AETC AIDS Education & Training Center Program Mountain West

HIV Clinical Controversies & Challenges

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echo

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No conflicts of interest to disclose

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Case 1

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Case 1

- 27 year-old cis-male presents to the emergency room with headache worsening over the last few weeks.
- PMH: Opiate dependence (smokes fentanyl); meth use – injects and smokes
- Social History: Living in his car, MSM
- While in ED, HIV Ag/Ab positive and he is admitted for further work-up
- Subsequent labs show CD4 4 cells/mm^3, HIV RNA 350,000
- CBC and CMP notable for Hgb 12
- LP shows: Opening pressure 36 cm H_2O; 17 WBCs (85% L), 0 RBCs, total protein 111
- CrAg – Serum & CSF CrAg > 1:512

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Cryptococcal Meningitis

What else would you be concerned about in a patient with headache and advanced HIV?

What is the preferred management of cryptococcal meningitis?

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Management of Cryptococcal Meningitis

Basic Principles

- Diagnosis
- **Medications**
- ICP Management
- Monitoring

Source:

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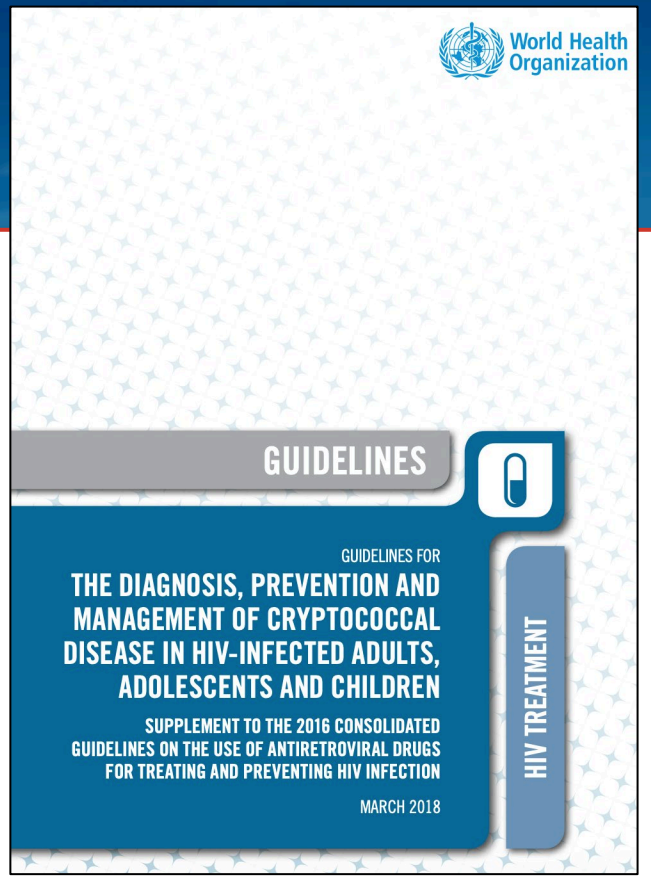
Cryptococcal Meningitis - Resources

- HHS OI Guidelines
- WHO Cryptococcal Disease Guidelines
- National HIV Curriculum

National HIV Curriculum



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Cryptococcal Meningitis Treatment

Induction: Liposomal amphotericin 3-4mg/kg daily + 5-FC 100mg/kg/day x 2 weeks

Need to document CSF clearance near end of induction

Consolidation: High dose fluconazole (800mg/day) x 8 weeks, though can reduced to 400mg/day

Maintenance: Low dose fluconazole (200mg/day) x at least 1 year and until CD4 count and HIV RNA suppressed

Source: Adult and Adolescent OI Guidelines (clinicalinfo.hiv.gov)

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Case 1 continued

- He states he wishes to leave the hospital as he is worried that his car will be towed
- Agrees to return to clinic to resume care and agrees to take medications prescribed

Source:

Case 1 continued

- He states he wishes to leave the hospital as he is worried that his car will be towed
- Agrees to return to clinic to resume care and agrees to take medications prescribed
- **Which of the following would you recommend?**

a. **Allow him to leave as a patient-directed discharge with fluconazole 1200mg po daily**

b. **Decline discharge and recommend he remain admitted for 2 weeks for amphotericin induction with 5-FC**

c. **Give one dose of amphotericin and discharge with high-dose fluconazole and 5-FC**

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Management of Cryptococcal Meningitis

