

# HIV Drug Resistance in Cases of Perinatal Transmission in IMPAACT 2010

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## **BACKGROUND**

- IMPAACT 2010/VESTED was a Phase III, three-arm, randomized, open-label trial in which 643 pregnant women living with HIV (**WLH**) initiated either DTG+FTC/TDF, DTG+FTC/TAF, or EFV/TDF/FTC between 14-28 weeks of gestation
- Mother-infant pairs were followed through 50 weeks postpartum; 90.3% breastfed
- 4/617 (0.6%) cases of vertical transmission (VT) detected<sup>1</sup>
- The purpose of this sub-study was to evaluate HIV drug resistance (**HIVDR**) and other parameters in cases of VT

#### **METHODS**

- HIVDR genotyping was performed on:
  - Infants' plasma or frozen whole blood from HIV-DNA positive specimens
  - Mothers' plasma from study enrollment and from time closest to suspected VT
- Single genome amplification (SGA) was used to generate 3 amplicons targeting:
   1) protease (PR) & reverse transcriptase (RT), 2) integrase (IN), and 3) 3'-polypurine tract (3'PPT)

Figure 1. HIVDR genotyping experimental design

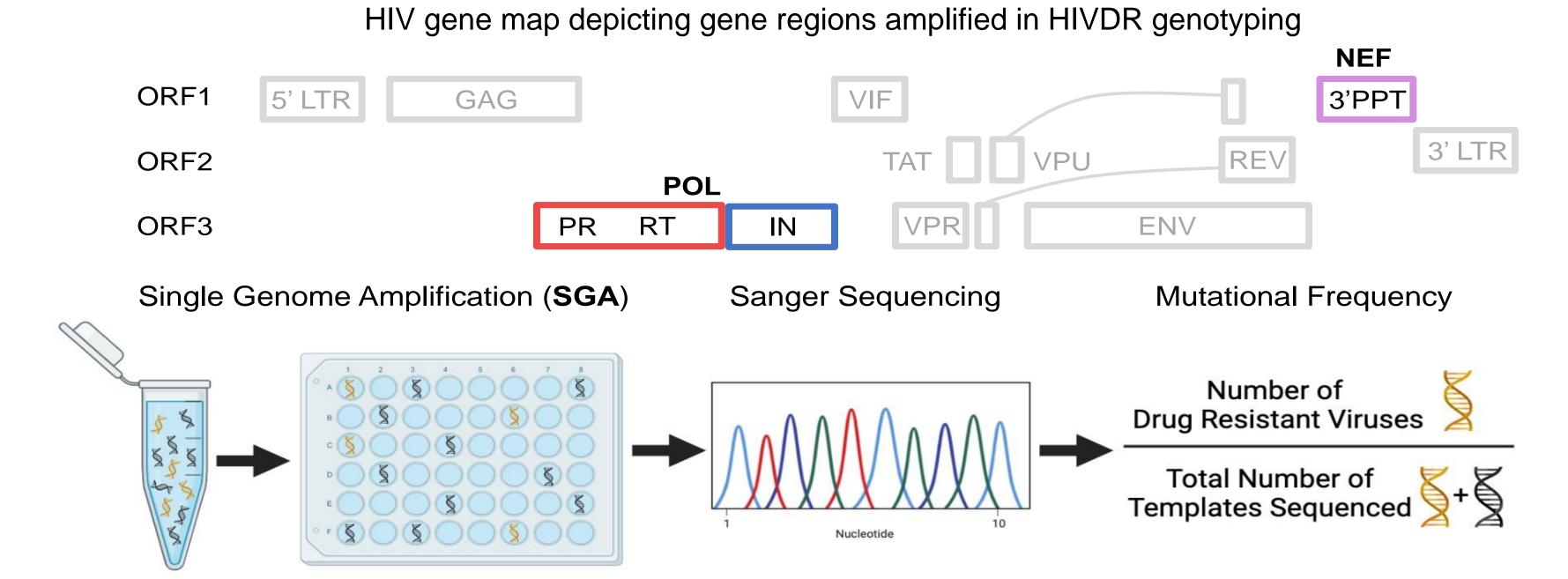


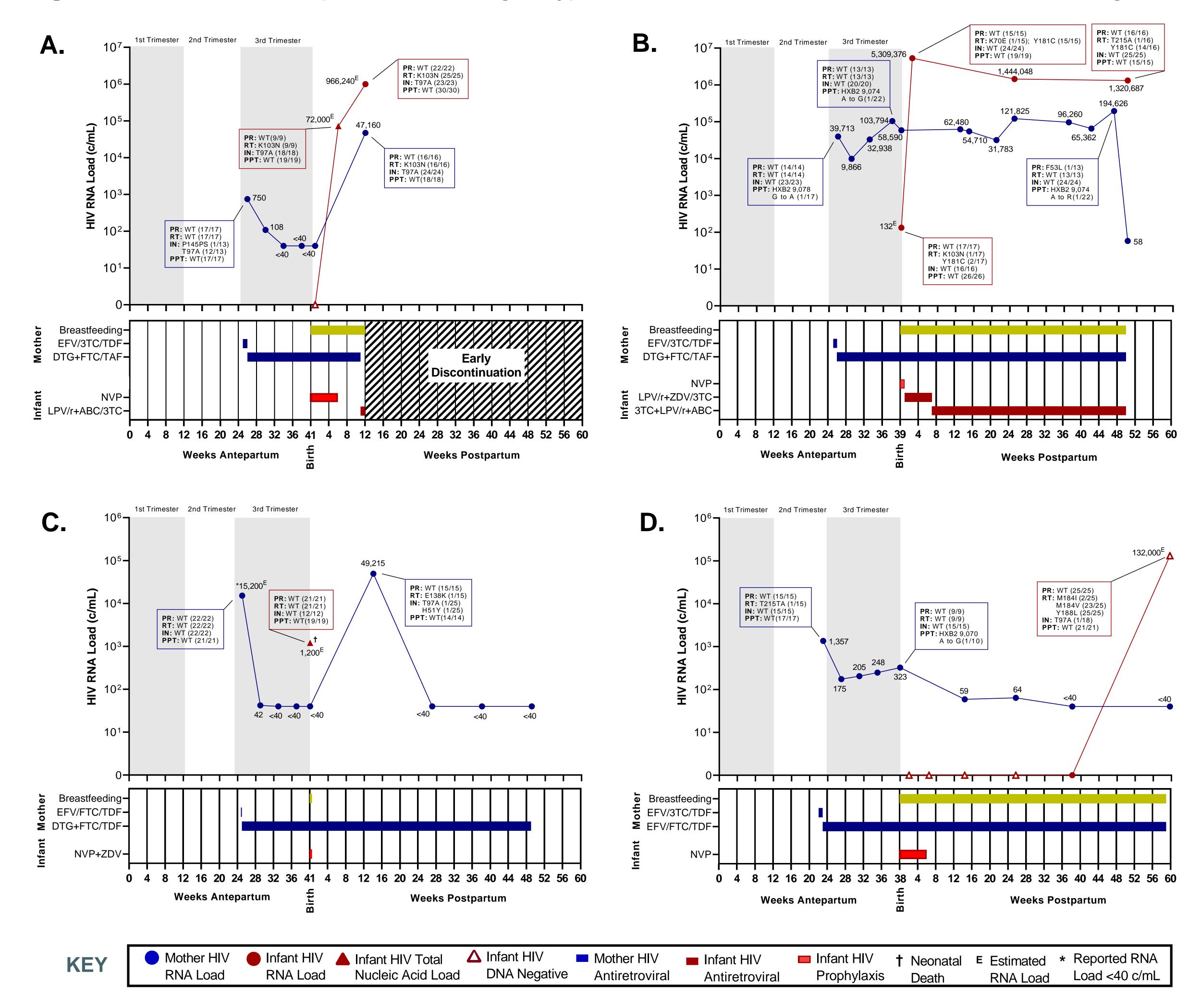
Table 1. Summary of clinical characteristics, HIVDR, and estimated time of transmission among mother-infant pairs in whom VT occurred

Characteristic	Pair A	Pair B	Pair C	Pair D
Country	Uganda	Zimbabwe	South Africa	Uganda
HIV-1 Subtype	Α	С	С	D
Maternal age at enrolment (years)	26	42	26	27
Gravidity	3	5	3	3
Maternal prophylaxis exposure during prior pregnancies*	None	None	None	None
