HIV Management Update 2015

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Pharmacist Learning Objectives
• Describe the HIV life cycle and recognize antiretroviral drug targets
• Classify an antiretroviral agent by its mechanism of action
• Summarize pertinent changes to the 2015 DHHS HIV guidelines
• List the antiretroviral agents which are recommended for the treatment of HIV+ patients
• List the antiretroviral agents which are recommended for post exposure prophylaxis (PEP)

Technician Learning Objectives
• Define HAART
• Identify the minimum number of antiretroviral drugs in an appropriate HAART regimen
• Understand the importance of HAART adherence
• List the antiretroviral agents which are recommended for post exposure prophylaxis (PEP)

Human Immunodeficiency Virus (HIV)
• Retrovirus (RNA)
• Two distinct groups: HIV-1, HIV-2
• Acquired Immune Deficiency Syndrome (AIDS)
• Transmission
  • Sex
  • Injection drug use
  • Perinatal
  • Breast milk
• HIV/AIDS among leading causes of morbidity/mortality in U.S.

Mature HIV Virion

Natural Progression of HIV

http://tuningpp.com/hiv-to-aids-progression/
Epidemiology

• 1.2 million persons 13 years and older living with HIV in U.S.\(^1\)
  • 168,300 (14%) are unaware of their infection\(^1\)
  • Undiagnosed responsible for over half of new HIV cases\(^2\)
• Only ~50% of U.S. adults ever tested\(^3\)
• CDC expanded screening 2006
• Annual incidence approximately 50,000 cases\(^1\)

“Late Testers” in New Mexico

• Diagnosed in stage 3
• 43.2% diagnosed with HIV AIDS diagnosis
• Relatively higher than U.S.

Living With HIV

![Graph showing New HIV Infections vs People living with HIV/AIDS over time]

Early Initiation of Therapy

• Improves outcomes\(^1\)
• Prevents progression to AIDS
• Reduce hospitalizations
• Decrease risk of opportunistic infections
• Long healthy life
• Reduces chance of transmitting to others\(^2\)
  • Undetectable viral load <4% risk
  • Condom use + undetectable viral load <1% risk

HAART

• Highly Active Anti-Retroviral Therapy
• 3 active antiretroviral drugs
• 2 nucleoside reverse transcriptase inhibitors
• Plus 3rd active agent:
  • Integrase strand transfer inhibitor
  • Non-nucleoside reverse transcriptase inhibitor
  • Protease inhibitor with pharmacokinetic enhancer (cobicistat, ritonavir)
• Adherence critical for success

Question

What is the minimum number of antiretroviral drugs that should be included in an ideal HIV treatment regimen?

A. One  
B. Two  
C. Three  
D. Four  
E. Five
Question
What is the percentage of adherence to HAART needed for optimal virologic suppression?

A. < 70%
B. 70 – 79.9%
C. 80 – 89.9%
D. 90 – 94.9%
E. ≥ 95%

Adherence Goal > 95%

The Drugs

Antiretroviral Drug Classes
- Entry inhibitor
- Fusion inhibitor
- Reverse transcriptase (RT) inhibitors
  - Nucleoside RT inhibitors (NRTI)
  - Non-nucleoside RT inhibitors (NNRTI)
- Integrase strand transfer inhibitors (INSTI)
- Protease inhibitors (PI)

HIV Life Cycle

Entry/Fusion Inhibitors
- Selzentry (maraviroc)
  - CCR5-inhibitor
  - Requires tropism assay
  - Twice a day
- Fuzeon (enfuvirtide)
  - Subcutaneous injection
  - Twice a day
NRTIs
- Truvada (tenofovir/emtricitabine)
  - Viread (tenofovir)
  - Emtriva (emtricitabine)
  - Once a day
- Epzicom (abacavir/lamivudine)
  - Ziagen (abacavir)
  - Epivir (lamivudine)
  - Once a day
- Combivir (zidovudine/lamivudine)
  - Retrovir (zidovudine)
  - Twice a day

NNRTIs
- Sustiva (efavirenz)
  - Atripla (efavirenz/tenofovir/emtricitabine)
- Edurant (rilpivirine)
  - Complera (rilpivirine/tenofovir/emtricitabine)
- Viramune (nevirapine)
- Intelenze (etravirine)

PIs
- Prezista (darunavir)
- Reyataz (atazanavir)
- Norvir (ritonavir)
- Prezobix (darunavir/cobicistat)
- Evotaz (atazanavir/cobicistat)

INSTIs
- Isentress (raltegravir)
  - Twice a day
- Vitekta (elvitegravir)
  - Needs to be boosted
- Tivicay (dolutegravir)
- Strible (elvitegravir/cobicistat/tenofovir/emtricitabine)
- Trumeq (dolutegravir/abacavir/lamivudine)

DHHS HIV Guidelines 2015
- Updated April 2015
- 5 recommended HAART regimens:
  - 4 integrase strand transfer inhibitor (INSTI)-based regimens
  - 1 ritonavir-boosted protease inhibitor (PI/r)-based regimen
- 2 regimens previously categorized as recommended moved to alternative

