Other Notable Interactions

- When coadministered with tenofovir, atazanavir must be boosted with ritonavir (mechanism of interaction unknown)
- Atazanavir needs acidic environment to be absorbed
  - Give atazanavir 2 hours before or 1 hour after antacids
  - Space atazanavir ≥ 10 hours from famotidine (or equivalent H_2-blocker)
  - Space atazanavir ≥ 12 hours from omeprazole 20 mg (or equivalent PPI dose)
    - When coadministered with a PPI, atazanavir must be boosted with ritonavir

Other Notable Interactions

- Complera® (emtricitabine/tenofovir/rilpivirine)
  - Do NOT coadminister with PPIs
  - Can take antacid ≥ 2 hrs before or ≥ 4 hrs after
  - Can take H2-Blocker ≥ 12 hrs before or ≥ 4 hrs after
- Stribild® (emtricitabine/tenofovir/elvitegravir/cobicistat)
  - Absorption affected by antacids containing aluminum, magnesium hydroxide, or calcium carbonate
  - Stribild® should be separated by 2 hrs from antacids
- Tivicay® (dolutegravir)
  - Dolutegravir should be given 2 hrs before or 6 hrs after medications with multivalent cations (Al^{+++}, Mg^{++}, Ca^{++}, Fe^{+++}, sucralfate)

Implications for Pharmacy

- Pharmacy can play an important role in treatment success:
  - Educate patients
  - Reinforce adherence
  - Highlight common side effects
  - Identify potential medication errors
  - Search for and evaluate potential drug interactions
- Develop an open, trusting, nonjudgmental relationship:
  - Minimizes barriers, stigma
  - Ensures strict confidentiality

Summary

- HIV is a chronic disease
- Great strides made, but much still needed
- Pharmacists are critical

Questions?