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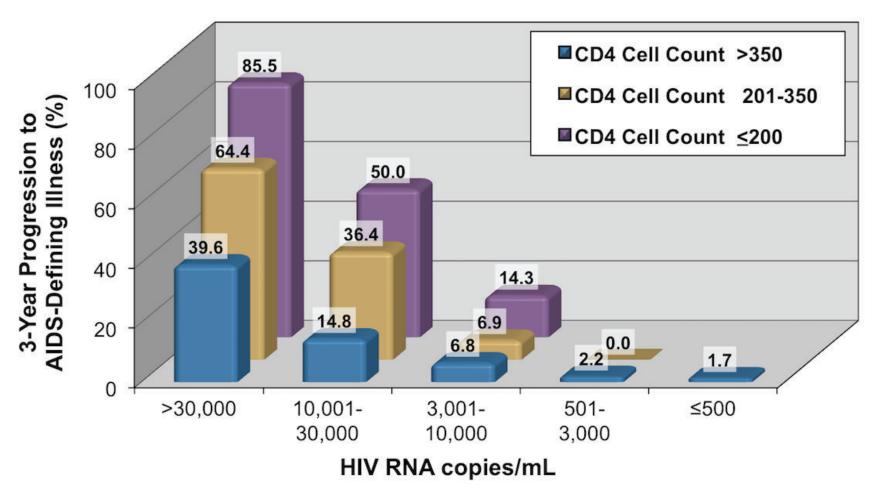
- Review HIV Care Continuum
- Basics of antiretroviral therapy (ART)
- Rapid-start ART
- When to delay start of meds
- Opportunistic infection prophylaxis
- Co-administration of other meds
- Vaccine schedules
- Health maintenance

## HIV MANAGEMENT IN PRIMARY CARE



## **HIV CARE CONTINUUM:**

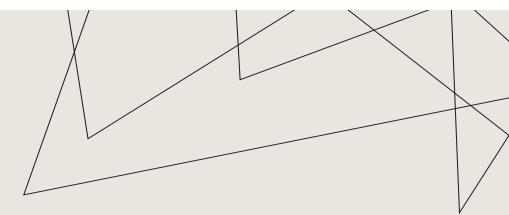
The series of steps a person with HIV takes from initial diagnosis through their successful treatment with HIV medication.



Source: Mellors JW, Rinaldo CR Jr, Gupta P, White RM, Todd JA, Kingsley LA. Prognosis in HIV-1 infection predicted by the quantity of virus in plasma. Science. 1996;272:1167-70.

### WHY SO SCARY?

- Unfamiliarity with current recommendations
- "So many" drug interactions
- "What if I mess it up?"
- Complexity of patient population
- "The meds have so many complications and sideeffects"
- "Rare" in clinical practice
- "It doesn't happen here"





# **Antiretroviral Therapy: What Does It Do?**

Antiretroviral therapy (ART) is the daily use of a combination of HIV medicines to treat HIV.

ART saves lives, but does not cure HIV.

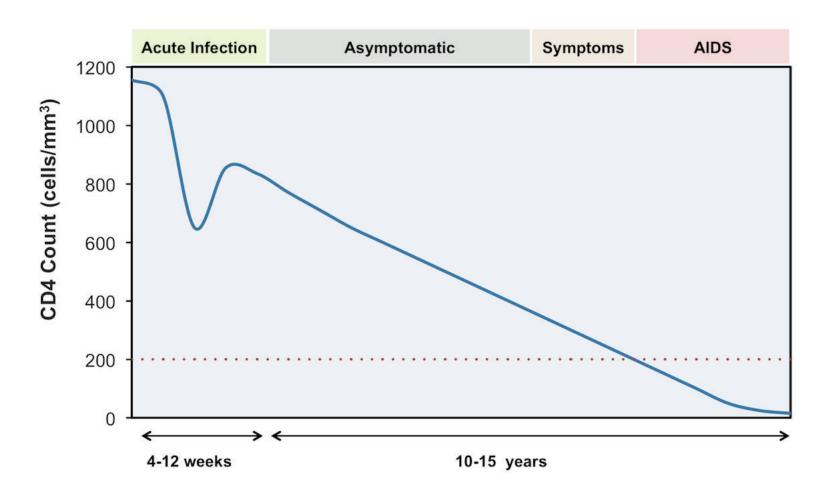


When a person with HIV has access to ART and takes it as prescribed, ART...

