48 – Antiretroviral Therapy for Special Populations

Speaker: Roy Gulick, MD

Antiretroviral Therapy (ART) for Special Populations

Roy M. Gulick, MD, MPH
Rochelle Belfer Professor in Medicine
Chief, Division of Infectious Diseases
Weill Cornell Medicine

Disclosures of Financial Relationships with Relevant Commercial Interests

- None

Special Populations

- acute/recent HIV infection
- acute opportunistic infection
- tuberculosis
- HIV-HBV co-infection
- HIV-HCV co-infection
- pregnancy
- post-HIV exposure (PEP)
  - occupational
  - non-occupational
- pre-HIV exposure (PrEP)

Question #1

PREVIEW QUESTION

A 22-year-old man presents with fever, mouth pain, and skin rash. PE reveals 3 small oral ulcers and diffuse macular rash. Labs show WBC 3K, platelets 89K, monospot negative, RPR NR, HIV antibody negative, HIV RNA 1,876,000 cps/ml.

Which statement is correct?

A. ART should not be offered.
B. ART would decrease his symptoms.
C. ART has long-term virologic benefits in this setting.
D. ART has long-term clinical benefits in this setting.

Acute or Recent HIV

- ART is RECOMMENDED.
- ART reduces symptoms and signs and reduces transmission.
- No long-term virologic, immunologic, or clinical data available.
- If ART is started, use standard regimens with goal of full virologic suppression.
- Obtain genotype prior to ART.
- If ART is started prior to genotype results, use **bictegravir, dolutegravir,** or **boosted darunavir,** together with tenofovir (TAF or TDF) + emtricitabine.
- Can modify regimen, if needed, when testing results return.

DHHS Guidelines 6/3/21

Question #2

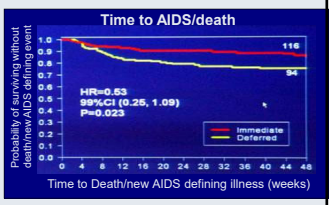
A 52-year-old woman is admitted for progressive SOB, is intubated, undergoes BAL and is found to have PCP. HIV Ab test is positive, CD4 103, HIV RNA 135,000 copies/ml. She is day 4 of IV trimethoprim-sulfa and corticosteroids and still intubated.

When should she start ART?

A. Immediately
B. In the next 2 weeks
C. After completing 21 days of trimethoprim-sulfa
D. At her first outpatient clinic visit

ACTG 5164: Immediate vs Delayed ART with an Acute OI

- 282 patients with treatable OI diagnosed within 14 days randomized to start ART within 48 hours vs. after 4 weeks
  - most common OI: PCP (63%)
- AIDS progression/death: immediate rx (14%) vs delayed rx (24%)
- No differences in safety/toxicity, IRIS, or week 48 responses



Zolopa PLoS One 2009;4:e5575

Acute Cryptococcal Meningitis

- Randomized clinical trial at Parirenyatwa Hospital in Harare, Zimbabwe
- Study population: 54 patients with CM treated with 800 mg fluconazole daily; median CD4 37
- Study Treatment: early ART (within 72 hours of diagnosis) or delayed ART (10 weeks after fluconazole)
- Results (through 3 years): 73% mortality rate overall
  - 88% (early ART) vs. 54% (late ART)
  - HR of death 2.85 (95% CI 1.1, 7.2)
- Conclusion: Early ART led to ↑ mortality

Makadzange CID 2010;50:1532

HIV-TB Co-infection

- Treat active TB the same with or without HIV.
- All HIV+ pts with TB should start TB meds immediately.
- In HIV+ patients with TB, timing of starting ART depends on CD4 count:
  - For CD4 <50, start ART ASAP, within 2 weeks of TB rx
  - For CD4 ≥50, start ART within 8 weeks of TB rx
- Start HIV+ pregnant women with TB on ART as early as feasible.

DHHS Guidelines 6/3/21

Question #3

A 39-year-old man with HIV disease, CD4 298, HIV RNA 23,000 cps/ml, never on ART is diagnosed with pulmonary TB. The plan is to start INH, RIF, PZA, and ETH pending susceptibilities. He agrees to start ART and genotype is wild-type.

Which ART regimen do you recommend?

A. TDF/emtricitabine/efavirenz
B. TAF/emtricitabine + atazanavir (boosted)
C. TDF/emtricitabine + atazanavir (unboosted)
D. TAF/emtricitabine + darunavir (boosted)

HIV-TB Co-infection (2)

- Include a rifamycin in the regimen.
  - rifampin
    - significantly ↓ **TAF** – current FDA label: not recommended
    - significantly ↓ ALL **PIs** – cannot use together
    - ↓ **Dolutegravir (DTG)** concentrations (need to ↑ DTG to 50 mg bid)
    - ↓ NNRTI concentrations: **Efavirenz** (**EFV**) 600 mg daily is recommended
  - rifabutin: preferred; more manageable drug interactions with protease inhibitors
- For IRIS, continue both ART and TB meds while managing the syndrome.
- Treatment support, including DOT of TB rx is strongly recommended.

