Pregnancy Hemoglobin A1c and glucose with DTG vs EFV, TDF vs TAF: IMPAACT 2010

Lameck Chinula[1], Evan Goldberg[2], Lauren Ziemba[2], Katie McCarthy[3], Chelsea Krotje[4], Kevin Knowles[4], Jyoti Mathad[5], Maria Leticia Santos Cruz[6], Risa Hoffman[7], Patrick Jean-Philippe[8], Tsungai Chipato[9], Deo Wabwire[10], Judith Currier[7], Shahin Lockman[11,12], Nahida Chakhtoura[13] for the IMPAACT 2010/VESTED Study Team and Investigators

[1]Division of Global Women's Health, Department of Obstetrics and Gynecology, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; UNC Project Malawi, Lilongwe, Malawi; [2]Center for Biostatistics in AIDS Research, Harvard TH Chan School of Public Health, Boston, MA, USA; [3]FHI 360, Durham, NC, USA; [4]Frontier Science Foundation, Amherst, NY, USA; [5]Department of Medicine, Weill Cornell Medical College, New York, NY, USA; [6]Hospital Federal dos Servidores do Estado, Rio de Janeiro, Brazil; [7]David Geffen School of Medicine, Division of Infectious Diseases, University of California, Los Angeles, CA, USA; [8]National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD, USA; [9]College of Health Sciences, University of Zimbabwe, Harare, Zimbabwe; [10]Makerere University - Johns Hopkins University Research Collaboration, Kampala, Uganda; [11]Division of Infectious Disease, Brigham and Women's Hospital, Boston, MA, USA; Department of Immunology and Infectious Diseases, Harvard TH Chan School of Public Health, Boston, MA, USA; [12]Botswana Harvard AIDS Institute Partnership, Gaborone, Botswana; [13]Eunice Kennedy Shriver National Institute of Child Health & Human Development, Bethesda, MD, USA.

BACKGROUND

In IMPAACT 2010, a trial comparing 3 antiretroviral treatment (ART) regimens initiated in pregnancy, found:

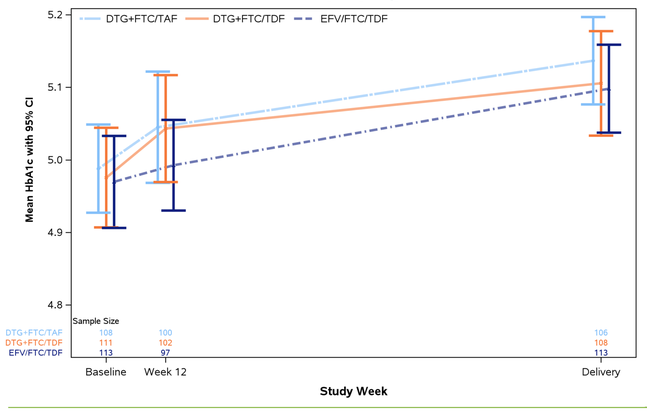
- Dolutegravir (DTG), particularly in combination with emtricitabine (FTC) and tenofovir alafenamide (TAF), was associated with more pregnancy weight gain, though lower than the Institute of Medicine's recommended weekly weight gain in 2nd and 3rd trimester
- DTG+FTC/TAF had better pregnancy outcomes than ART containing FTC with efavirenz (EFV) or tenofovir disoproxil fumarate (TDF)

The impact of these weight gain patterns during pregnancy on gestational diabetes is unknown. We evaluated glycated hemoglobin (HbA1c) and glucose levels and their association with maternal ART regimen in a subset of IMPAACT 2010 participants.

METHODS

- 643 pregnant women with HIV in 9 countries were randomized 1:1:1 to start open-label DTG+FTC/TAF, DTG+FTC/TDF, or EFV/FTC/TDF at 14-28 weeks' gestation
- Following protocol amendment, in a subset of participants, we sampled maternal HbA1c and random glucose at study entry, 12 weeks on study (antepartum) and delivery; and neonatal glucose within 48 hours of birth
- We assessed by-arm differences in mean levels and time-averaged area under the curve (AUC) of HbA1c and glucose in women (and glucose in infants) using student's t-tests
- We assessed by-arm differences in the proportions of women with post-baseline HbA1c ≥5.7% (marker of pre-diabetes) or ≥6.5% (marker of diabetes) using Wald Tests

FIGURE 1. Mean HbA1C (%) by randomized arm



We observed **no significant differences in maternal HbA1C** and no clinically meaningful differences in maternal or infant random glucose in women starting DTG+FTC/TAF, DTG+FTC/TDF, vs EFV/FTC/TDF in pregnancy or their newborns, despite differences in pregnancy weight gain among the regimens

