Measures of ART Adherence Associated With Virological Failure in Rakai, Uganda

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Background: Adherence is a major predictor of antiretroviral therapy failure; however, viral load monitoring, which is the gold standard for monitoring the efficacy of HIV treatment and measuring validity of adherence reports, is often not feasible in resource limited settings. Simple adherence measures are available in the ART program in Rakai, Uganda, including measures based on pharmacy refill (PR), appointments and pill count. We examined whether these measures were associated with the occurrence of first virological failure (VF).

Methodology: We analyzed ART adherence and virological failure in 2710 patients aged 15 years or older who initiated ART from 2004 to 2012 in Rakai, Uganda. Adherence was measured using pill counts, pharmacy-refills and appointment attendance based on visits scheduled at two weeks during the first 3 months, then once per month for the first year, and once every two months after the first year. Viral load assays were done at six month intervals. We defined adherent patients as individuals who had at least 95% of pill count, appointment attendance or Pharmacy refills during the 6 months prior to viral load (VL) monitoring. The primary outcome was the occurrence of first VF using WHO’s 2013 criterion >=1000 copies/ml. Three types of adherence measures (AM) were considered, based on 1) Pill count: ((Dispensed-Returned pills)/ (Pills prescribed during the 6 months))*100%; 2) Appointments: ((total appointments attended with no delay)/ (total expected appointments over a 6 months interval))*100%; and 3) Pharmacy refill: ((Dispensed medication)/ (pills prescribed during the 6 months))*100%. Multivariate proportional hazards Cox model adjusted for age at VL visit, baseline regimen, WHO stage, CD4, Year of initiating ART and ART experience, was used to examine whether each AM was associated with time from ART initiation to first VF.

Results: The median follow-up time was 46.4 months; IQR 23.8-69.5 months. VF during follow-up was observed in 16% patients (n=426) and 6% (n=27) of these persons subsequently died. The hazard ratios (HR) adherent to non-adherent associated with VF were: pill count (HR: 0.50, 95%CI 0.38-0.67), appointment (0.46, 95%CI 0.37-0.58) and pharmacy-refill adherence (HR: 0.29, 95%CI 0.22-0.37). Younger age (15-29) was associated with a two-fold significant increase in VF. The CBV/EFV regimen combination and the later year of initiating ART were associated with a significant reduction in risk for VF.

Conclusions: All adherence measures were predictive of VF. Because monitoring appointments requires the least effort in clinical settings, it may be a preferred method of assessing adherence in resource-poor settings and early detection of VF.