Injectable contraception and HIV-1 acquisition in the VOICE study (MTN-003)

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Background

Several observational studies have reported an increased risk of HIV acquisition among women using injectable HC, particularly depot medroxyprogesterone acetate (DMPA), compared to women using non-hormonal methods

- Few studies have disaggregated specific injectable type
- Noradrenosterone enanthate (NET-EN) is a different type of injectable HC commonly used in South Africa

Examining the association of HC type with HIV acquisition within a single delivery method (injection) may reduce behavioral confounding (e.g., differential condom use) present when comparing HC users with non-users

Objective: To compare the impact of DMPA to NET-EN exposure on HIV-1 acquisition among women enrolled in South African sites in the VOICE Study

Methods

- The MTN-003 (VOICE) trial was a Phase 2B, multi-site, randomized, placebo-controlled trial conducted between 2009 – 2012 that assessed the safety and effectiveness of tenofovir-based oral and topical HIV-1 chemoprevention in women
- Participants using protocol-defined effective contraception (HC, intrauterine device or sterilization) were eligible for enrollment
- Contraceptive use, pregnancy status and HIV status were assessed monthly during 1 – 3 years of participant follow-up
- Condom use and other behaviors related to HIV risk were assessed by interview-administered questionnaire and audio computer assisted self-interview (ACASI)
- Midpoint between last negative and first confirmed positive test was used to calculate estimated time of HIV-1 seroconversion
- In a planned secondary analysis of all VOICE enrollees, we used a Cox proportional hazards model to compare directly the rates of HIV acquisition between women using DMPA and those using NET-EN at 11 South African VOICE sites
- We conducted additional comparisons stratifying by baseline (BL) herpes simplex virus type 2 (HSV-2) status

Results

- 3,163 women were enrolled at South African sites and met other pre-specified criteria for inclusion (Figure 1)
- Of injectable HC users included in the analysis, 2,055 (65.0%) used DMPA, 1,363 (43.1%) used NET-EN and 255 (8.1%) used both DMPA and NET-EN during follow-up
- Proportion of DM patients (27 – 73%) and HIV-1 incidence (1.7 – 8.9/100 person-years) varied by site
- Median (IQR) age at baseline for DMPA users was 24 (21 – 27) and for NET-EN users was 23 (20 – 26) years old

Table 1. Baseline characteristics of injectable HC users

Table 2. Results of Cox proportional hazards models

Conclusions

- This observational study is the first specifically designed to compare risk of HIV-1 acquisition between DMPA and NET-EN use.
- Lack of a non-HC comparator group prevented estimation of risk associated with either method compared to non-use.
- Among women willing to use effective contraception while participating in an HIV prevention trial, we observed an overall increased risk of HIV-1 acquisition among women currently using DMPA compared to those using NET-EN.
- This observed difference in HIV acquisition was modified when stratifying by baseline HSV-2 status. However, findings in observational analyses, especially those in select sub-groups, are subject to bias and should be interpreted with caution.

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Figure 1. Study population

Table 2. Results of Cox proportional hazards models