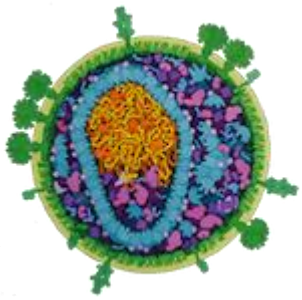

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SAFETY AND EFFICACY OF DTG VS EFV AND TDF VS TAF IN PREGNANCY: IMPAACT 2010 TRIAL

Author(s):

Lameck Chinula[1], Sean S. Brummel[2], Lauren Ziemba[2], Lynda Stranix-Chibanda[3], Anne Coletti[4], Chelsea Krotje[5], Patrick Jean-Philippe[6], Lee Fairlie[7], Tichaona Vhembo[3]

[1]University of North Carolina Project–Malawi, Lilongwe, Malawi,[2]Harvard T.H. Chan School of Public Health, Boston, MA, USA,[3]University of Zimbabwe, Harare, Zimbabwe,[4]FHI 360, Durham, NC, USA,[5]Frontier Science & Technology Research Foundation, Inc, Amherst, NY, USA,[6]DAIDS, NIAID, Rockville, MD, USA,[7]Wits Reproductive Health and HIV Institute, Johannesburg, South Africa,[8]Makerere University–Johns Hopkins University Research Collaboration, Kampala, Uganda,[9]University of California Los Angeles, Los Angeles, CA, USA,[10]Brigham and Women's Hospital, Boston, MA, USA,[11]University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Abstract Body:

We compared the safety and virologic efficacy of dolutegravir (DTG) + emtricitabine (FTC)/tenofovir alafenamide fumarate (TAF) vs. DTG + FTC/tenofovir disoproxil fumarate (TDF) vs. efavirenz (EFV)/FTC/TDF in pregnant women.

Pregnant women with HIV-1 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 gestational age (GA). Up to 14 days' pre-entry antiretroviral treatment (ART) was permitted. In primary efficacy analysis, we compared the combined DTG-containing arms to the EFV arm for non-inferiority (-10% margin), then superiority, with regard to delivery HIV RNA<200 cp/mL. Safety outcomes compared between all arms were a) composite adverse pregnancy outcome (preterm delivery [PTD]<37 weeks, small for GA [SGA]<10th centile, stillbirth [SB] or spontaneous abortion [SAB]); b) maternal grade≥3 adverse event (AE) through 14 days postpartum; and c) infant grade≥3 AE through 28 days. Neonatal death (NND, ≤28 days) was also evaluated.

We randomized 643 women: 217 to DTG+FTC/TAF, 215 to DTG+FTC/TDF, and 211 to EFV/FTC/TDF. Baseline medians were: GA 21.9 weeks, HIV RNA 903 cp/mL, CD4 count 466 cells/uL; 83% took ART prior to entry (median 6 days). Median antepartum follow-up was 17.4 weeks. Delivery HIV RNA, available for 605 (94.1%) women, was <200 cp/mL in 395 of 405 (97.5%) in the combined DTG arms vs 182 of 200 (91.0%) in the EFV/FTC/TDF arm (difference 6.5% [95%CI 2.0%, 10.7%]; p=0.005). Pregnancy outcomes were available for 640 (99.5%). Fewer women in the DTG+FTC/TAF arm (24.1%) had an adverse pregnancy outcome than in DTG+FTC/TDF (32.9%, p=0.043) or EFV/FTC/TDF (32.7%, p=0.047) arms. Although SB was more frequent with DTG+FTC/TAF (3.7%) and DTG+FTC/TDF (5.2%) than EFV/FTC/TDF (1.9%) (all by-arm p-values 0.05; post-hoc), NND was more frequent with EFV+FTC/TDF (4.8%) than DTG+FTC/TAF (1.0%, p=0.019) or DTG+FTC/TDF (1.5%, p=0.053). Combined SB or NND rates were similar by arm (post-hoc analysis). At least one grade>3 AE occurred in 148 (23.0%) women and 105 (17.0%) infants (all by-arm p-values 0.05). Two babies were diagnosed with HIV at <14 days, one each in DTG+FTC/TAF and DTG+FTC/TDF arms (maternal delivery HIV-1 RNA 58,590 and <40 cp/mL, respectively).