

Violet Korutaro¹, Lauren Ziemba², Sean Brummel², Anne Coletti³, Katie McCarthy³, Patrick Jean-Philippe⁴, Benjamin Johnson⁵, Lynda Stranix Chibanda^{6,12}, Lee Fairlie⁷, Roger Shapiro^{8,13}, Deo Wabwire⁹, Patricia Nahirya Ntege¹, Lameck Chinula¹⁰, Shahin Lockman^{8,11,13}, on behalf of the IMPAACT 2010/VESTED team

¹Baylor College of Medicine Children's Foundation Uganda, Kampala, Uganda; ²Center for Biostatistics in AIDS Research, Harvard TH Chan School of Public Health, Boston, MA, USA; ³FHI 360, Durham, NC, USA; ⁴National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, USA; ⁵Frontier Science & Technology Research Foundation, Inc., Amherst, NY, USA; ⁶Child and Adolescent Health Unit, University of Zimbabwe Faculty of Medicine and Health Sciences, Harare, Zimbabwe; ⁷Wits RHI, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; ⁸Department of Immunology and Infectious Diseases, Harvard T.H. Chan School of Public Health, Boston, Massachusetts, USA; ⁹MU-JHU Research Collaboration, Kampala, Uganda; ¹⁰University of North Carolina Project-Malawi, Lilongwe, Malawi; ¹¹Division of Infectious Disease, Brigham and Women's Hospital, Boston, Massachusetts, USA; ¹²University of Zimbabwe Clinical Trials Research Centre, Harare, Zimbabwe; ¹³Botswana Harvard Health Partnership, Gaborone, Botswana

BACKGROUND

- The IMPAACT 2010 (VESTED) randomized trial compared efficacy/safety of dolutegravir (DTG)+ emtricitabine/tenofovir alafenamide fumarate(FTC/TAF); DTG+FTC/tenofovir disoproxil fumarate (TDF) and efavirenz (EFV)/FTC/TDF started in pregnancy.
- 643 ART-naïve pregnant women with HIV in 9 countries (predominantly in Africa) were randomized at 14-28 weeks of gestation.
- Previous analyses showed superior virologic efficacy and pregnancy outcomes with DTG-based compared with EFV-based ART. The fewest adverse pregnancy outcomes were observed in the DTG+FTC/TAF arm.
- We conducted an exploratory analysis of infant mortality approximately one year after birth and associated maternal and infant factors.

METHODS

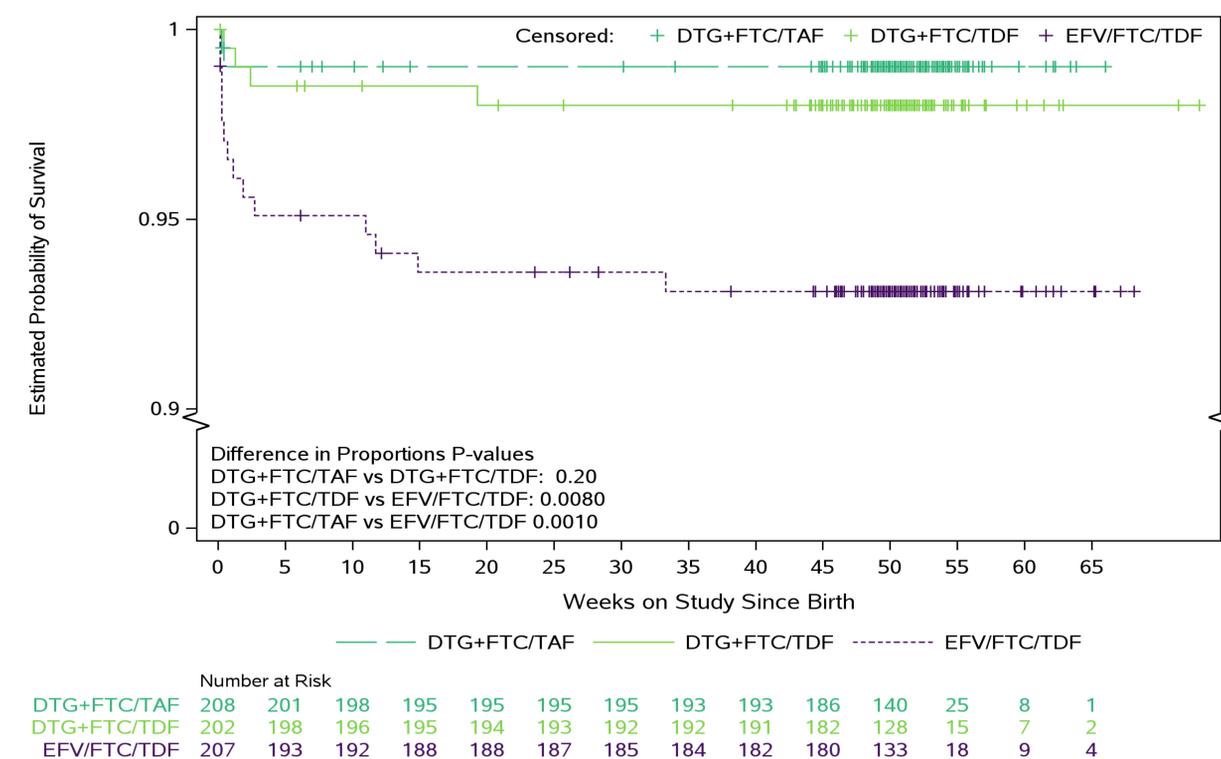
- We estimated the probability of death through 50 weeks after birth among liveborn infants, overall and by randomized maternal ART regimen (Kaplan–Meier).
- We examined potential risk factors for infant death in univariable log-binomial models:
 - Maternal factors: baseline (at study entry) age, gestational age, CD4 count, HIV-1 viral load, RBC folate and HbA1c; antepartum weight gain, HIV-1 viral load at delivery; RBC folate and HbA1c at delivery
 - Infant factors: preterm birth [PTB], low birth weight [LBW], small-for-gestational-age [SGA], major congenital anomaly, HIV infection.

