

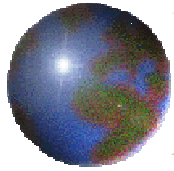


# New Antiretroviral Drugs and Treatment Guidelines for HIV Infected Patients

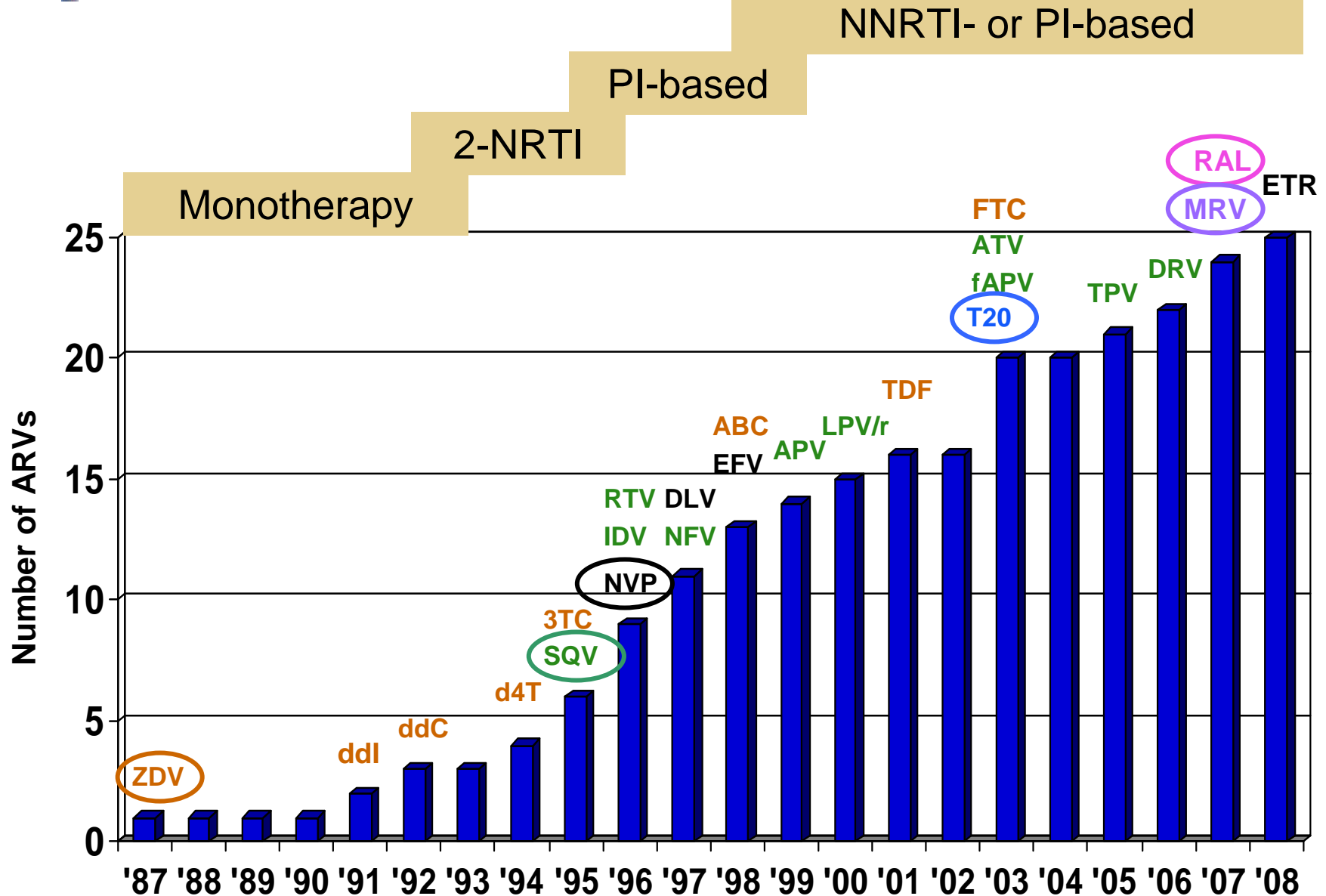
Jorge A. Tavel, M.D.  
National Institute of Allergy and Infectious Diseases  
National Institutes of Health  
Bethesda, Maryland USA