- Reduces the amount of HIV in the body
- Reduces the risk of HIV transmission
- Prevents HIV from advancing to AIDS
- Protects the immune system
- Prolongs life expectancy to near-normal

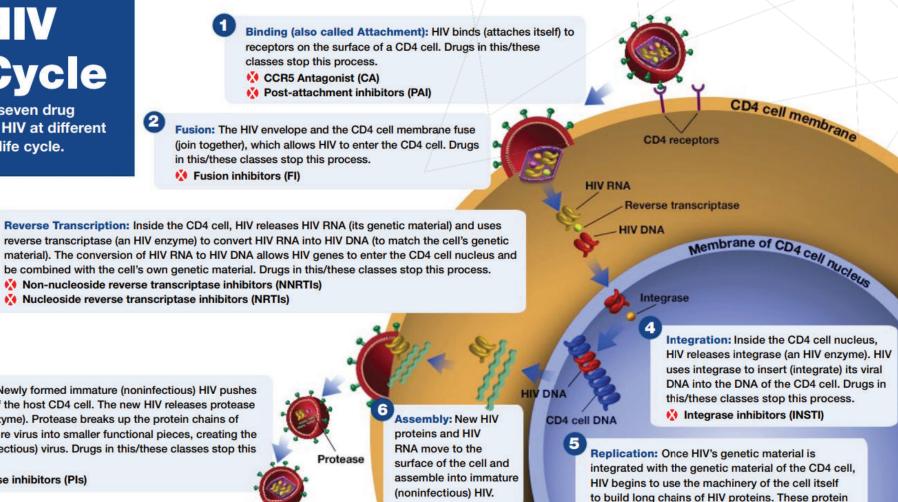


#### NATURAL HISTORY OF HIV INFECTION WITHOUT ART



## The HIV **Life Cycle**

**HIV** medicines in seven drug classes stop (X) HIV at different stages in the HIV life cycle.

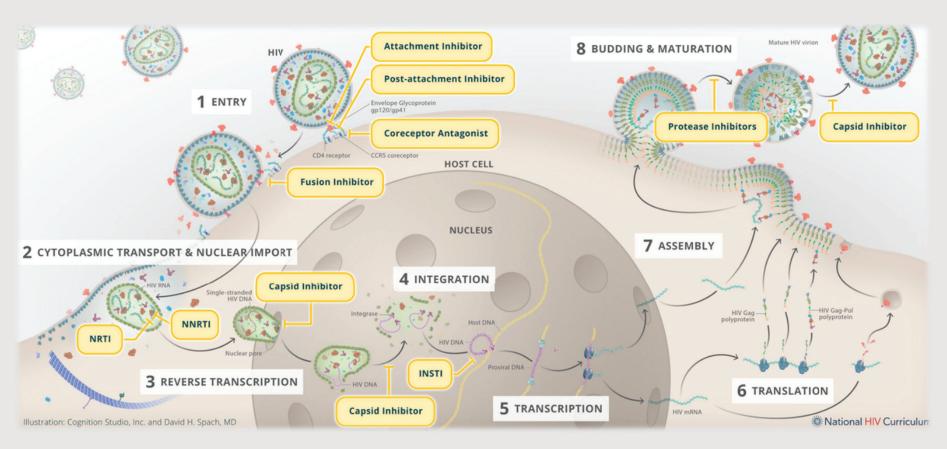


**Budding:** Newly formed immature (noninfectious) HIV pushes itself out of the host CD4 cell. The new HIV releases protease (an HIV enzyme). Protease breaks up the protein chains of the immature virus into smaller functional pieces, creating the mature (infectious) virus. Drugs in this/these classes stop this process.

Protease inhibitors (PIs)

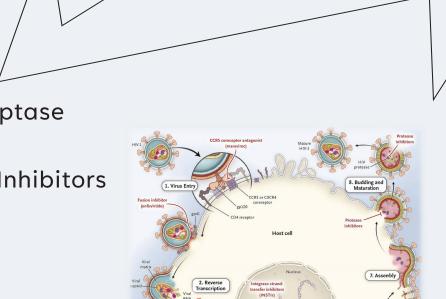
chains are the building blocks for more HIV.