DISCUSSION

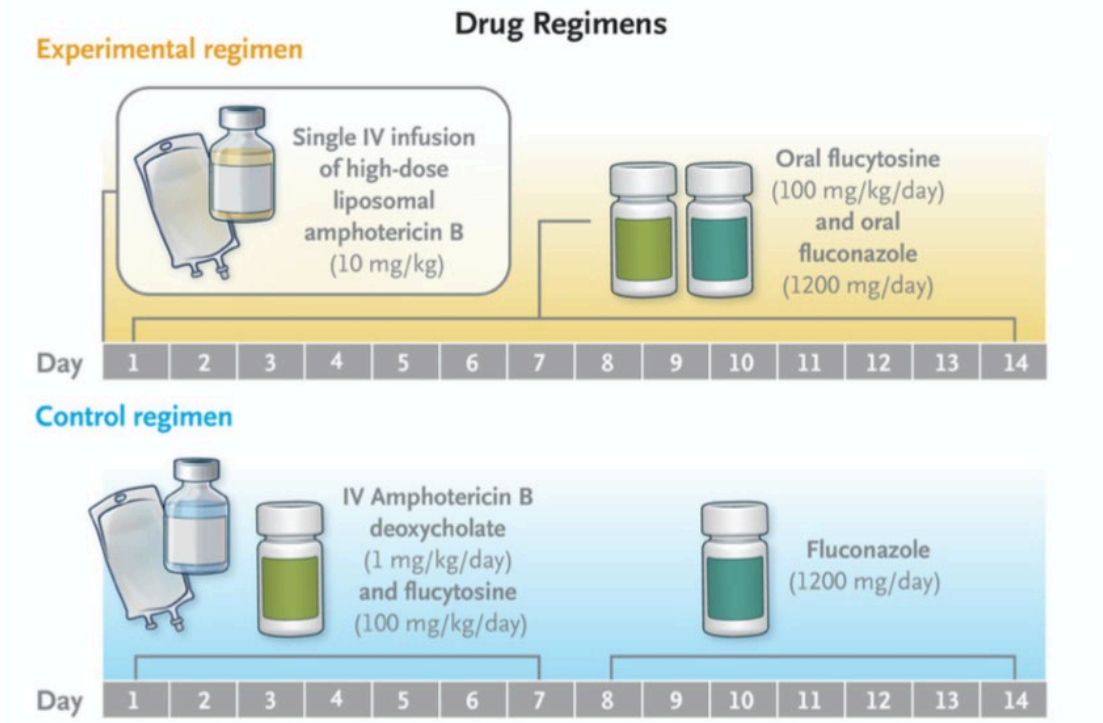
Source:

Cryptococcal Meningitis: Single Dose Liposomal Ampho

ORIGINAL ARTICLE

Single-Dose Liposomal Amphotericin B Treatment for Cryptococcal Meningitis

Joseph N. Jarvis, M.R.C.P., Ph.D., David S. Lawrence, M.B., Ch.B., David B. Meya, Ph.D., Enock Kagimu, M.B., Ch.B., John Kasibante, M.B., Ch.B., Edward Mpoza, M.B., Ch.B., Morris K. Rutakingirwa, M.B., Ch.B., Kenneth Ssebambulidde, M.B., Ch.B., Lillian Tugume, M.B., Ch.B., Joshua Rhein, M.D., David R. Boulware, M.D., Henry C. Mwandumba, Ph.D., et al., for the Ambition Study Group*



