

# Breast Milk Transfer and Infant Exposures to DTG, TAF, and TFV: Results From IMPAACT 2010/VESTED

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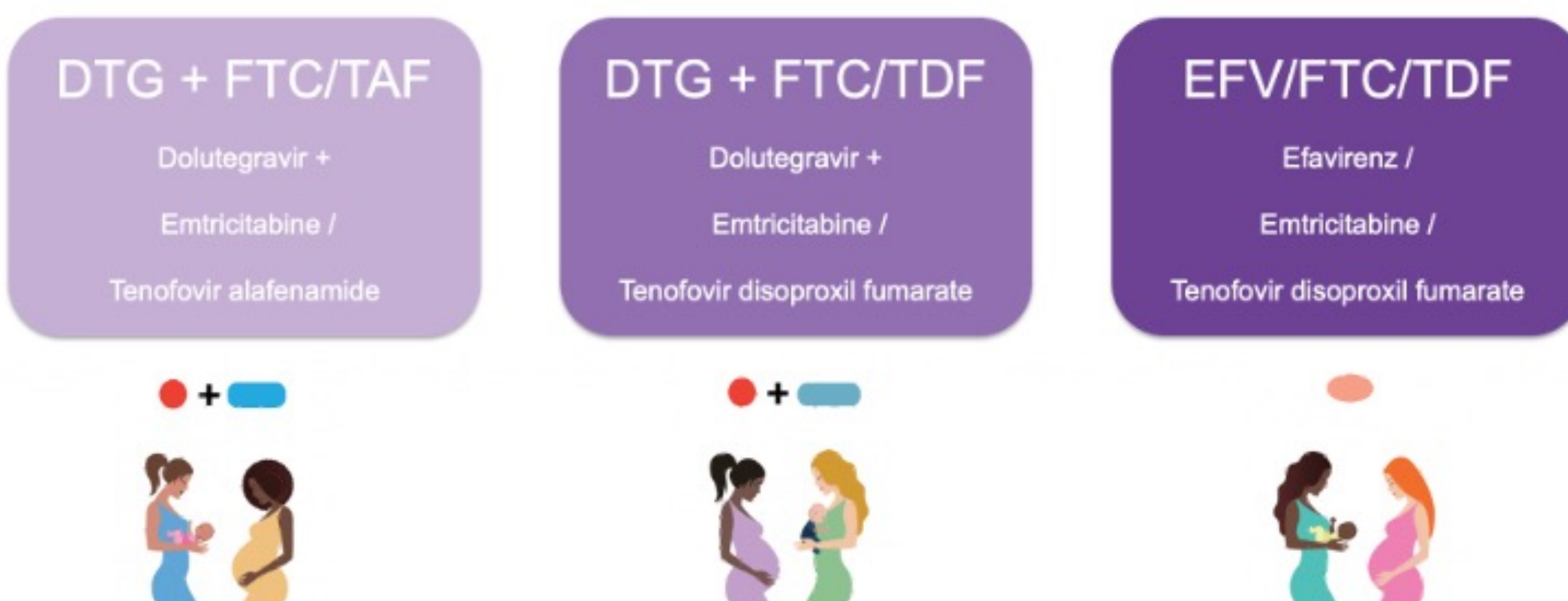
Breast milk transfer of DTG, TAF, and TFV is low but should be considered in the context of risk of drug resistance in infants who acquire HIV.

## BACKGROUND

- Limited information is available on breast milk transfer and subsequent infant systemic exposure to dolutegravir (DTG), tenofovir alafenamide (TAF), and tenofovir (TFV).
- This analysis evaluated concentrations of DTG, TAF, and TFV in time-matched samples (maternal plasma, breast milk, and infant plasma) from IMPAACT 2010, a randomized trial that assessed three antiretroviral treatment (ART) regimens in pregnancy.

## METHODS

- Pregnant women with HIV in 9 countries were randomized 1:1:1 to start one of three open-label ART regimens at 14-28 weeks of gestation.



- Infants received non-study antiretroviral prophylaxis consistent with local standards of care.
- Matched maternal (plasma and breast milk) and infant (plasma) samples were prospectively collected at random at Week 6 postpartum.
- DTG was measured in samples from the DTG +FTC/TAF and DTG+FTC/TDF arms; TAF was measured in samples from the DTG+FTC/TAF arm; TFV was measured in samples from the DTG+FTC/TDF arm.
- Validated liquid chromatography-tandem mass spectrometry (LC-MS/MS) assays were used to quantitate plasma and whole breast milk concentrations of DTG, TAF, and TFV.
- Samples below the quantitation limit (BQL) were imputed to 0.
- The relative infant dose for DTG, TAF, and TFV was estimated by using a standard target feeding milk volume of 150 mL/kg/day and observed whole breast milk concentrations.