### HOW ART WORKS

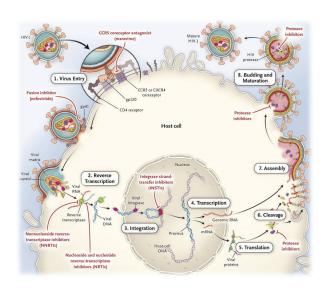




- Nucleoside/Nucleotide Reverse Transcriptase Inhibitors (NRTI)
- Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)
- Integrase Inhibitors (INSTI)
- Protease Inhibitors (PI)
- Entry Inhibitors
- Boosting Agents



### NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS (NRTI)



Emtriva (emtricitabine) -FTC

Epivir (lamivudine) -3TC

Retrovir (zidovudine) -ZDV

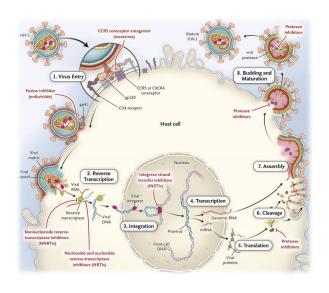
Viread (tenofovir DF) -TDF

Vemlidy (tenofovir AF) -TAF

Ziagen (abacavir) -ABC

Act as host nucleotide decoys and cause termination of the elongating HIV DNA chain

NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS (NNRTI)



Edurant (rilpivirine) -RPV

Intelence (etravirine) -ETR

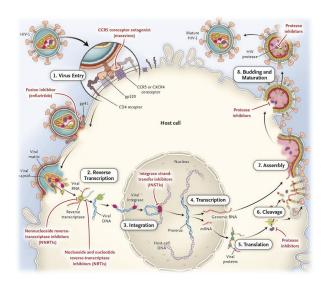
Pifeltro (doravirine) -DOR

Sustiva (efavirenz) -EFV

Viramune (nevirapine) -NVP

Bind directly to HIV reverse transcriptase enzyme and inhibit the function of the enzyme

## INTEGRASE INHIBITORS (INSTI)



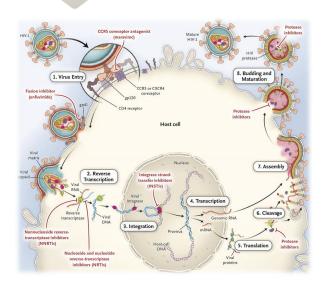
Isentress (raltegravir) – RAL

Isentress HD (Raltegravir) –RAL

Tivicay (dolutengravir) - DTG

Utilize multiple mechanisms to block the integrase enzyme

#### PROTEASE INHIBITORS (PI)



Lexiva (fosamprenavir) – FPV

Prezista (darunavir) –DRV

Reyataz (atazanavir) –ATV

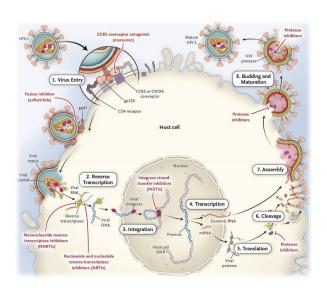
Viracept (nelfinavir) – NFV

### Some are boosted Protease inhibitors

- Kaletra (lopinavir with ritonavir) LPV/RTV
- Evotaz (atazanavir with cobicistat)
- Prezcobix (darunavir with cobicistat)

Bind to the active site of HIV protease and inhibit protease enzyme activity

#### **ENTRY INHIBITORS**



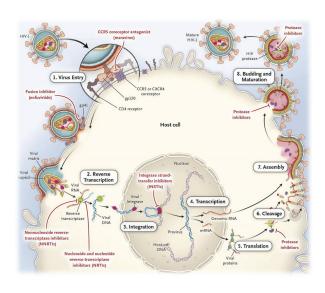
Fuzeon (enfuvirtide) – T-20 - Fusion Inhibitor

Selzentry (maraviroc) – MVC – CCR5 Antagonist

Trozargo (ibalizumab) – IBA – Post attachment inhibitor

In short, they prevent HIV from entering the host cell [attachment, receptor binding, fusion with membrane]

#### **BOOSTING AGENTS**



Norvir (ritonavir) – RTV

Tybost (cobicistat) - COBI

Act as host nucleotide decoys and cause termination of the elongating HIV DNA chain

