

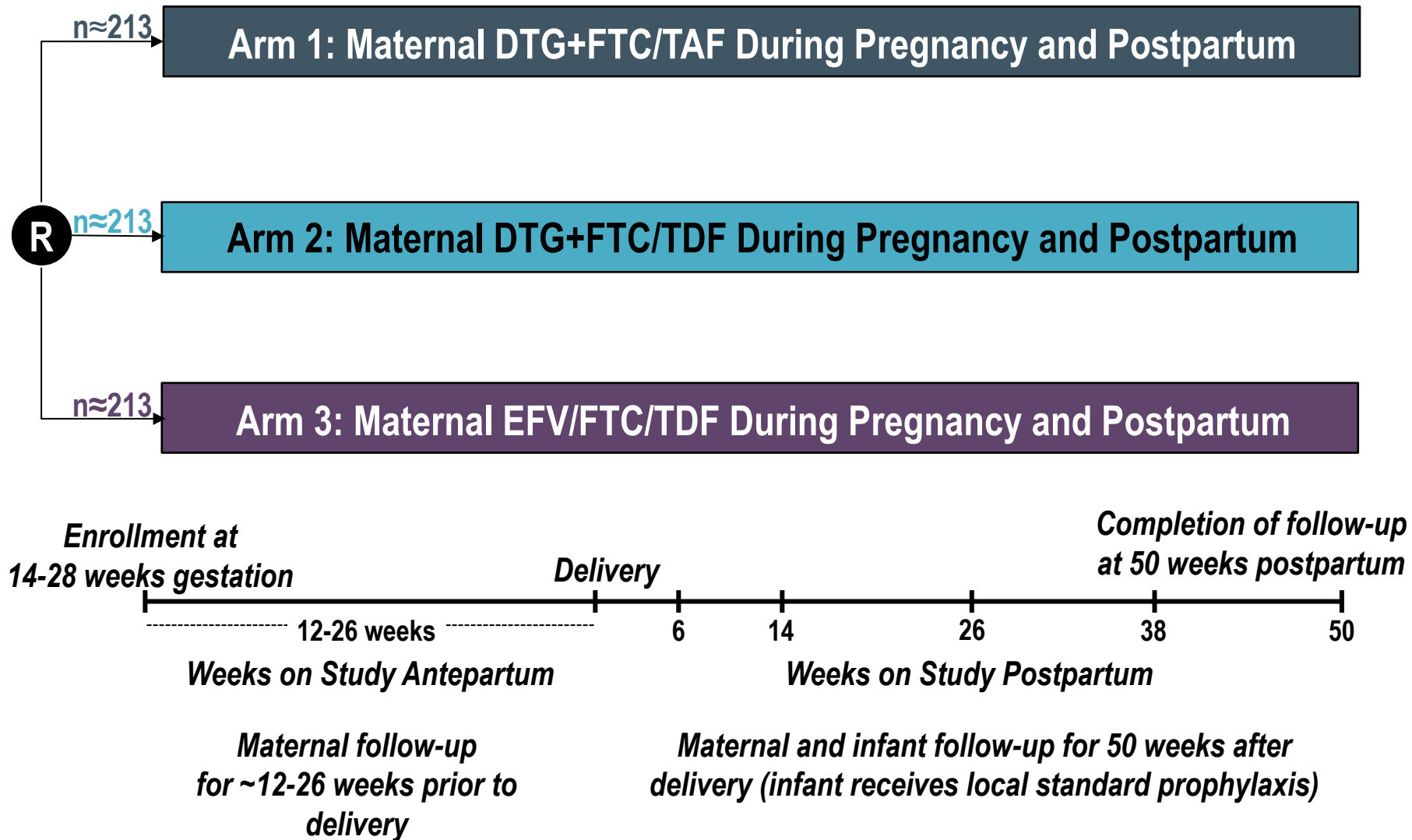
# Safety/Efficacy of DTG vs EFV, TDF vs TAF in Pregnancy/Postpartum: IMPAACT 2010

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# Background and Rationale

- ▶ We conducted a Phase III, 3-arm, randomized, open-label trial to compare the safety and virologic efficacy of three regimens started during pregnancy by women living with HIV
  - Dolutegravir + Emtricitabine/Tenofovir Alafenamide (DTG+FTC/TAF)
  - Dolutegravir + Emtricitabine/Tenofovir Disoproxil Fumarate (DTG+FTC/TDF)
  - Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate (EFV/FTC/TDF)
- ▶ We previously reported the virologic efficacy of combined DTG-containing triple therapy arms vs. EFV arm and pairwise comparison of safety outcomes of the 3 study arms through delivery outcome
  - DTG three-drug ART regimens had superior virologic efficacy to EFV/FTC/TDF; DTG+FTC/TAF had lowest rate of adverse pregnancy outcomes
- ▶ We now present virologic efficacy and safety data from enrollment through 50 weeks postpartum

