Alcohol Drinkers’ Exposure to Preventive Therapy for TB (ADEPT-TB)

or: Uganda Cohort

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Alcohol Drinking Effects on Progression prior to Treatment (ADEPT) Study

Study accomplishments

- Recruitment and retention of a large cohort of HIV-infected drinkers in Uganda:
  - 450 participants (60% current drinkers)
  - Plus 300 drinkers from precursor study
  - 90% retention at 6- and 12- months
  - Frequent PEth testing and specimen collection/storage

- Publications: 11 published manuscripts, 4 under review, 7 conference abstracts

- Main study aims: To determine the effect of heavy alcohol consumption on HIV disease progression prior to the start of ART. Presented at RSA 2015.
Proposed new study

Alcohol Drinkers’ Exposure to Preventive Therapy for TB -- ADEPT-TB
ADEPT-TB background

• Tuberculosis (TB) is the leading cause of mortality in persons with HIV.
  • 20-30% of deaths

• Heavy drinkers are at 3-fold greater risk for active TB compared to others.
  • Increased risk for poorer TB outcomes including mortality
  • Approximately 25% of persons with HIV in SSA are heavy drinkers

• TB preventive therapy (with isoniazid – INH) decreases mortality by 30-50% above and beyond the benefits of ART.
ADEPT-TB background

• TB preventive therapy is recommended by the World Health Organization for all persons with HIV in resource-constrained settings.
  • 6-9 months INH

• EXCEPT… for those with “regular and heavy alcohol use”
  • Due to concerns about INH-related toxicity

• BUT… toxicity for drinkers has not been well studied
  • It is not known whether the benefits of TB preventive therapy outweigh the risks

• Adherence to TB preventive therapy could also be a problem
  • Short course therapy (3 months) may be the solution
Aim 1: To examine the **safety and tolerability** of TB preventive therapy for HIV-infected drinkers, measured by hepatotoxicity and treatment discontinuation rates.

- We will randomize to either 6 months of INH or 3 months INH + rifampin (RIF)

Aim 2: To compare the level of TB preventive therapy **adherence** by regimen.

Aim 3: To determine whether the **benefits** of providing TB preventive therapy to HIV-infected drinkers in resource-limited settings **outweigh the risks** compared to no treatment.
ADEPT-TB methods

- Randomized trial (n=380)
  - Arm 1: 6 months INH (n=190)
  - Arm 2: 3 months INH/rifampin (RIF) (n=190)
- Eligibility: Current drinker, HIV-infected, on ART
- Exclusion: Suspected TB, on ART regimens that might interact with INH or INH/RIF, pregnant or breastfeeding
- Frequent monitoring for toxicity
  - The US standard of care for INH for drinkers
- Monthly visits while on therapy, every 6 months thereafter
- Objective measurement
  - Alcohol use measured by PEth
  - Preventive therapy adherence measured via electronic pill count monitoring
  - Additional novel measure of INH exposure via hair concentration
Figure. ADEPT-TB study flow chart.

Eligibility visit: Eligibility assessed, ALT/AST testing, TST placed
If symptomatic: Chest X-ray and sputum collection to rule out active TB

Baseline study visit: Enrollment, baseline study survey, specimen collection, randomization, and month 1 pills dispensed

6 months INH
N=190

3 months INH + RIF
N=190

Week 2: Assessment for hepatotoxicity and other side effects

Months 1 + 2: Assessment for hepatotoxicity and side effects; pharmacy pill count, refill, EMM download, alcohol and adherence assessments

Month 3: Assessment for hepatotoxicity and side effects; pharmacy pill count, refill, EMM download
Study survey, blood draw for PEth, hair collection

Months 4 + 5: INH arm only: Assessment for hepatotoxicity and side effects; pharmacy pill count, refill, EMM download, alcohol and adherence assessments

Month 6: INH arm only: Assessment for hepatotoxicity and side effects; pharmacy pill count, EMM download
Both arms: Study survey, blood draw for PEth, hair collection

Months 12, 18, 24, etc.: Interview, specimen collection for PEth and repository, assessment for active TB
ADEPT-TB expected outcomes

• Precise estimates of rates of toxicity of TB preventive therapy among HIV-infected drinkers
  • Level of drinking well-characterized

• Determination of adherence to TB preventive therapy, comparing standard to short course
  • Objective measures of adherence

• Decision analysis modelling will compare the known benefits of TB preventive therapy to the risks for this high risk population
  • We will also examine optimal monitoring strategies

→ These outcomes will provide critical data for guidelines for TB preventive therapy in drinkers with HIV to reduce morbidity and mortality.
ADEPT-TB: Rich data with many deliverables

1. Liver injury among HIV-infected drinkers in Uganda (baseline data)
2. Latent TB infection and newly diagnosed active TB among HIV-infected drinkers in Uganda (baseline data)
3. Safety and tolerability of 2 regimens of TB preventive therapy for drinkers with HIV in Uganda (Aim 1)
4. Predictors of hepatotoxicity of TB preventive therapy among drinkers with HIV on ART in Uganda (Aim 1)
5. Adherence to standard versus short-course TB preventive therapy in HIV-infected drinkers (Aim 2)
6. INH concentration in hair by TB preventive therapy compared to other measures of adherence (Aim 2)
8. Patterns of alcohol use among HIV-infected drinkers on TB preventive therapy (longitudinal data)
ADEPT-TB collaborative effort

The team
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Nneka Emenyonu, DrPh                                                               Project director
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