## COMBINATION MEDS – THE MAJORITY!

#### **Single-Tablet Regimens**















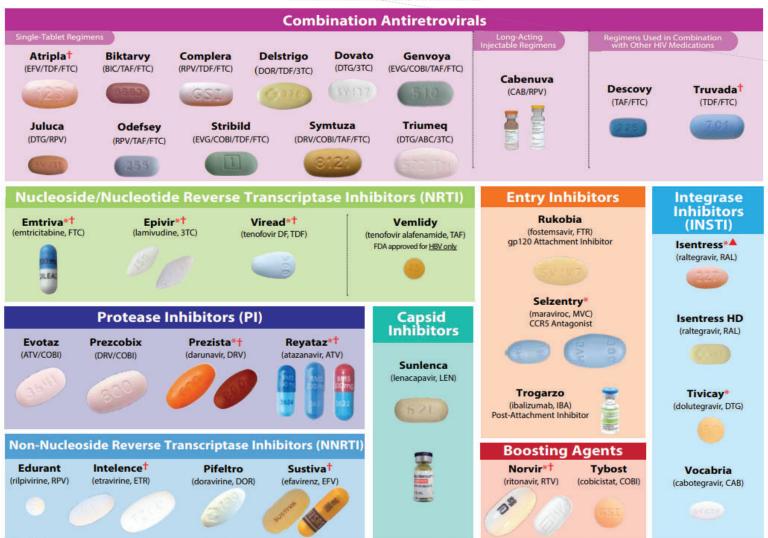








#### **HIV Medication Chart**



All pills shown in relative size/scale. Medication brand names appear in bold. Generic names and commonly used abbreviations appear in parentheses.

## LONG-ACTING ART

Drug	Optional Oral Lead-in <sup>a</sup> (at Least 28 Days)	Intramuscular (Gluteal)Initiation Injections(One-Time Dosing)	Intramuscular (Gluteal)Continuation Injections(Once-Monthly Dosing)
	Month (at Least 28 Days) Prior to Starting Injections	Initiate Injections at Month 1 <sup>b</sup>	One Month after Initiation Injection and Monthly Onwards
Cabotegravir	30 mg once daily with a meal	600 mg (3 mL)	400 mg (2 mL)
Rilpivirine	25 mg once daily with a meal	900 mg (3 mL)	600 mg (2 mL)

#### A DIFFERENT WAY TO TREAT HIV

Every other month, and you're good to go.

CABENUVA is given by a healthcare provider as 2 injections, initially 1 month apart for 2 months. Attend all appointments.



Unlike daily pills, **CABENUVA** is a longacting, complete HIV regimen you can get monthly or every other month that's as few as 6 times a year.



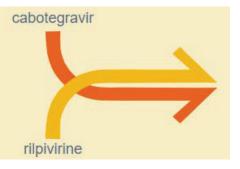
It's an injectable treatment that works continuously to help you stay undetectable\* for up to 2 months, depending on the treatment plan.



With regular injections, you won't have to take any more daily HIV pills.<sup>†</sup>

#### HOW DOES LONG-ACTING CABENUVA WORK?

It contains 2 HIV medicines, cabotegravir and rilpivirine, to help keep you undetectable.\* These 2 medicines slowly release over time to keep around the same level of medicine in your body between appointments.



<sup>\*</sup>Undetectable means the amount of HIV in the blood is below the level that can be measured by a lab test. Results may vary.

<sup>&</sup>lt;sup>†</sup>Before your first injections, you may take daily starter pills for about a month to see how your body reacts.



#### SCHEDULING CABENUVA TREATMENT

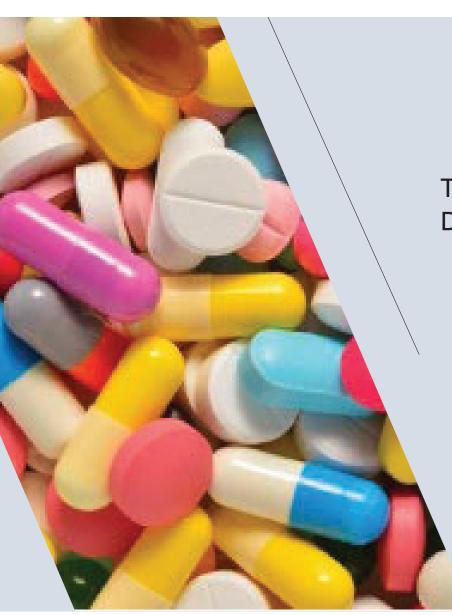
CABENUVA injections can be given by a healthcare professional once a month or every other month, depending on your treatment plan. To help stay undetectable, it's important to keep your planned appointments.