## RESULTS

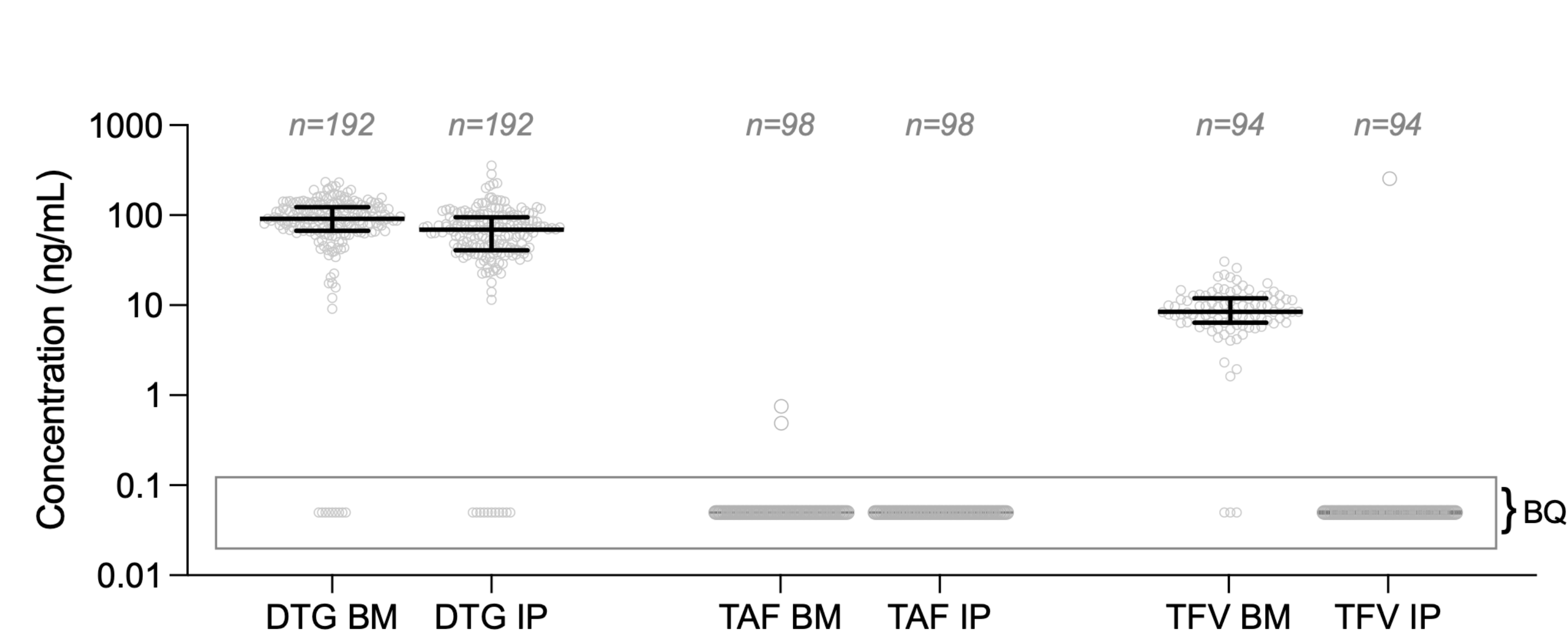
Data were available from 192 postpartum lactating women and their 192 breastfed infants.

- The mean age of mothers at enrollment was 26 years, and most of the participants lived in Zimbabwe, Uganda, or Tanzania (**Table 1**).
- About 55% of infants were female at birth with a mean gestational age of 40 weeks (**Table 1**).
- Median (interquartile range; IQR) DTG concentrations in breast milk and infant plasma samples were 91 ng/mL (67-123) and 69 ng/mL (41-95), respectively (**Figure 1**).
- TAF was BQL in nearly all breast milk and infant plasma samples (**Figure 1**).
- Median (IQR) TFV concentrations in breast milk were 8 ng/mL (6-12); nearly all infant plasma were BQL for TFV (**Figure 1**).

**Table 1: Maternal and Infant Characteristics**

		Median (SD) or N (%)
Maternal	Age (years)	26 (6)
	Race	
	Asian	2 (1%)
	Black	190 (99%)
	Ethnicity	
	Hispanic	-
	Not Hispanic	189 (98%)
	Unknown	3 (2%)
	Country	
	Botswana	9 (5%)
Infant at birth	Age (gestational weeks)	40 (2)
	Female Sex	106 (55%)
	Weight (g)	3089 (490)
	Length (cm)	50 (3)

**Figure 1: DTG, TAF, and TFV Concentrations in Breast Milk (BM) and Infant Plasma (IP)**



- Data represented as median and IQR.
- The lower limit of quantitation (LLOQ) for DTG, TAF, and TFV in breast milk and plasma was 7.8, 0.195, and 0.0977 ng/mL and 9.8, 3.9, and 0.977 ng/mL, respectively.
- Samples below the quantitation limit (BQL) are shown in the box.
- In breast milk, 9, 96, and 3 samples were BQL for DTG, TAF, and TFV, respectively.
- In infant plasma, 11, 98, and 93, samples were BQL for DTG, TAF, and TFV, respectively.

## RESULTS cont.

- Median (range) maternal plasma concentrations of DTG, TAF, and TFV were 2810 (0.0-7460), 0.0 (0.0-158), and 96.1 (0.0-353) ng/mL, respectively (**Table 2**).
- The estimated median relative infant dose from breastfeeding for DTG was 1.92%; the estimated relative infant dose for TAF and TFV was nearly zero (**Table 2**).

**Table 2: DTG, TAF, and TFV Concentrations in Maternal Plasma and Relative Infant Dose**

	DTG	TAF	TFV
Maternal plasma concentrations (ng/mL)	2810 (0.0 – 7460)	0.0 (0.0 – 158)	96.1 (0.0 – 353)
Relative infant dose from breastfeeding	1.92% (0.00 – 4.89)	0.00% (0.00 – 0.03)	0.03% (0.00 – 0.11)

## CONCLUSIONS

- TAF and TFV plasma concentrations in breastfeeding infants were below the quantitation limit in nearly all samples.
- For DTG, median breast milk and infant plasma concentrations were 91 ng/mL and 69 ng/mL, respectively, and the median relative infant dose from breastfeeding was 1.92%.
- The clinical relevance of low breast milk transfer of DTG, TAF, and TFV is unknown but should be considered in the context of risk of drug resistance in infants who acquire HIV.

## ACKNOWLEDGEMENTS

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