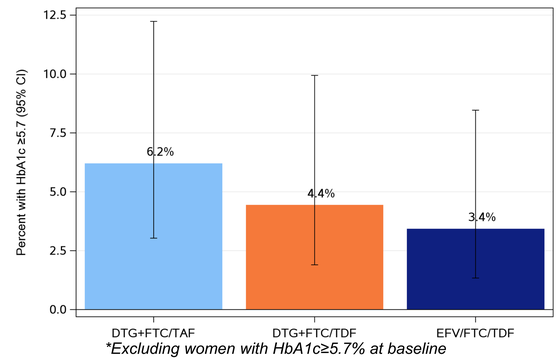
RESULTS

- 348 mothers and 65 infants included in this analysis: DTG+FTC/TAF (114), DTG+FTC/TDF (116), EFV/FTC/TDF (118) arms
- Maternal enrolment medians were: age 25.9 years, gestational age 21.5 weeks, BMI 24.1 kg/cm², HIV-1 RNA 3.1 log10, and CD4 466 cells/mm³
- Maternal mean HbA1c levels and mean time-averaged HbA1c AUC did not differ significantly between arms (Table 1, Figure 1)
- 7.0% of women in the DTG+FTC/TAF arm, 6.0% in the DTG+FTC/TDF arm, and 3.4% in the EFV/FTC/TDF arm had at least one post-baseline HbA1c ≥5.7% (p≥0.21 for between-arm comparisons) (Table 1). A similar pattern was observed across the randomized arms when women with HbA1c ≥5.7% at baseline were excluded (Figure 2)
- No women had a diabetes diagnosis at entry; one woman in the DTG+FTC/TAF arm developed HbA1c ≥6.5% after enrollment
- The DTG+FTC/TDF arm had slightly higher mean time-averaged AUC glucose (4.80 mmoL/L) than the EFV/FTC/TDF arm (4.63 mmoL/L, mean difference [95% CI]: 0.17 [0.00, 0.34] mmol/L) (Table 1)
- Infant glucose levels ≤48 hours of birth were similar by arm (Table 1)

TABLE 1. Maternal antepartum HbA1c and maternal and infant random glucose by randomized arm

	DTG+FTC/TAF	DTG+FTC/TDF	EFV+FTC/TDF	Treatment Arm Comparison	Difference in Means or Percentages (95% CI)	P-value
Mean (standard deviation) HbA1c at delivery (%)	5.14 (0.31)	5.11 (0.38)		DTG+FTC/TAF vs DTG+FTC/TDF	0.03 (-0.06, 0.12)	0.51
		5.11 (0.38)	5.10 (0.32)	DTG+FTC/TDF vs EFV/FTC/TDF	0.01 (-0.09. 0.10)	0.88
	5.14 (0.31)		5.10 (0.32)	DTG+FTC/TAF vs EFV/FTC/TDF	0.04 (-0.05, 0.12)	0.37
% (n/N) of women with HbA1c ≥ 5.7% at either antepartum week 12 or delivery	7.0% (8/114)	6.0% (7/116)		DTG+FTC/TAF vs DTG+FTC/TDF	-1.0% (-7.9%, 5.8%)	0.76
		6.0% (7/116)	3.4% (4/118)	DTG+FTC/TDF vs EFV/FTC/TDF	-2.6% (-8.9%, 3.2%)	0.34
	7.0% (8/114)		3.4% (4/118)	DTG+FTC/TAF vs EFV/FTC/TDF	-3.6% (-10.2%, 2.4%)	0.21
Mean (sd) time-averaged maternal glucose AUC (mmol/L)	4.66 (0.72)	4.80 (0.66)		DTG+FTC/TAF vs DTG+FTC/TDF	-0.14 (-0.32, 0.04)	0.13
		4.80 (0.66)	4.63 (0.64)	DTG+FTC/TDF vs EFV/FTC/TDF	0.17 (0.00, 0.34)	0.045
	4.66 (0.72)		4.63 (0.64)	DTG+FTC/TAF vs EFV/FTC/TDF	0.03 (-0.15, 0.21)	0.72
Mean (sd) infant glucose within 48 hours of birth (mmol/L)	3.43 (1.09)	3.40 (1.06)		DTG+FTC/TAF vs DTG+FTC/TDF	0.03 (-0.63, 0.69)	0.93
		3.40 (1.06)	3.49 (1.03)	DTG+FTC/TDF vs EFV/FTC/TDF	-0.09 (-0.72, 0.53)	0.77
	3.43 (1.09)		3.49 (1.03)	DTG+FTC/TAF vs EFV/FTC/TDF	-0.06 (-0.74, 0.62)	0.86

FIGURE 2. HbA1c≥5.7% at Antepartum Week 12 or at Delivery by randomized arm



*Excluding women with HbA1c≥5.7% at baseline

LIMITATIONS

- Modest sample size
- Glucose was not measured after fasting state

CONCLUSIONS

In this randomized trial comparing DTG+FTC/TAF, DTG+FTC/TDF, and EFV/FTC/TDF started in pregnancy, we observed:

- No significant differences in maternal antepartum/ delivery HbA1C by ART regimen
- No clinically meaningful differences in maternal or infant random glucose

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