Target
Treatment
Date

You and your doctor will choose an ongoing date that works best for your injection appointments. This is called your **Target Treatment Date**. If you can't make your appointment, be sure to contact your doctor right away.

Flexible Treatment Window You have a **Flexible Treatment Window** to schedule your appointment within—from 7 days before to 7 days after your Target Treatment Date.



## THAT'S ALL GREAT... BUT WHAT DO I START?

#### Start with a "backbone" of two NRTIs

- Tenofovir-emtricitabine
- Avoid abacavir whenever possible
- Avoid Tenofovir DF if kidney disease/osteoporosis

Then add a third "anchor" drug – can be NNRTI, PI, or INSTI

Bictegravir or dolutegravir

## Rapid ART

Starting antiretroviral therapy (ART) immediately after HIV diagnosis is recommended by U.S. federal guidelines. Rapid ART (aka immediate ART) can result in earlier HIV viral suppression, improved retention in care, and reduced HIV transmission.



#### INDICATIONS

#### Rapid ART is appropriate for:

- Individuals with a confirmed HIV diagnosis (i.e., HIV Ag, Ab, and/or HIV RNA viral load)
- Persons with suspected acute HIV infection, with or without confirmed HIV diagnosis (HIV Ag or Ab test results may be negative or indeterminate at the time of evaluation)

#### Rapid ART is not appropriate for:

 Persons with certain untreated opportunistic infections (OIs)—e.g., the CNS infections cryptococcal or TB meningitis; begin OI treatment before starting ART (consult with experts)

#### COMPRESSED HIV INTAKE

- · Review of HIV test results
- Targeted health history
- HIV risk behaviors
   Date of last negative HIV test
- Use of PrEP or PEP
- Psychoemotional counseling, support
- HIV education (including ART benefits, possible adverse effects, adherence, preventing transmission)
- Targeted physical exam
- Benefits counseling, insurance enrollment or optimization

#### **Baseline Labs**

- Repeat HIV testing (if indicated)
- . HIV RNA (quantitative viral load)
- CD4 cell count
   HIV genetype, inc.
- HIV genotype, including integrase
- HLA-B\*5701
   CBC/differential
- · Complete metabolic panel (kidney & liver tests, glucose)
- STI testing: syphilis test (RPR, VDRL, or treponemal), chlamydla and gonorrhea NAAT tests (urine, pharynx, rectum as indicated by sites of exposure)
- . TB screening test (e.g., Quantiferon)
- Hepatitis serologies (HAV IgG, HBsAb, HBsAg, HBcAb, HCV IgG)
- · Pregnancy test (if appropriate)

AIDS Education and Training Center Program, January 2023. AIDSETC.org

#### Offer ART

- If patient agrees and there are no contraindications, prescribe 30-day supply, give starter pack if available
- If patient declines immediate ART, follow up within 1-2 weeks, re-offer ART, continue HIV education

#### RECOMMENDED REGIMENS

These can be modified based on results of baseline labs.

- Dolutegravir (Tivicay), 50 mg once daily + [TAF/FTC (Descovy), TDF/FTC (Truvada), or TDF/3TC] 1 once daily
   Bictegravir/TAF/FTC (Biktarvy) 1 once daily
- . Darunavir/cobicistat/TAF/FTC (Symtuza) 1 once daily

If taking PrEP or PEP at or since the time of HIV infection:

- Consider an enhanced regimen: boosted PI + integrase inhibitor + TAF/FTC (Descovy), TDF/FTC (Truvada), or TDF/3TC: seek consultation
- If on injectable cabotegravir PrEP, consider boosted
   PI + TAF/FTC (Descovy), TDF/FTC (Truvada), or TDF/3TC

If **pregnant** or trying to conceive (some antiretrovirals are notrecommended during pregnancy):

- Dolutegravir (Tivicay), 50 mg once daily + [TAF/FTC (Des-
- covy), TDF/FTC (Truvada), or TDF/3TC) 1 once daily

  Other options may be appropriate; consult with expert

Abbreviations: 3TC: lamivudine; FTC: emtricitabine; PI: protease inhibitor; TAF: tenofovir alafenamide; TDF: tenofovir disoproxil fumarate; BID: twice daily

#### FOLLOW UP

Schedule a follow-up visit for 1-2 weeks, then at least monthly until well established in care