Source: Jarvis JN et al. N Engl J Med 2022

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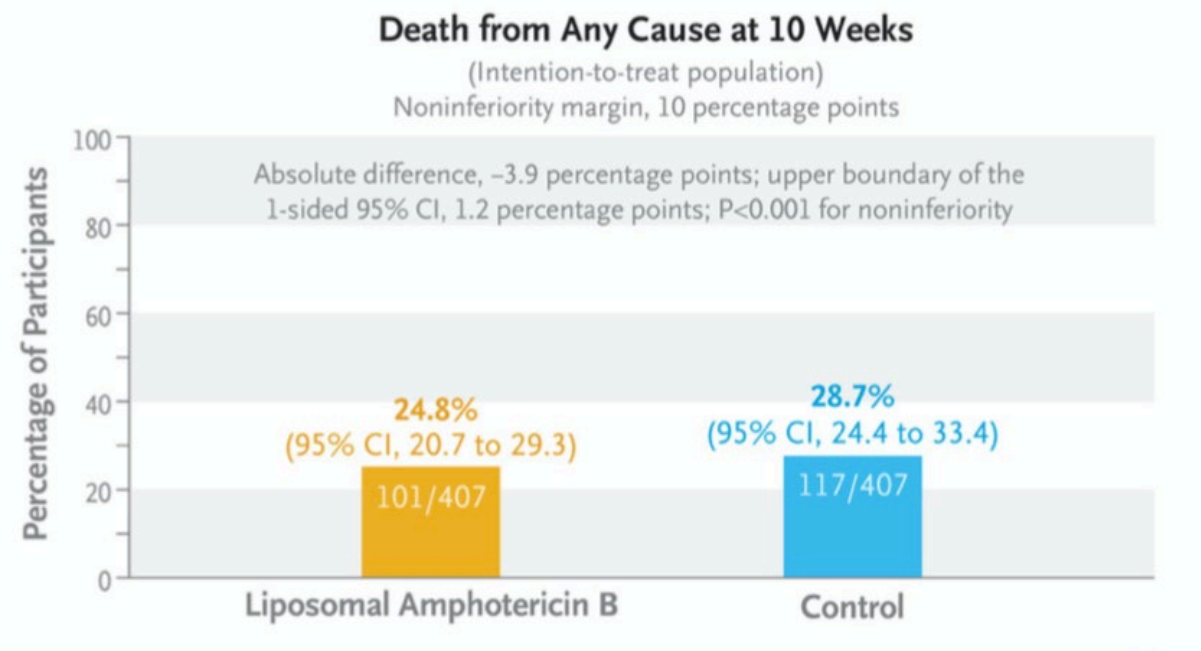
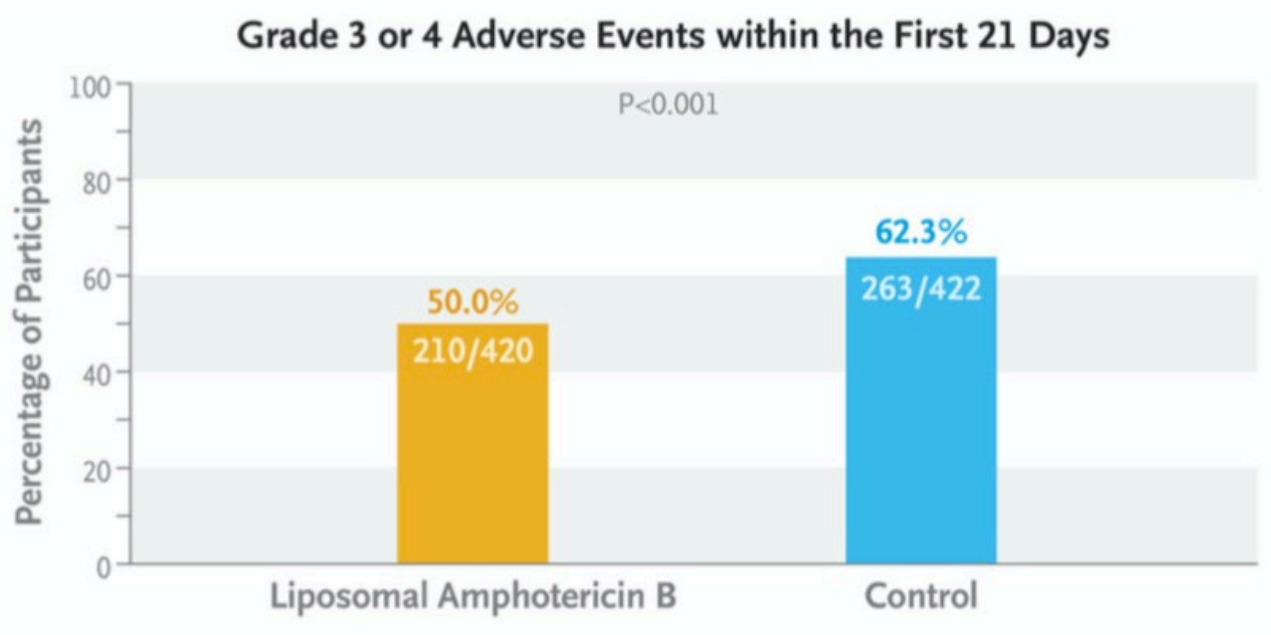
Single-Dose Amphotericin Non-Inferior, Less Side Effects





Source: Jarvis JN et al. N Engl J Med 2022

Alternative Regimens – What do the Guidelines Say?

- **HHS OI Guidelines:**
  - Fluconazole (1,200 mg daily) plus flucytosine is also a potential alternative to amphotericin B regimens **(BII)** but is inferior to ampho B for induction and is only recommended for patients who cannot tolerate standard treatment
  - The **preferred regimen** for primary induction therapy for patients with normal renal function is 2 weeks of an amphotericin B formulation once daily plus flucytosine 25 mg/kg four times daily **(AI)**
- **WHO Guidelines:**
  - Single-dose amphotericin regimen is now strongly recommended for induction therapy

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Case 1 continued

- He receives a single dose of liposomal amphotericin and is discharged with fluconazole and 5-FC.
- He returns to clinic a few days later for follow-up and notes he is taking his medications and is tolerating them well so far. He notes his headache has improved.
- You discuss his HIV diagnosis further at his clinic visit. He asks for treatment for HIV.

Source:

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Case 1 continued

- He receives a single dose of liposomal amphotericin and is discharged with fluconazole and 5-FC.
- He returns to clinic a few days later for follow-up and notes he is taking his medications and is tolerating them well so far. He notes his headache has improved.
- You discuss his HIV diagnosis further at his clinic visit. He asks for treatment.