INSTI-Based Regimens
- Dolutegravir/abacavir/lamivudine (AI)
  - Only if HLA-B*5701 negative
- Dolutegravir plus tenofovir/emtricitabine (AI)
- Elvitegravir/cobicistat/tenofovir/emtricitabine (AI)
- Raltegravir plus tenofovir/emtricitabine (AI)
## PI-Based Regimen
- Darunavir/ritonavir + tenofovir/emtricitabine (A1)
- Atazanavir/ritonavir has been moved to alternative list

## Alternative List
- Limitations for use in certain patient populations
- May be the preferred regimen for some patients
- NNRTI-based regimens
  - Efavirenz/tenofovir/emtricitabine (B1)
  - Rilpivirine/tenofovir/emtricitabine (B1)
- PI-based regimens
  - Atazanavir/ritonavir + tenofovir/emtricitabine (B1)
  - Atazanavir/cobicistat* + tenofovir/emtricitabine (B1)
  - Darunavir/ritonavir + abacavir/lamivudine (BII)

## Triumeq
- Dolutegravir/abacavir/lamivudine
- One pill once a day, with/without food
- Adverse effects
  - Headache
  - Insomnia
  - Rash, hypersensitivity reaction
  - HLA-B*5701 negative only
- Drug interactions
  - Polyvalent cations, separate

## Prezincobix
- Darunavir/cobicistat
- One pill once a day, with food
- Adverse effects
  - Diarrhea, nausea, vomiting
  - Rash
  - Increased serum creatinine
- Treatment-naive only
- Drug interactions
  - CYP-3A4 substrates

## Evotaz
- Atazanavir/cobicistat
- One pill once a day, with food
- Adverse effects
  - Elevated bilirubin levels, jaundice, scleral icterus
  - Diarrhea, nausea, vomiting
  - Increased serum creatinine
- Drug interactions
  - CYP-3A4 substrates

## Tenofovir Alafenamide (TAF)
- In phase III trials
- Prodrug of the nucleotide analog tenofovir
- Conversion occurs intracellularly
  - Lower plasma exposure than tenofovir disoproxil fumarate (TDF)
  - Higher active [drug] in mononuclear cells
- Benefits over TDF:
  - Less toxicities (nephrotoxicity, BMD/fractures)
  - Smaller dose required (pill size)
Question
(True/False) All 3 INSTIs are listed as recommended agents in the 2015 DHHS HIV treatment guidelines.
A. True
B. False

Post Exposure Prophylaxis (PEP)
• Last updated 2013
• Elimination of risk stratification for exposure incidents
• 3-drug PEP regimen for all
• Expanded list of ARVs for PEP
• Emphasis on tolerability and convenience of PEP regimen
• New recommendations for follow-up HIV testing

Occupational Risk Exposures
• Percutaneous injury or contact of mucous membrane or non-intact skin
• Blood
• Tissue
• Body fluids that are potentially infectious
  • CSF, pleural, pericardial, peritoneal, amniotic, semen, vaginal secretions
• Not considered infectious:*
  • Feces, nasal secretions, saliva, sputum, sweat, tears, urine, vomitus

* Unless visibly bloody

Toxicity of PEP Regimens
• Previous PEP boosted PI-based regimens
  • GI side effects common
  • Major reason for not completing PEP
  • Ritonavir has many drug interactions
• Tolerability major emphasis for recommended PEP
  • Potential side effects should be discussed

HIV PEP Recommendations
• Newer agents better tolerated and have better toxicity profiles than previous agents
  • 3 or more tolerable agents now recommended for all occupational exposures to HIV
    • 2 NRTIs (backbone)
    • 1 INSTI, ritonavir-boosted PI or NNRTI
  • Other classes may be indicated (resistant virus)
• To facilitate completion of PEP
  • Optimize side effect and toxicity profiles
  • Optimize dosing convenience

Preferred PEP Regimen
Raltegravir 400 mg BID + Truvada 1 tab QD
Alternative PEP Regimens

1 from each column

- Raltegravir
- Darunavir + ritonavir
- Etravirine
- Rilpivirine
- Atazanavir + ritonavir
- Lopinavir/ritonavir
- Stribild®
- Tivicay#
- Tenofovir + emtricitabine
- Tenofovir + lamivudine
- Zidovudine + lamivudine
- Zidovudine + emtricitabine

Timing and Duration of PEP

- Most effective when begun soon after the exposure in animal studies
- Start as soon as possible after the exposure, preferably within hours (72 hours)
- Point at which no benefit gained not defined
- Duration of PEP is full 4 weeks (28 days)

Question

Which of the following statements is TRUE regarding occupational exposure HIV PEP?

A. The recommended duration of PEP is 2 weeks
B. A positive HIV test is required before initiation of PEP
C. An ideal PEP regimen includes abacavir + lamivudine backbone
D. PEP should be started as soon as possible after exposure
E. Dolutegravir is included as part of the preferred PEP regimen