#### RESOURCES / REFERENCES

- AETC National Clinician Consultation Center
   Monday Friday 9 AM to 8 PM ET / 800-933-3413
- See full Rapid ART guide at https://aidsetc.org/rapid-art
- Based on: Getting to Zero San Francisco. Rapid ART: Immediate ART initiation at HIV diagnosis and re-engagement in care at: www.gettingtozerosf.org

#### RAPID START ART

- Ideally, ART would be started the same day as diagnosis
- Benefits
  - Prevention of low CD4 is shown to prevent decreased overall morbidity/mortality
- Why aren't we doing this a primary care providers?
  - Fear
  - Lack of education
  - Poor collaboration



## WHEN TO DELAY START OF ART IN PRIMARY CARE

- Rather than delay make urgent referral to infectious disease
- RARE to delay
- Patient preference
- Multiple severe, poorly managed co-morbidities
- Prior history of multiple ART regimens

## WHAT NOT TO DO!

- Monotherapy with ANY ARV Regimen
- Dual Therapy with two NRTIs
- Triple therapy with three NRTIs
- TAF plus TDF

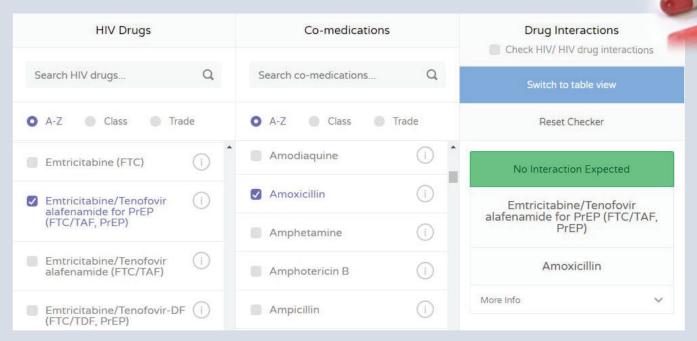


## MONITORING RESPONSE TO MEDS

- Baseline HIV viral load and CD4
- ANY time there is a change in clinical status recheck labs
- Recheck a CD4 every 3-6 months for the first 2 years of therapy
  - THEN:
    - If less than 300 every 3-6 months
    - 300-500 every 12 months
    - If consistently greater than 500 optional (CHCBH still checks every 12mo)
- Repeat viral load in 2-8 weeks, no later than 8 weeks
  - Recheck VL every 4-8 weeks until virally suppressed
  - After fully suppressed extend VL to every 3-4 months for 1-2 years
  - Long-term suppression VL every 6 months

## BUT MY PATIENT IS ON OTHER MEDS, NOW WHAT DO I DO?

**HIV and HCV Drug Interactions: Quick Guides for Clinicians** 



HIVinfo.NIH.gov: HIV treatment - side effects

**University of Liverpool: HIV Drug Interactions Checker** 

### MEDICATIONS - KEY CONCEPTS

#### **Steroids**

- HIV medications can increase concentrations
  - Cushing's syndrome adrenal suppression
- More common with "boosters"
- Adjust dosing for:
  - Most inhaled steroids
  - Prednisone
- AVOID Flonase

#### **Over the Counter (OTC)**

- St. John's Wort CP450 3A4
  - May reduce concentration of PIs and NNRTIs by as much as 82%
- Garlic topic of debate
- PPIs and H2 receptor antagonists
- Antacids magnesium and/or aluminum
  - neutralize stomach acids and may interfere with absorption of ART



Other common opportunistic infections in PLWH

Coccidiodomycosis | Cryptococcal meningitis | Cytomegalovirus Histoplasmosis | Kaposi Sarcoma | Toxoplasmosis



## OPPORTUNISTIC INFECTIONS (OI): PREVENTION

Primary care providers need a basic understanding of what opportunistic infections are and how to prevent them from occurring

Opportunistic infections are more frequent or severe due to immunosuppression

- Most common in undiagnosed HIV, those with late diagnosis, or those with poor retention in care
- Typically occur with a CD4 count less than 200
- AIDS-defining infections

### **OPPORTUNISTIC INFECTIONS:**

#### Prevention of *Pneumocystis* Pneumonia

#### Pneumocystis pneumonia

- Prior to ART, this infected up to 80% of patients with AIDS
- 90% of those who get PCP have a CD4 less than 200