ART taken in pregnancy prior to enrolment during screening (days)	7	5	1	6
Gestational age at initiation of ART (weeks)	26	26	25	23
Maternal CD4 at enrolment (cell/uL)	123	218	396	592
Biological sex of the infant	Male	Female	Male	Female
Birth weight (kg)	3.20	3.14	2.99	3.50
Estimated time of transmission	Early Breastfeeding	In Utero	In Utero	Late Breastfeeding
Age of infant at HIV DNA diagnosis	6.1 weeks	4 days	2 days	59.7 weeks
Major maternal HIVDR detected	K103N	None	None	None
Major infant HIVDR detected	K103N	K103N; Y181C	None	M184I/V; Y188L

<sup>\*</sup>Women were ART-naïve except for previous antiretroviral regimens taken for the prevention of perinatal transmission or pre-exposure (TDF or FTC/TDF)

#### RESULTS

Figure 2. Mothers' & infants' plasma HIV RNA, genotypic resistance, antiretroviral treatment, & breastfeeding duration



### **SUMMARY & CONCLUSIONS**

- In utero transmission likely occurred in 2/4 pairs and transmission during breastfeeding in 2/4 pairs, one early and one later possibly during weaning
- HIVDR potentially influenced transmission in 1/4 pairs (Figure 2, Panel A)
- Major NNRTI mutations were detected in 3/4 infants, 2/3 potentially selecting HIVDR due to infant NVP prophylaxis
  - Use of infant prophylaxis with a higher genetic barrier to resistance may further reduce the risk of VT and HIVDR

REFERENCE: 1. Lockman S, et al. Lancet Lond Engl. 2021 Apr 3;397(10281):1276–92.

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