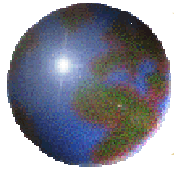
**May 5, 2008**  
**Second Eastern European  
and Central Asian AIDS Conference**



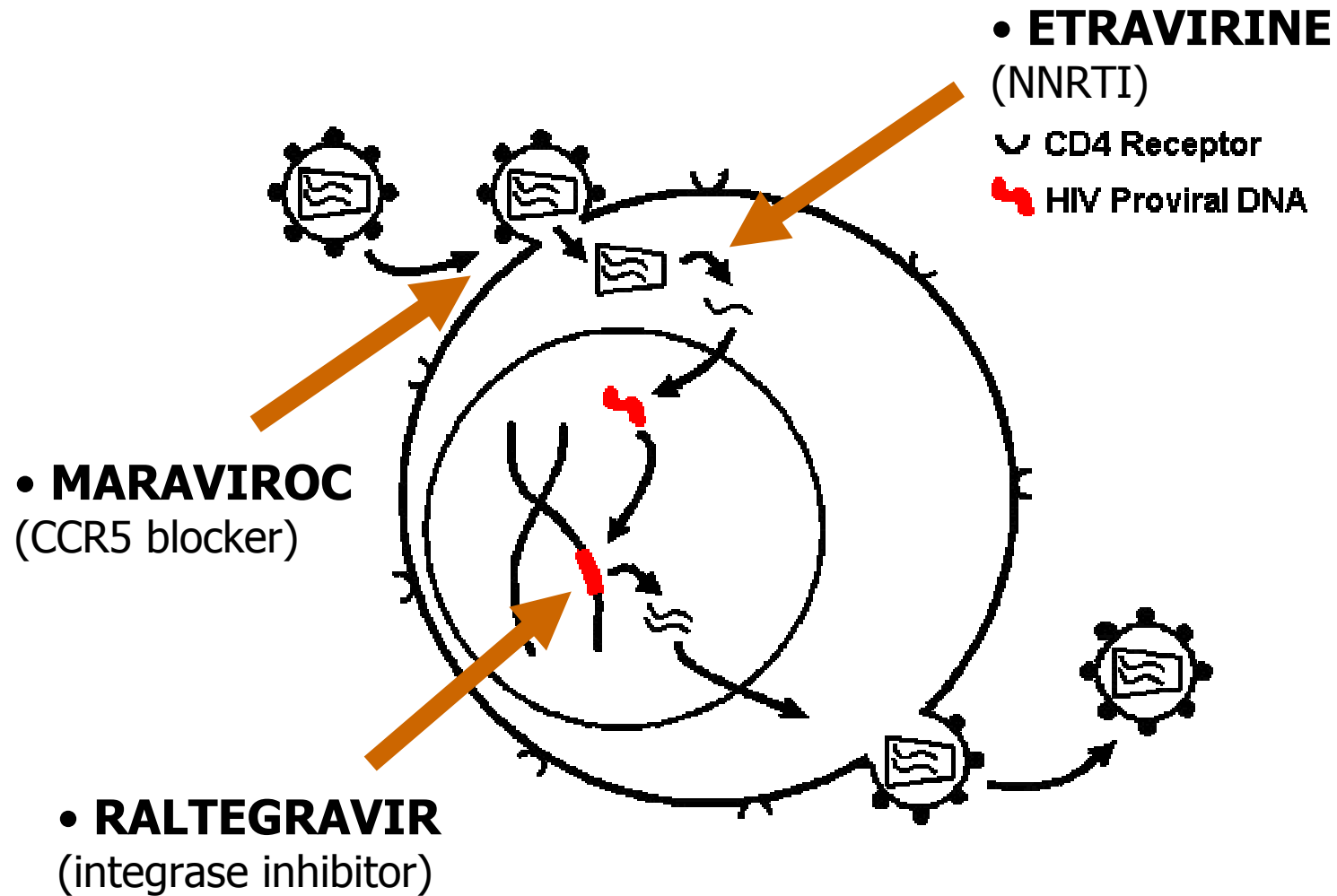


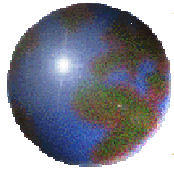
# FDA Approved Antiretroviral Drugs





# Three New Antiretrovirals





# HIV Management Evolves Rapidly

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

December 1, 2007

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

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the **AIDSinfo** Web site (<http://AIDSinfo.nih.gov>).