#### Indications for primary prophylaxis

- CD4 less than 200
- CD4 percentage less than 14%
- CD4 200-250 and ART needs to be delayed and unable to monitor CD4 every 3 months

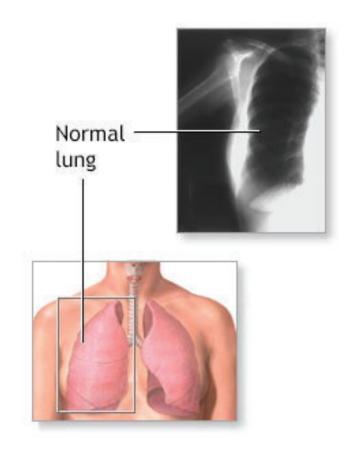
#### Regimen: Trimethoprim-sulfamethoxazole tablet daily

#### When to discontinue primary prophylaxis

■ CD4 greater than 200 for at least 3 months or CD4 100-200 for 3-6 months with an undetectable viral load

## PNEUMOCYSTIS CARINII PNEUMONIA (PCP)

- Fever
- Cough
- Shortness of breath
- Chest pain
- Chills
- Fatigue
- Weight Loss





Infection of lungs by Pneumocystis carinii



### **OPPORTUNISTIC INFECTIONS:**

Prevention of Disseminated Mycobacterium avium Complex (MAC)

**MAC:** Non-tubercular mycobacterium found in environment – infection causes fever, night sweats, weight loss, fatigue, diarrhea, anemia

- Usually in those not on ART or with resistance
- If disseminated may take several weeks for culture to be positive

#### Indications for primary prophylaxis

- CD4 less than 50
  - ➢ If suspect active MAC get cultures before starting treatment

#### Regimen:

Azithromycin 1200mg/week or 600mg 2x/week

#### When to discontinue primary prophylaxis

Effective ART has been started – regardless of CD4 count

#### HEALTH MAINTENANCE

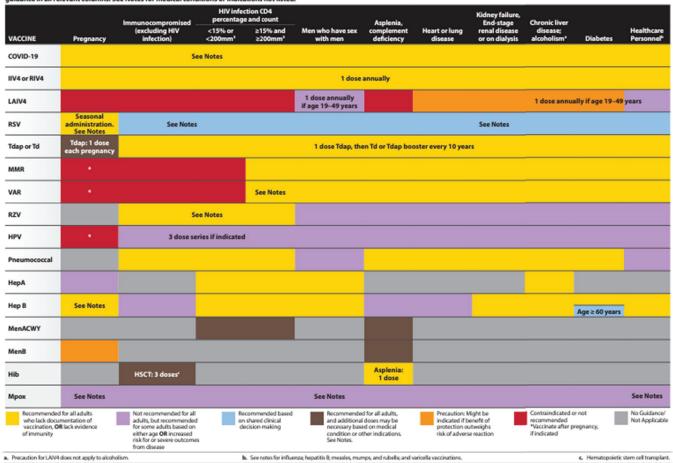
- STI testing and Trichomoniasis at diagnosis then every 3 months, and at least annually
- Syphilis at diagnosis every 3 months, and at least annually
- Pap at diagnosis then routine if normal, if abnormal follow ASCCP guidelines
- Anal Pap smear at diagnosis research pending
- Mental health/substance use disorder screening bi-annually
- Cholesterol panel at diagnosis then 1-3 months after starting meds
- DEXA scan at age 50 then based on sex assigned at birth
- People with HIV should receive evidence-based, patient-centered counseling to support shared decision-making about infant feeding

### HEALTH MAINTENANCE

- TB screening at diagnosis and annually
- Hep A/B/C testing at diagnosis and annually
- HPV vaccine all PLWH up to age 45
- STOP SMOKING
- Dentist every 6 months
- Yearly eye exam

#### Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2024

Always use this table in conjunction with Table 1 and the Notes that follow. Medical conditions or indications are often not mutually exclusive. If multiple medical conditions or indications are present, refer to quidance in all relevant columns. See Notes for medical conditions or indications not listed.



## **IMMUNIZATIONS**

- NO LIVE VACCINES avoid FluMist
- Know your CD4 before giving vaccinations
  - No varicella, MMR, or Zoster if CD4 less than 200
- Yes, they need a Covid vaccine.
- Vaccinations for Adults with HIV Infection



# It takes a team to stay healthy with HIV. Who's on your team?