What is your advice to him regarding timing of initiation of ART?

a. Start ART today

b. Start ART after completion of induction therapy for crypto meningitis

c. Start ART in 4-6 weeks

d. Other

Source:

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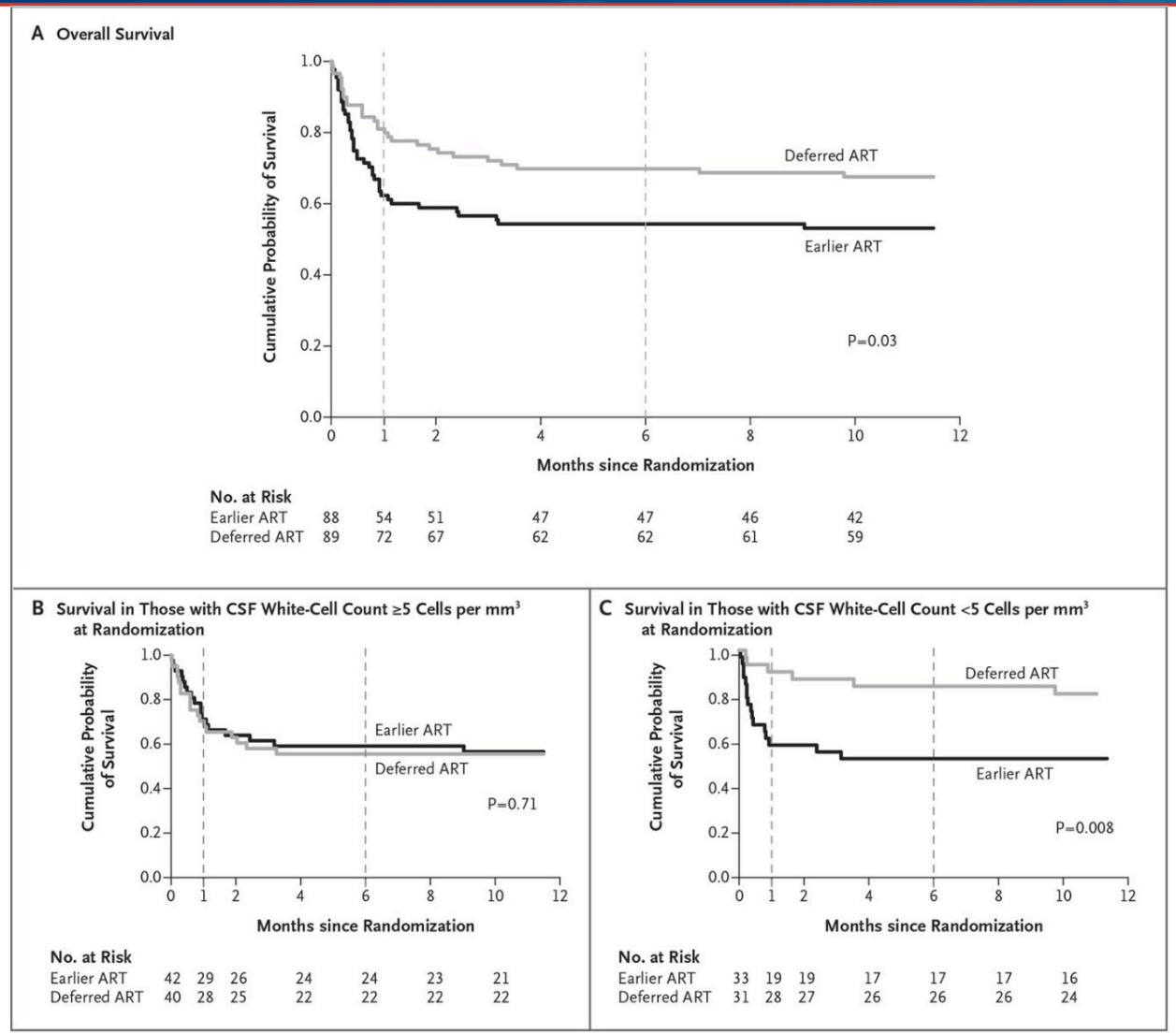
Management of Cryptococcal Meningitis

DISCUSSION

Source:

Cryptococcal Meningitis: Timing of ART Initiation



Source: Boulware D et al. N Engl J Med 2014

Cryptococcal Meningitis: Timing of ART Initiation – Other Clinical Controversies

DISCUSSION

Source:

Case 1 continued

Would you start LA-ART to treat HIV?

a. Yes

b. No

LA-ART as initial therapy: Eligibility

DISCUSSION

Source:

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Case 2

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Case 2

57 year-old man with long-standing HIV well controlled (HIV RNA UD, CD4 count 470) on fixed dose combination Dolutegravir + Abacavir + Lamivudine

He presents for routine visit after recent screening labs showed HbA1c 6.4 and fasting lipids significant for total cholesterol 245, LDL 130, HDL 51, TG 175.

He is otherwise well without any complaints. He is on losartan for essential hypertension.

BMI at this visit is 32 and BP 120/70.

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Current 10-year ASCVD risk is calculated at 13.8%

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Case

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He presents for routine visit after recent screening labs showed HbA1c 6.4 and fasting lipids significant for total cholesterol 245, LDL 130, HDL 51, TG 175.