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

January 29, 2008

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

### How to Cite the Adult and Adolescent Guidelines:

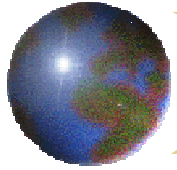
Panel on Antiretroviral Guidelines for Adult and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents. Department of Health and Human Services. January 29, 2008; 1-128. Available at <http://www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf>. Accessed (insert date) [insert page number, table number, etc. if applicable]

It is emphasized that concepts relevant to HIV management evolve rapidly. The Panel has a mechanism to update recommendations on a regular basis, and the most recent information is available on the **AIDSinfo** Web site (<http://AIDSinfo.nih.gov>).



**What  
antiretrovirals  
should be  
started?**

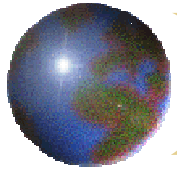




## What NNRTI to Start (29 Jan 2008)

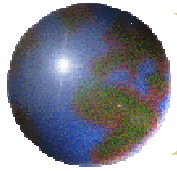
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- **Efavirenz**
  - remains as preferred NNRTI
- **Nevirapine**
  - alternative NNRTI
- **Etravirine**
  - not recommended as initial therapy
- **2 NNRTI**
  - not recommended to use in combination



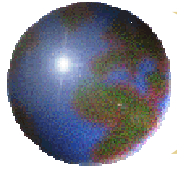
## What PI to Start (29 Jan 2008)

<b>Preferred</b>	<ul style="list-style-type: none"><li>• RTV-boosted atazanavir</li><li>• RTV-boosted fosamprenavir (BID)</li><li>• lopinavir/ritonavir (BID)</li></ul>
<b>Alternative</b>	<ul style="list-style-type: none"><li>• atazanavir (unboosted)</li><li>• RTV-boosted fosamprenavir (QD)</li><li>• lopinavir/ritonavir (QD)</li><li>• RTV-boosted saquinavir</li></ul>
<b>Not Recommended</b>	<ul style="list-style-type: none"><li>• nelfinavir</li><li>• indinavir (boosted or unboosted)</li><li>• RTV-boosted darunavir</li><li>• RTV-boosted tipranavir</li></ul>



## What NRTI to start (29 Jan 2008)

<b>Preferred</b>	<ul style="list-style-type: none"><li>• abacavir + lamivudine (for pts tested negative for HLA-B*5701)</li><li>• tenofovir + emtricitabine</li></ul>
<b>Alternative</b>	<ul style="list-style-type: none"><li>• zidovudine + lamivudine</li><li>• didanosine + lamivudine</li></ul>
<b>Not Recommended</b>	<ul style="list-style-type: none"><li>• stavudine + lamivudine (high incidence of mitochondrial toxicities)</li><li>• didanosine + tenofovir (CD4 decline, virologic non-response, interactions)</li></ul>



## Abacavir: New Data

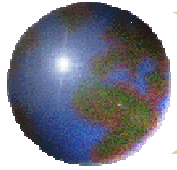
- **D:A:D Study:**

- 33,347 patients enrolled
- 157, 912 person-years follow-up
- 517 subjects diagnosed with myocardial infarction
  - 192 used ABC within the previous 6 months
  - 124 used ddl within the previous 6 months
- Recent, but not past (>6 month) or cumulative use of ABC or ddl, predicted risk of infarction.