DHHS Guidelines 6/3/21

Question #4

A 55-year-old treatment-naïve man with HIV disease, CD4 320 and HIV RNA 67,000 cps/ml

Lab testing reveals: toxoplasma Ab+; CMV Ab+; HAV total Ab+; HBV surface Ag+, core Ab+, surface Ab-; HCV Ab-; RPR NR

Of the following, which ART regimen would you recommend?

A. abacavir/lamivudine/dolutegravir
B. abacavir/lamivudine + atazanavir (boosted)
C. tenofovir (TAF or TDF)/emtricitabine + zidovudine
D. tenofovir (TAF or TDF)/emtricitabine + darunavir (boosted)

HIV-HBV Co-infection

- Some ART has activity against HBV
  - lamivudine (3TC), emtricitabine (FTC), tenofovir (TDF and TAF)
- Some HBV drugs have activity against HIV
  - entecavir (can select M184V) *McMahon NEJM 2007;356:2614*
- If treatment started, treat both optimally
  - 2 active agents for HBV
  - + 3rd drug for HIV (preferred = BIC or DTG)

DHHS Guidelines 6/3/21

HIV-HCV Co-Infection

- Anyone with HCV should be screened for HIV.
- High-risk HIV+ patients should be screened for HCV annually.
- ART should be started in those with concomitant HCV.
  - Same initial regimens recommended, but caution with drug-drug interactions and overlapping toxicities.
- Patients with HIV and HCV should be evaluated for HCV therapy (including assessing liver fibrosis stage).
  - Also evaluate for HBV co-infection.
- HCV direct-acting antiviral regimens → high cure rates

DHHS Guidelines 6/3/21

Question #5

A 26-year-old woman with HIV disease on abacavir/lamivudine + efavirenz with CD4 630 and VL suppressed below detection becomes pregnant.

What do you recommend regarding ART?

A. Discontinue ART until 2nd trimester.
B. Change abacavir to zidovudine.
C. Change efavirenz to bictegravir.
D. Continue current regimen.

Antiretrovirals in Pregnancy

- ART recommended for prevention of MTCT for all pregnant women, as early as possible, regardless of CD4 or VL level
  - Perform drug-resistance testing if VL >500-1000 cps/ml and adjust regimen, based on results
  - ART does NOT increase the risk of birth defects
  - Start (or continue) standard ART as early as possible:
    - 2 NRTIs + 3rd drug (PI, II, or NNRTI)
    - NO 2-drug regimens
- Near delivery, if HIV RNA >1000 (or unknown), use intravenous zidovudine, and recommend Cesarean section at 38 weeks

DHHS Perinatal Guidelines 2/10/21 <www.clinicalinfo.hiv.gov>

ART in Pregnancy: NRTI

- Preferred:
  - abacavir/lamivudine
  - tenofovir (TDF)/(emtricitabine or lamivudine)
- Alternative:
  - tenofovir alafenamide (TAF)/emtricitabine
  - zidovudine/lamivudine
- Not recommended:
  - zidovudine/lamivudine/abacavir (3 NRTIs) (insufficient virologic activity)

- IV zidovudine recommended close to delivery if HIV RNA >1000

DHHS Perinatal Guidelines 2/10/21 <www.clinicalinfo.hiv.gov>

ART in Pregnancy: NNRTI

- Alternative:
  - efavirenz (birth defects reported in primate studies, NO evidence in human studies and extensive experience; screen for depression)
  - rilpivirine (NOT with baseline VL >100K or CD4 <200 or PPIs)
- Insufficient data: doravirine
- Not recommended:
  - etravirine (not for treatment-naïve)
  - nevirapine (toxicity, need for lead-in dosing, low barrier to resistance)

DHHS Perinatal Guidelines 2/10/21 <www.clinicalinfo.hiv.gov>

48 – Antiretroviral Therapy for Special Populations

Speaker: Roy Gulick, MD

ART in Pregnancy: PI

- Preferred:
  - atazanavir/ritonavir
  - darunavir/ritonavir (use bid)
- Not recommended:
  - cobicistat (↓ drug concentrations, limited experience)
  - lopinavir/ritonavir (side effects)

DHHS Perinatal Guidelines 2/10/21 <www.clinicalinfo.hiv.gov>

ART in Pregnancy: II

- Preferred:
  - dolutegravir (small, but statistically significant, risk of neural tube defects)
  - raltegravir
- Insufficient data: bictegravir
- Not recommended:
  - elvitegravir/cobicistat (↓ drug concentrations)

DHHS Perinatal Guidelines 2/10/21 <www.clinicalinfo.hiv.gov>

ART in Pregnancy: Other

- Not recommended:
  - 2-drug regimens (e.g. dolutegravir/lamivudine, dolutegravir/rilpivirine)
  - enfuvirtide (not for treatment-naïve)
  - maraviroc (tropism testing; not recommended in treatment-naïve)
- Insufficient data: ibalizumab

DHHS Perinatal Guidelines 2/10/21 <www.clinicalinfo.hiv.gov>

Question #6

PREVIEW QUESTION

A 34-year-old HIV-negative nurse sustains a needlestick from an HIV-positive patient who has not taken ART for 2 years.