Current 10-year ASCVD risk is calculated at 13.8%

In addition to starting metformin, what do you advise regarding management?

a. Change ART and start a statin

b. Change ART

c. Start a statin

d. Other

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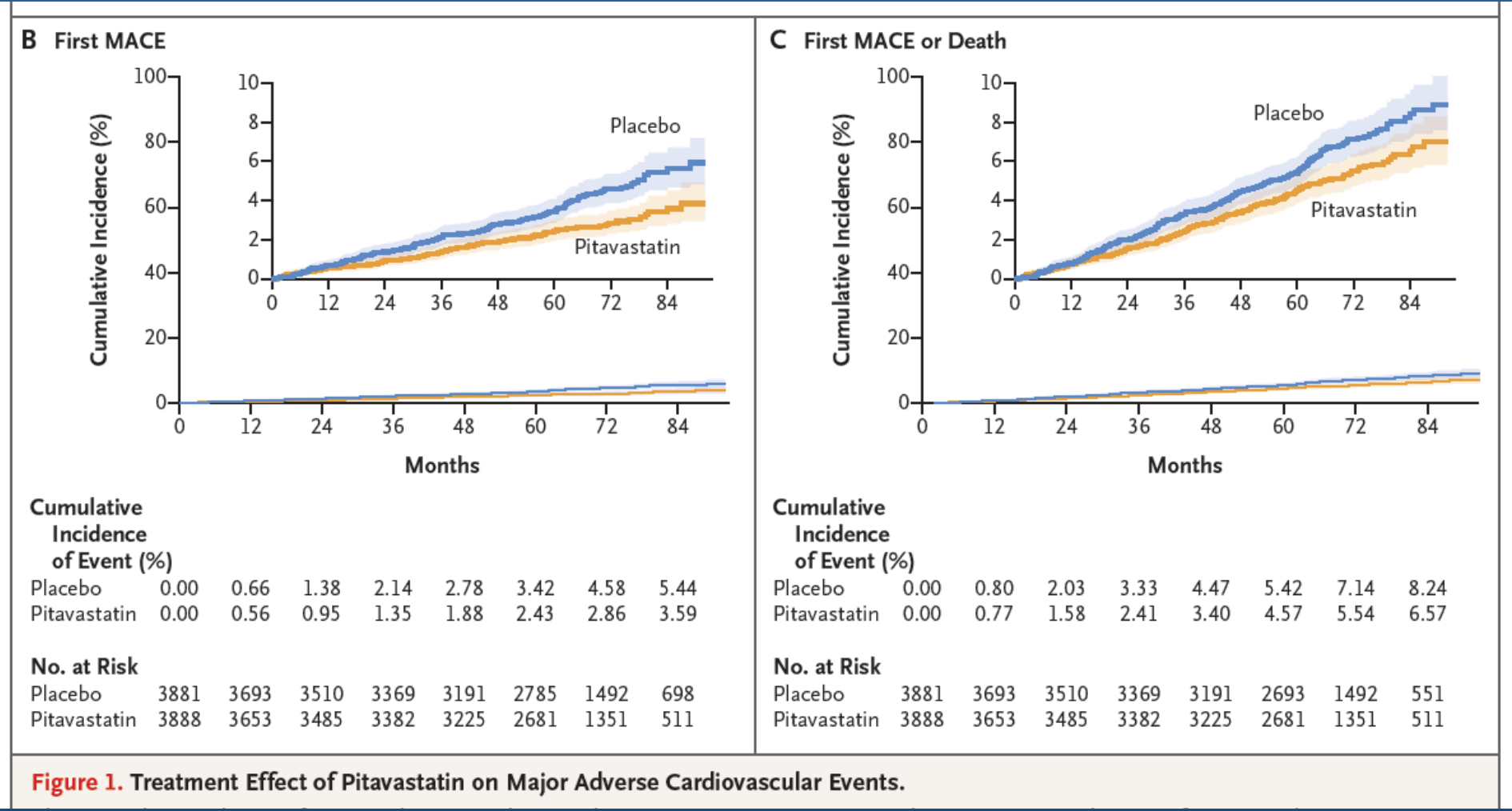
Would you start a statin?

DISCUSSION

Source:

Statin Drugs Can Reduce the Risk of Heart Attacks and Strokes in People with HIV



Cumulative Incidence of Event (%)								
Placebo	0.00	0.66	1.38	2.14	2.78	3.42	4.58	5.44
Pitavastatin	0.00	0.56	0.95	1.35	1.88	2.43	2.86	3.59
No. at Risk								
Placebo	3881	3693	3510	3369	3191	2785	1492	698
Pitavastatin	3888	3653	3485	3382	3225	2681	1351	511

Cumulative Incidence of Event (%)								
Placebo	0.00	0.80	2.03	3.33	4.47	5.42	7.14	8.24
Pitavastatin	0.00	0.77	1.58	2.41	3.40	4.57	5.54	6.57
No. at Risk								
Placebo	3881	3693	3510	3369	3191	2693	1492	551
Pitavastatin	3888	3653	3485	3382	3225	2681	1351	511

Figure 1. Treatment Effect of Pitavastatin on Major Adverse Cardiovascular Events.

