Protocol Title: Virologic failure in HIV-positive women treated with ATV/r

Background and Significance

Human immunodeficiency virus (HIV) infection requires treatment for the lifetime of the patient, and success is achieved by reducing viral load to undetectable levels. The recommended therapy for Human Immunodeficiency Virus (HIV) infection in adults is combination anti-retroviral therapy (ART), where multiple anti-retroviral drugs are given in combination in order to maximize inhibition of viral replication and minimize the development of resistance mutations in the virus (1). Currently, ART is recommended in all HIV infected patients, regardless of CD4 cell count, disease symptoms, or other factors, as it preserves the patient's immune system and has the additional public health benefit of preventing transmission to others (3,4,5). Based on clinical guidelines, there are a number of preferred initial regimens which include the following combinations (3, 4):

a) a non-nucleoside reverse transcriptase inhibitor (NNRTI): efavirenz plus two nucleoside reverse transcriptase inhibitors (NRTI): tenofovir/emtricitabine,
   or
b) boosted protease inhibitor (PI): atazanavir-ritonavir once daily or darunavir-ritonavir once daily plus two NRTIs
   or
c) An integrase inhibitor, raltegravir (400 mg twice daily) with two NRTIs.

The choice of regimen for an individual patient depends on anti-virus activity, toxicity, drug interaction potential, viral resistance development, pill burden and comorbidities (4, 5). Atazanavir, which is used with ritonavir booster (ATV/r), a protease inhibitor, is a component in both preferred and alternative ART regimens, and is widely used due to its efficacy and its relatively high barrier to development of HIV resistance mutations (6). It has also been shown to have better GI, cardiac, and liver profile which would make it a safe alternative in patients with liver disease or those with cardiovascular disease for whom other protease inhibitors would not be tolerated (8).

ART treatment success is defined as viral suppression or undetectable levels being achieved while on ART (the lowest limit of detection depends on the assay used; our clinic uses the assay with the undetectable level of HIV PCR of < 40 copies/ml). Virologic failure is defined as persistent viremia (ie, HIV PCR >40 copies/ml if using our assay) at $\geq$ 6 months after initiation of treatment. Virologic failure is most often a result of poor adherence, and is typically dealt with by intensifying patient education and eventually testing for HIV Genotype to detect resistance mutation(s) which can lead to switching to an alternative ART regimen. The consequences of virologic failure can be profound, including increased risk of clinical progression to HIV-related disease, increased risk of transmission of disease, and potentially limited choices of active ART. Consequently, it is important that treatment-naïve HIV-infected patients be prescribed ART regimens with the lowest risk of virologic failure.

Recent studies have shown that female HIV patients on an ART regimen containing ATV/r had a disproportionate rate of virologic failure (8, 9). Although clinical guidelines address some issues unique to HIV-infected women (ie, avoidance of tenofovir as initial treatment for post-menopausal women) (4), there is no single regimen considered as optimal for women. In this study, we intend to compare the virologic outcomes of females receiving ART containing ATV/r to those receiving a non-ATV/r antiretroviral regimen who received care at [**Name of clinic**] between Jan 2010 and Dec 2014 to determine the virologic failure rate of ATV/r compared to other regimens in women.

Objectives:
The objective of this research is to determine if treatment-naïve HIV-positive women treated with ATV/r have increased virologic failure compared to women treated with other protease inhibitors

Research Design and Methods

This study involves a retrospective review of medical records of HIV-positive women. Subjects will be adult females diagnosed with HIV who had received initial prescription of ART between January 2010 and December 2014, with no prior ART treatment prior to 2010, and follow up after initiation of therapy of at least 12 months.

Procedures
The study is retrospective chart review. From the medical records described above, data will be collected on patient demographics, insurance status, pregnancy, comorbidities and several HIV-related factors. HIV-related factors are:

- Serum HIV-1 RNA PCR copies at baseline and various times after initiation of ART, with 400 copies/ml serum being cutoff for negative (<400) and virologic failure (≥400). Multiple sets of data may be collected per patient if the treatment was altered and T4 and TSH levels were re-measured. Medical records will be accessed from [name of clinic] computers.
- CD4 cell count at baseline and various times after initiation of treatment
- Co-infection with Hepatitis B or C

Investigators involved in the study will access patient medical records for extraction of data. Data extraction will only occur in Dr. So-and-So's office using limited access, password-protected computers. A correlation tool will be employed, with each subject being assigned a Study Identification Number to be associated with the medical record number for that patient. A separate data collection sheet will contain all of the health and demographic data being collected for each patient, along with the patient Study Identification Number. No identifying information will be included in the data collection sheet. Data will be stored in password protected Excel files and saved on password-protected computers in Dr. So-and-So's office.

Role of Student in Research Project

Student will collect all data from medical records, enter data into data collection sheet, perform preliminary data analysis (generation of summary data), contact and interact with statistician regarding statistical analysis of data, prepare figures and tables, and begin writing abstract for submission of results to a conference or research day.

References

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