RESULTS

- Among 640 deliveries, 23 (3.6%) were stillborn and excluded from this analysis (4 [2%] EFV/FTC/TDF, 8 [4%] DTG+FTC/TAF, 11 [5%] DTG+FTC/TDF); rates of PTB and SGA were lowest in the DTG+FTC/TAF arm (both as previously published).
- Twenty (3.3%) of the 617 liveborn infants died by 50 weeks, with 15 (75%) deaths occurring within the first 28 days.
- Infant mortality was higher with maternal EFV/FTC/TDF (6.9%) compared with DTG+FTC/TAF (1.0%; difference 5.9%, 95%CI 2.2%, 9.7%) and DTG+FTC/TDF (2.0%; difference 4.9%, 95%CI 0.9%, 8.9%) [Figure 1].
- 13 (65%) of 20 infants who died were born either preterm or SGA

Infant mortality was 3.3%, with most (75%) deaths in the neonatal period. Lower maternal CD4, high delivery VL, later ART start, and maternal EFV/FTC/TDF in pregnancy were key predictors of infant mortality, as were infant PTB and LBW. Findings underscore the need for optimized antenatal, ART, and neonatal care.

FIGURE 1. Time to Infant Death among Liveborn Infants by Randomized ART Regimen



RESULTS (cont.)

Risk factors for infant mortality		
	Factors	Risk Ratio,95% CI
Maternal	Lower enrollment CD4 (<500 vs. ≥500 cells/uL)	RR 2.4, 95% CI [0.86, 6.35]
	Higher viral load at delivery (>1,000 vs. <50 cp/mL)	RR 4.5, 95% CI [1.2, 17.5]
	Initiated ART at 24-28 weeks of gestation vs 14-18 weeks	RR 2.4, 95% CI [0.99, 5.9]
Infant	Preterm birth	RR 6.6, 95% CI [2.8, 15.4]
	Low birth weight	RR 6.8, 95%CI [2.7, 17.2]
	Small for gestational age	RR 2.8, 95% CI [1.1, 7.3]
	Major congenital anomaly†	RR 8.1, 95%CI [1.4, 46.6]
	Infant HIV infection	RR 8.1, 95% CI [1.4, 46.6]

- † 1 baby with anomaly (duodenal atresia) died, and 3 other babies with anomalies survived.
- There were no apparent associations between infant mortality and maternal viral load at enrollment, maternal age, RBC folate, HbA1c, or antepartum weight change.

CONCLUSIONS

- Risk factors of infant mortality included lower maternal CD4, higher delivery viral load, later ART start, and use of EFV/FTC/TDF versus both DTG regimens in pregnancy, in addition to known risk factors of PTB, LBW, SGA, congenital anomaly, and infant HIV infection.
- Findings highlight the importance of optimized maternal ART regimens, viral suppression, and preserved CD4 cell count in pregnancy, and targeted neonatal care to reduce infant mortality.

ACKNOWLEDGEMENTS

The IMPAACT 2010/VESTED Protocol Team gratefully acknowledges the dedication and commitment of the 643 mother-infant pairs, their communities, and CAB representatives, without whom this study would not have been possible.

The authors also wish to acknowledge the IMPAACT 2010 /VESTED Protocol team, NIAID, NICHD, and NIMH, and the 22 IMPAACT sites and staff. The study products were provided by ViiV Healthcare Ltd, Gilead Sciences, and Mylan.

PLAIN LANGUAGE SUMMARY

Most infant deaths occurred in the first month of life. In addition to preterm birth and LBW, maternal ART regimen and high viral load had substantial associations with infant mortality, highlighting the need for good maternal and newborn care