Source: https://www.nejm.org/doi/full/10.1056/NEJMc2311117

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Recommendations for the Use of Statin Therapy as Primary Prevention of Atherosclerotic Cardiovascular Disease in People with HIV

For people with HIV who have low-to-intermediate (<20%) 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimates:

Age 40-75 years

- When 10-year ASCVD risk estimates are 5% to <20%, initiating at least moderate-intensity statin therapy is recommended **(AI).**
- Recommended options for moderate-intensity statin therapy include the following:
    - Pitavastatin 4 mg once daily **(AI)**
    - Atorvastatin 20 mg once daily **(AII)**
    - Rosuvastatin 10 mg once daily **(AII)**

Source: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/statin-therapy-people-hiv

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Recommendations for the Use of Statin Therapy as Primary Prevention of Atherosclerotic Cardiovascular Disease in People with HIV

For people with HIV who have low-to-intermediate (<20%) 10-year atherosclerotic cardiovascular disease (ASCVD) risk estimates:

Age 40-75 years

- When 10-year ASCVD risk estimates are <5%, at least moderate-intensity statin therapy is recommended **(CI).**
- The absolute benefit from statin therapy is modest in this population; therefore, the decision to initiate a statin should take into account the presence or absence of HIV-related factors that can increase ASCVD risk.

Source: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/statin-therapy-people-hiv

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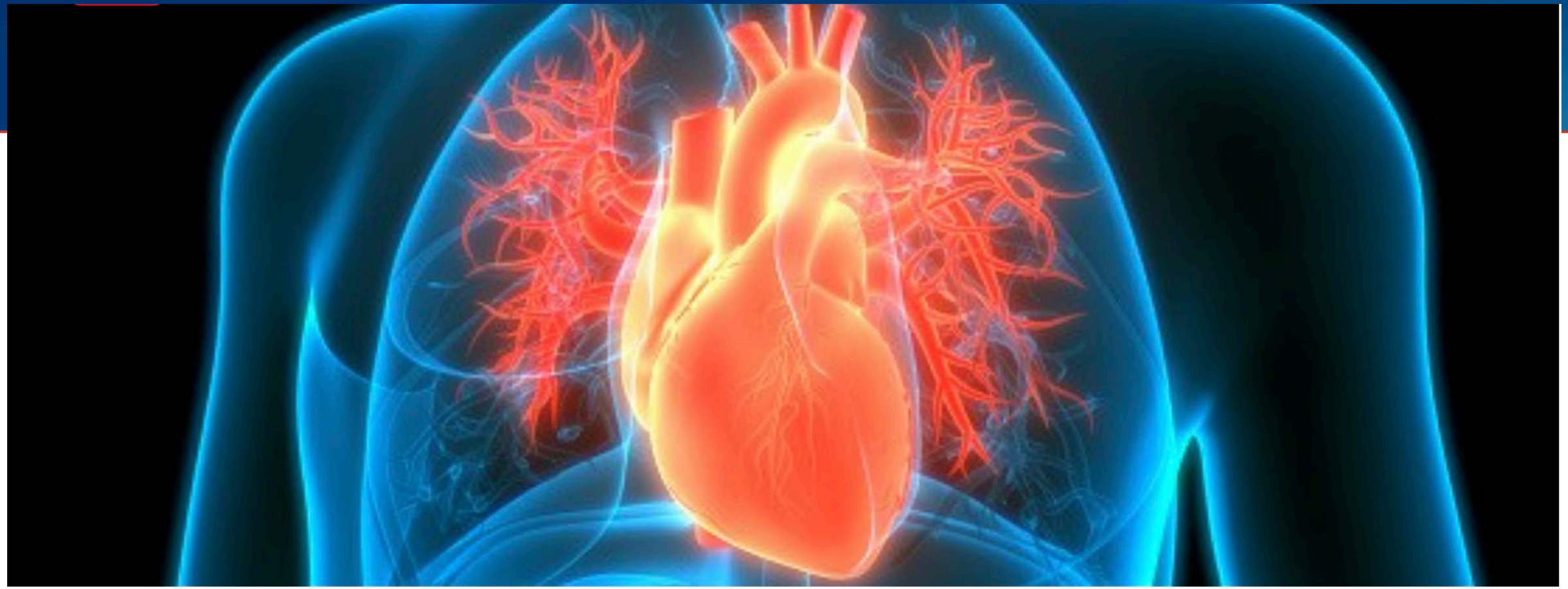
Should we switch off of abacavir in patients at risk for CV disease?

