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Oral presentation

Tolerance and viral resistance after single-dose nevirapine (NVP) and short-course of tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) to prevent mother-to-child transmission (PMTCT) of HIV-1: the TEmAA ANRS 12109 phase II trial, step 1

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Background

Viral resistance occurs with high frequency after single-dose nevirapine (sdNVP) for PMTCT and alternative regimens are urgently needed [1]. The objective of this study was to evaluate the safety and resistance profile of a combination of TDF (300 mg) and FTC (200 mg) in HIV-1 infected pregnant women and their newborns.

Methods

The TEmAA ANRS 12109 trial is an open label phase II trial conducted in Ivory Coast, Cambodia and South Africa. SdNVP (200 mg) and 2 tablets of TDF/FTC were given to HIV-1-infected pregnant women at the beginning of labor. One daily tablet of TDF/FTC was given for 7 days postpartum. All women received zidovudine (ZDV, 300 mg BID) from the day of enrollment, between the 28th and 38th week of gestation, until the beginning of labor. All infants received sdNVP syrup on Day 2 (2 mg/kg) and ZDV syrup (4mg/kg BID) for 7 days. Mothers and infants were followed for two months. Serious adverse events (SAEs) and HIV-1 infection status of the infants at 3 days and 4 weeks of life were assessed using plasma RNA PCR. Maternal HIV-1 RNA plasma viral load (VL) was performed at enrolment, day 2 postpartum (PP) and at week 4 PP. Genotypic resistance tests were performed at week 4 PP.

Results

Thirty-eight HIV-1 infected pregnant women were enrolled (19 in Abidjan, 12 in Phnom Penh and 7 in Soweto): median age 27 years (interquartile range [IQR]: 23–30), median CD4 count 450 cells/mm3 (IQR: 314-596) and median HIV-1 RNA VL 4.08 log copies/mL (IQR: 3.60-5.03). All women received TDF/FTC at a median of 4.9 hours before delivery (IQR: 3.0-8.2). Nine (24%) transient grade 3/4 biological events occurred in mothers during postpartum follow-up (3 anaemia, 5 neutropenia and 1 elevation of liver enzymes). Among 39 livebirths (one pair of twins), 9 infants had clinical SAEs (23%) and 2, transient grade 3 anaemia (5%). Four children died (1 meningitis, 1 gastroenteritis with malnutrition, 1 intestinal occlusion and 1 unexplained neurological disease) while the other SAEs, with infectious origin (gastroenteritis, bronchopneumonia, meningitis, conjunctivitis and

neonatal sepsis), resolved. SAEs and deaths were unlikely to be related to TDF/FTC. Two infants out of 38 tested at 4 weeks of life had detectable RNA plasma viral load, also detectable at D3, suggesting *in utero* HIV infection (5.3%, 95% Confidence Interval [CI]: 0.6-17.8). Median maternal HIV VL was 3.3 log_{10}copies/ml at day 2 PP and 4.2 log_{10}copies/ml at week 4 PP. No viral resistance mutations to ZDV, NVP, FTC, and TDF were found in 19 mothers tested at week 4 PP. Remaining tests are ongoing.

Conclusion

A TDF/FTC combination for PMTCT was well tolerated in women and exposed newborns with no intrapartum HIV transmission reported. Providing 7 days of additional PP antiretroviral exposure with TDF/FTC immediately after sdNVP+TDF/FTC extended the suppression of viral replication avoiding a PP exposure to sdNVP. The second step of the trial will now look for the optimal neonatal dose of TDF and FTC to introduce in this PMTCT regimen.

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References

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