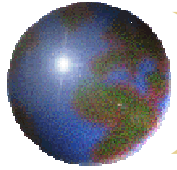
- **ACTG5202: ABC/3TC vs TDF/FTC + EFV or ATZ/rtv**

- in patients with viral load >100,000 copies/mL, those on ABC/3TC had a significantly shorter time to virologic failure



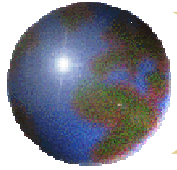
## HLA-B\*5701 Testing

- Panel recommends screening of HLA-B\*5701 before starting patients on ABC-containing regimen to reduce risk of hypersensitivity reaction
- HLA-B\*5701 positive patients should not be prescribed ABC
- The positive status should be recorded as an ABC allergy in the patient's medical record
- If HLA-B\*5701 testing is not available, it is reasonable to initiate ABC with appropriate clinical counseling and monitoring for signs of HSR



# Coreceptor Tropism Testing

- Tropism assay should be performed whenever a CCR5 inhibitor is being considered.
- Coreceptor tropism testing might also be considered for patients who exhibit virologic failure on a CCR5 inhibitor.
- Limitations of *Trofile*<sup>TM</sup> assay:
  - Takes 2 weeks to perform
  - Requires VL > 1,000 copies/mL
  - Not sensitive in detecting minor variants (more sensitive assay is currently under investigation)
  - Expensive - US\$1,960 per test



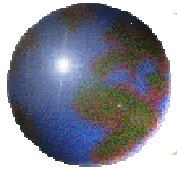
## Treatment Experienced Patients

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- Goal of therapy: maximal viral suppression
- More likely to achieve with newer agents
- At least 2, and possibly more fully active agents are needed when changing regimens
- Roles of raltegravir, maraviroc, and etravirine