DISCUSSION

Source:



Antiretroviral abacavir linked with cardiovascular events in REPRIEVE trial

Source: https://www.uc.edu/news/articles/2024/07/antiretroviral-abacavir-linked-with-cardiovascular-events-in-reprieve-trial.html

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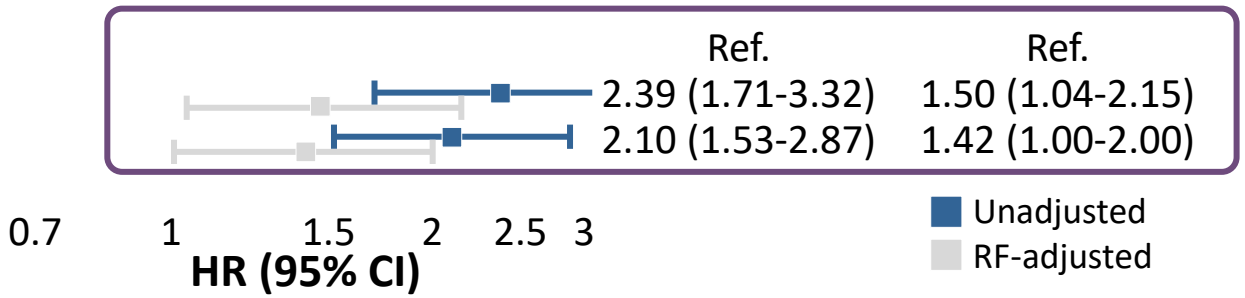
REPRIEVE: Abacavir and Major Cardiovascular Events

	Events	Participants	Unadjusted HR (95% CI)	RF-Adjusted HR (95% CI)
History of ABC exposure				
No	161	6092	Ref.	Ref.
Yes	96	1677	2.23 (1.73-2.87)	1.44 (1.09-1.91)
ABC use at randomization				
No	205	6785	Ref.	Ref.
Yes	52	984	1.83 (1.35-2.48)	1.29 (0.93-1.79)
ABC exposure				
Never	160	6067	Ref.	Ref.
Former	45	718	2.39 (1.71-3.32)	1.50 (1.04-2.15)
Current	52	984	2.10 (1.53-2.87)	1.42 (1.00-2.00)



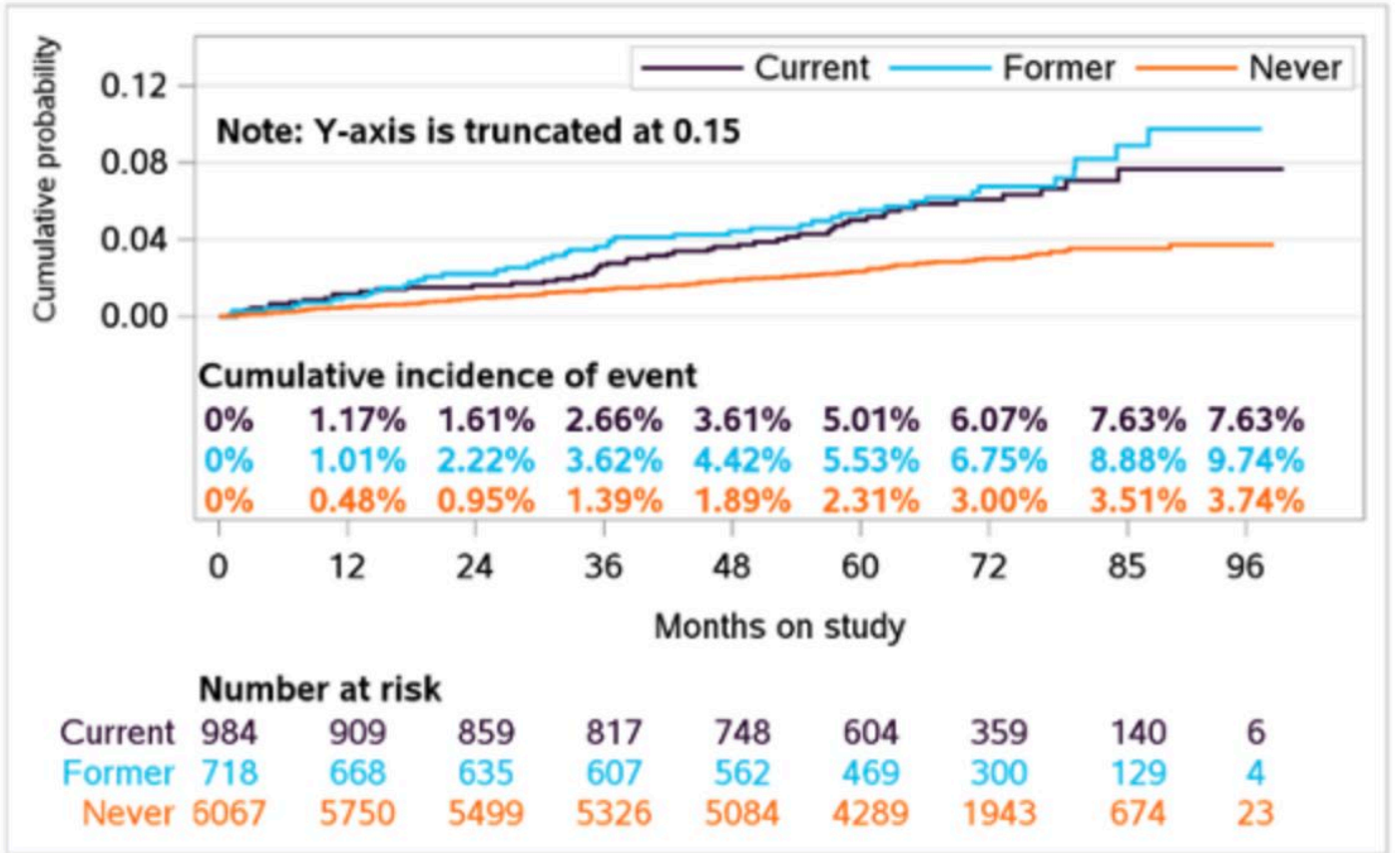
- Current and former use of **ABC** was associated with a **~42%-50% higher risk of subsequent MACE**
  - ABC effect on MACE was *not* changed by exposure to INSTIs, NNRTIs, or PIs
- Current and former use of TDF, PIs, and thymidine analogs were *not* associated with subsequent MACE