Which of these post-exposure (PEP) regimens do you recommend?

A. tenofovir (TDF)/emtricitabine
B. tenofovir (TDF)/emtricitabine + integrase inhibitor
C. tenofovir (TAF)/emtricitabine + integrase inhibitor
D. tenofovir (TDF)/emtricitabine + protease inhibitor

Antiretrovirals for PEP (1)

Postexposure prophylaxis (PEP) for occupational exposure:

- Assess nature of exposure:
  source fluid, volume of fluid, type of exposure, timing
- Assess exposure source; HIV and hepatitis testing
- Testing (baseline, 6 + 12 wks + 6 months with standard HIV Ab or 6 wks + 4 months if new HIV Ab/p24 test used) and counseling
- Offer 4 weeks of rx for recognized transmission risk
  - start ASAP (within 72 hours)
  - **tenofovir (TDF)/emtricitabine + dolutegravir** (not in women in early pregnancy or sexually active and not on birth control) or **raltegravir**
  - adjust regimen for possibility of resistance in source patient
  - f/u within 72 hours

PHS Guidelines updated 5/23/18

Antiretrovirals for PEP (2)

PEP for non-occupational exposure:

- Presentation ≤72 hours with substantial risk exposure from HIV+ source – recommended
- Presentation ≤72 hours with substantial risk exposure from source with unknown HIV status – case-by-case basis
- Presentation >72 hours or no substantial risk of exposure – not recommended

- Testing: rapid HIV (Ag)/Ab test or if results not available, start PEP
- Treatment: 4 weeks of
  - Preferred: **TDF/FTC + dolutegravir** (not in women in early pregnancy or sexually active and not on birth control) or **raltegravir**
  - Alternative: **TDF/FTC + darunavir/ritonavir**

PHS Guidelines update 5/23/18 <www.clinicalinfo.hiv.gov>

Question #7

PREVIEW QUESTION

23 year old HIV-negative man with an HIV+ partner on ART with HIV RNA suppressed below detection asks about starting pre-exposure prophylaxis (PrEP).

In addition to safer sex counseling, which of these do you recommend?

A. Nothing – PrEP is not indicated.
B. PrEP with tenofovir (TDF)/emtricitabine daily.
C. PrEP with tenofovir (TAF)/emtricitabine "on demand".
D. PrEP with bictegravir/tenofovir (TAF)/emtricitabine daily.

CDC Guidance for PrEP:

https://www.cdc.gov/hiv/pdf/risk/prep/cdc-hiv-prep-guidelines-2017.pdf

- Before starting:
  - document HIV Ab negative and r/o acute infection within a week of starting
  - document CrCl ≥60, screen for STIs and HBV infection
- Prescribe tenofovir (TDF)/emtricitabine 1 po daily X 90 days
  - provide risk reduction, adherence counseling, condoms
- On treatment:
  - HIV testing every 3 months
  - check CrCl every 6 months
  - risk reduction, condoms, STI assessments/rx
  - evaluate the need to continue PrEP
- 2019 FDA approved TAF/FTC for PrEP for ♂ (NOT ♀), based on DISCOVER

Conclusions

1. Acute (and recent) HIV – ART recommended.
2. Acute OI – ART within 2 weeks of diagnosis reduces mortality; caution with CNS opportunistic infections.
3. TB – Early ART prolongs survival; caution with rifamycin drug interactions.
4. Hepatitis B and C co-infection – Consider antiviral activity, drug-drug interactions, drug toxicities.
5. Pregnancy – Treat to reduce MTCT; modify ART recommendations based on safety and experience.
6. Post-exposure prophylaxis (PEP) – ART within 72 hours; give for 4 weeks; adjust for known drug resistance.
7. Pre-exposure prophylaxis (PrEP) – TDF/FTC (♂+♀), TAF/FTC (♂)

Acknowledgments

- **Cornell HIV Clinical Trials Unit (CCTU)**
- Division of Infectious Diseases
- Weill Cornell Medicine
- AIDS Clinical Trials Group (ACTG)
- HIV Prevention Trials Network
- Division of AIDS/NIAID/NIH
- The patient volunteers!