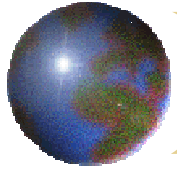


**When  
should  
antiretrovirals  
be started?**

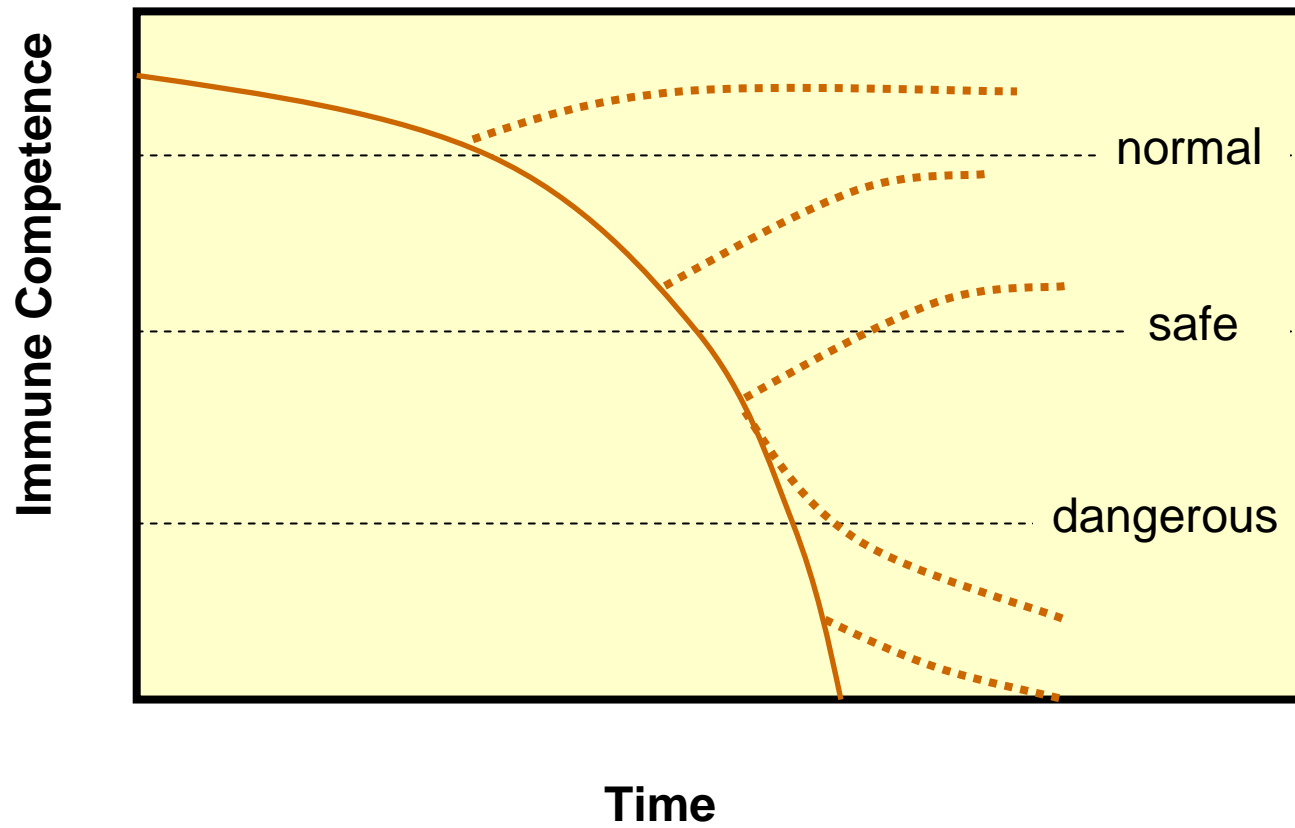


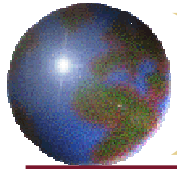
# When to Start: Old Recommendations

<b>Category</b>	<b>CD4 count (cells/mm<sup>3</sup>)</b>	<b>HIV RNA (copies/mL)</b>	<b>Recommendation</b>
AIDS or severe symptoms	Any value	Any value	Treat
Asymptomatic	<200	Any value	Treat
<b>Asymptomatic</b>	<b>200-350</b>	<b>Any value</b>	<b>Offer ARV, discuss pros &amp; cons w/ pts</b>
Asymptomatic	>350	≥100,000	Most will defer ARV, some may treat
Asymptomatic	>350	<100,000	Defer therapy



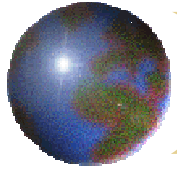
# When to Start





# When to Start: New Recommendations

<b>Category</b>	<b>CD4 count (cells/mm<sup>3</sup>)</b>	<b>HIV RNA (copies/mL)</b>	<b>Recommendation</b>
AIDS or severe symptoms	Any value	<b>Any value</b>	<b>Treat</b>
Asymptomatic	< 200		
<b>Asymptomatic</b>	<b>200-350</b>		
Pregnancy	Any value		
HIV nephropathy	Any value		
HBV infected pts requiring HBV Tx	Any Value		



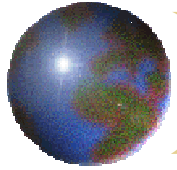
## ARVs at CD4 > 350 cells/mm<sup>3</sup>

### Benefits:

- Maintain high CD4 & prevent irreversible damage to immune system
- ↓ risk of HIV-associated complications & non-OI conditions that can be seen w/ high CD4
- ↓ risk of HIV transmission with suppressed HIV-RNA

### Risks:

- ARV side effects/toxicities
- Development of drug resistance due to incomplete suppression
- ↑ total time on ARV, greater chance of tx fatigue
- Premature use of ARV
- If not virologically suppressed, transmission of resistant HIV

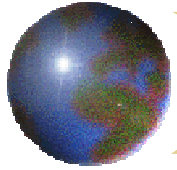


# Resistance Testing

## Genotypic Testing in ARV-Naive Patients

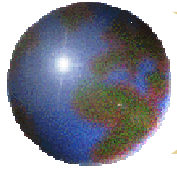
Previous Recommendation	New Recommendation
Prior to Initiation of ARV	When enter into care
Earlier testing may be considered	Repeat testing at the time of ARV initiation may be considered

Rationale: Transmitted resistance mutation may be detected at a time point more proximal to the time of infection.



## Acute HIV Infection

- Resistance testing should be done regardless of whether ART is to be initiated.
- If ART is to be started before genotypic resistance testing results, one may consider using a PI-based regimen, as acquired PI resistance is less common than NNRTI resistance.



# Conclusions

- ❖ Guidelines for management of HIV infected patients change frequently.
- ❖ New antiretroviral classes offer opportunities for virological suppression in heavily pretreated patients.
- ❖ As demonstrated in multiple studies, treatment by a physician experienced in the management of HIV infection is key.

Acknowledgement: Alice Pau, Pharm.D.  
Executive Secretary  
DHHS Panel on Antiretroviral Guidelines for Adults & Adolescents