Source: Fichtenbaum. AIDS 2024. Abstr OAB3406LB.

Slide credit: clinicaloptions.com

REPRIEVE: Abacavir and Major Cardiovascular Events

Cumulative Incidence of MACE with Abacavir



Source: Fichtenbaum. AIDS 2024. Abstr OAB3406LB.

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REPRIEVE: Abacavir and Major Cardiovascular Events

Conclusion from the authors:

Controlling HIV is most important
Avoid Abacavir if possible

Source: Fichtenbaum. AIDS 2024. Abstr OAB3406LB.

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Updated HIV Treatment Guidelines 9/12/2024

Table 6a. Recommended Initial Regimens for Most People With HIV

For people who do not have a history of using CAB-LA as PrEP, one of the following regimens is recommended[a]:

- BIC/TAF/FTC **(AI)**
- DTG plus (TAF or TDF)[b] plus (FTC or 3TC) **(AI)**
- DTG/3TC **(AI),** except for individuals with HIV RNA >500,000 copies/mL, HBV coinfection, or in whom ART is to be started before the results of HIV genotypic resistance testing for reverse transcriptase or HBV testing are available.

Source: https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/what-start-initial-combination?view=full

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Case 3

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Case 3

32 year-old woman with asymptomatic, CD4 count 700's diagnosed as part of routine screening

- Started on DTG + F/TDF at initial visit
- Screening labs at initial visit are significant for positive quantiferon-TB. CXR normal. No pulmonary symptoms.
- She immigrated to US from Mexico 5 years prior

Source:

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What would you start for LTBI treatment?

32 year-old woman with asymptomatic, CD4 count 700's diagnosed as part of routine screening

- Started on DTG + F/TDF at initial visit
- Screening labs at initial visit are significant for positive quantiferon-TB. CXR normal. No pulmonary symptoms.
- She immigrated to US from Mexico 5 years prior

1. INH for 9 months
2. INH + rifapentine weekly for 3 months
3. INH + rifapentine daily for 1 months
4. Rifampin daily for 4 months
5. No LTBI treatment necessary

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LTBI Treatment in HIV

Indications:

- Positive screening test for LTBI (≥5 mm of induration at 48–72 hours in people with HIV or positive IGRA) regardless of BCG status AND no evidence of active TB disease, and no prior history of treatment for active disease or latent TB infection
- Close contact with a person with infectious TB (such as someone who has shared air space, such as in a household or close congregate setting, with a person with active pulmonary TB)

Source: https://clinicalinfo.hiv.gov/

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Latent TB Treatment-Antiretroviral Options – updated 9/12/2024!

Regimen	TB Med(s)	Duration, Dosing	ART Options*
Preferred			
3HP	INH & rifaPentine	3 months, weekly	TXF/FTC + DTG QD EFV/TXF/FTC
1HP	INH & rifaPentine	1 month, daily	EFV/TXF/FTC, **DTG BID**
Alternative			
9H or 6H	INH	9 or 6 months, daily	No change to ART
4R	Rifampin	4 months, daily	TXF/FTC + DTG BID EFV/TXF/FTC

RAL can also be combined with rifampin or rifapentine, but must be 800 mg BID with rifampin.
TXF = TDF or TAF
ABC/3TC is also an acceptable NRTI backbone for all regimens listed.

Source: Hillary Liss, MD and Adrienne Shapiro, MD based on clinicalinfo.hiv.gov, updated 9/12/2024

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TB Medications and ART Drug-Drug Interactions

DISCUSSION

Source:

Summary

- Cryptococcal meningitis treatment – single dose ampho may be considered but standard therapy remains 2 week induction
- Patients with low CSF WBC's have higher risk of immune reconstitution with cryptococcal meningitis
- Be aware of factors associated with increased risk of virologic failure with long-acting injectable ART as initial therapy
- Abacavir no longer part of preferred initial ART regimen
- Consider indications for statin therapy in people with HIV
- Remember drug-drug interactions with latent TB therapy and note new 1 month preferred regimen

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