# IMPAACT 2010 Study Design



- ### Key Eligibility Criteria
- Pregnant WLHIV 14-28 weeks gestation
  - ART-naïve (up to 14 days ART in current pregnancy allowed)

Participants were enrolled at 22 sites in 9 countries

# Objectives: Safety Outcomes

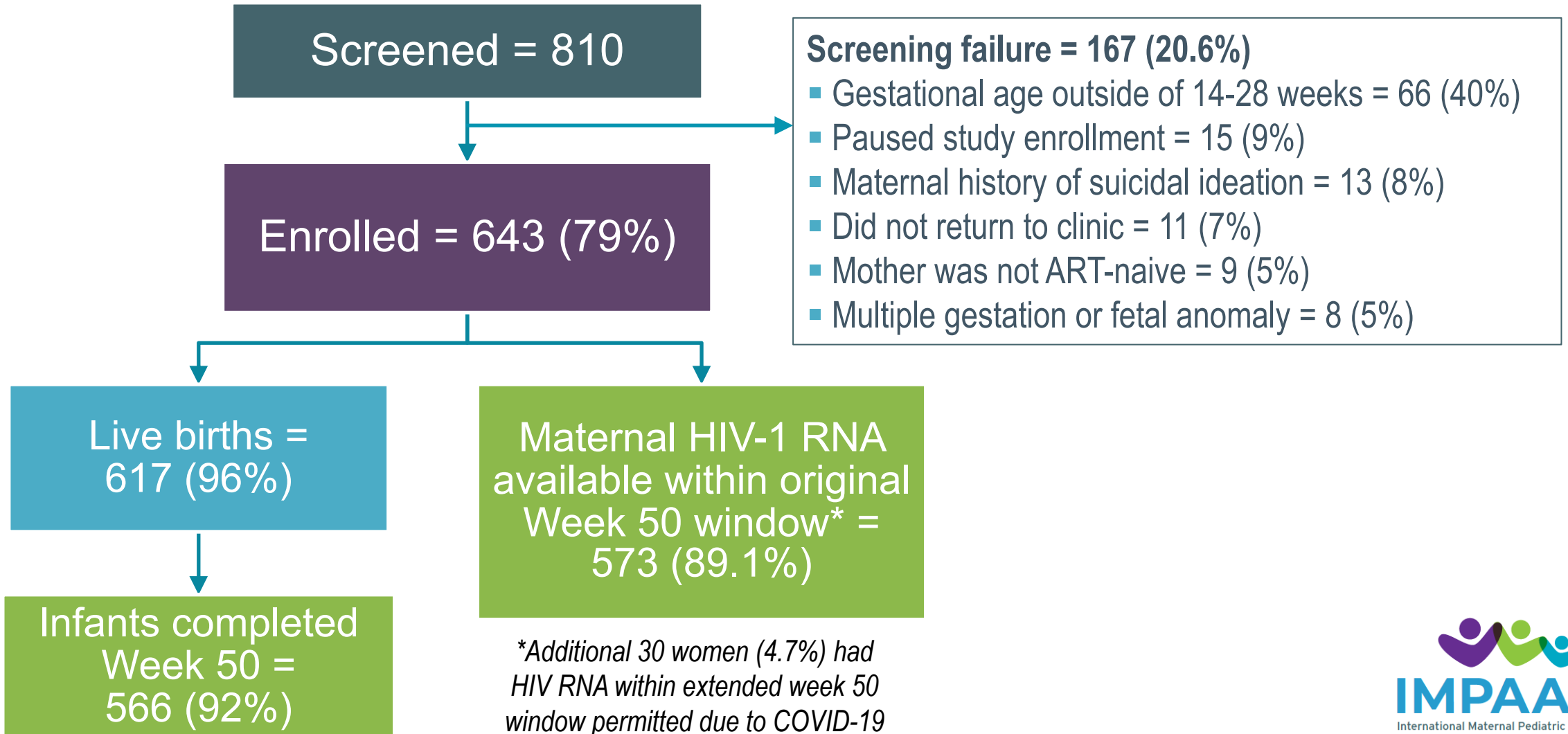
Whether rates of the following outcomes differ for any pairwise between-arm regimen comparison:

- ▶ **Maternal grade 3 or higher adverse events** through 50 weeks postpartum
- ▶ **Infant grade 3 or higher adverse events** through 50 weeks after birth
- ▶ **Infant mortality** through 50 weeks after birth
- ▶ **Infant HIV infection** through 50 weeks after birth

# Objectives: Virologic Efficacy

Whether proportions of mothers with HIV-1 RNA  $<200$  copies/mL at 50 weeks postpartum differ when comparing a **DTG-containing 3-drug regimen (DTG arms combined)** initiated during pregnancy to **EFV/FTC/TDF**

# Enrollment and Retention

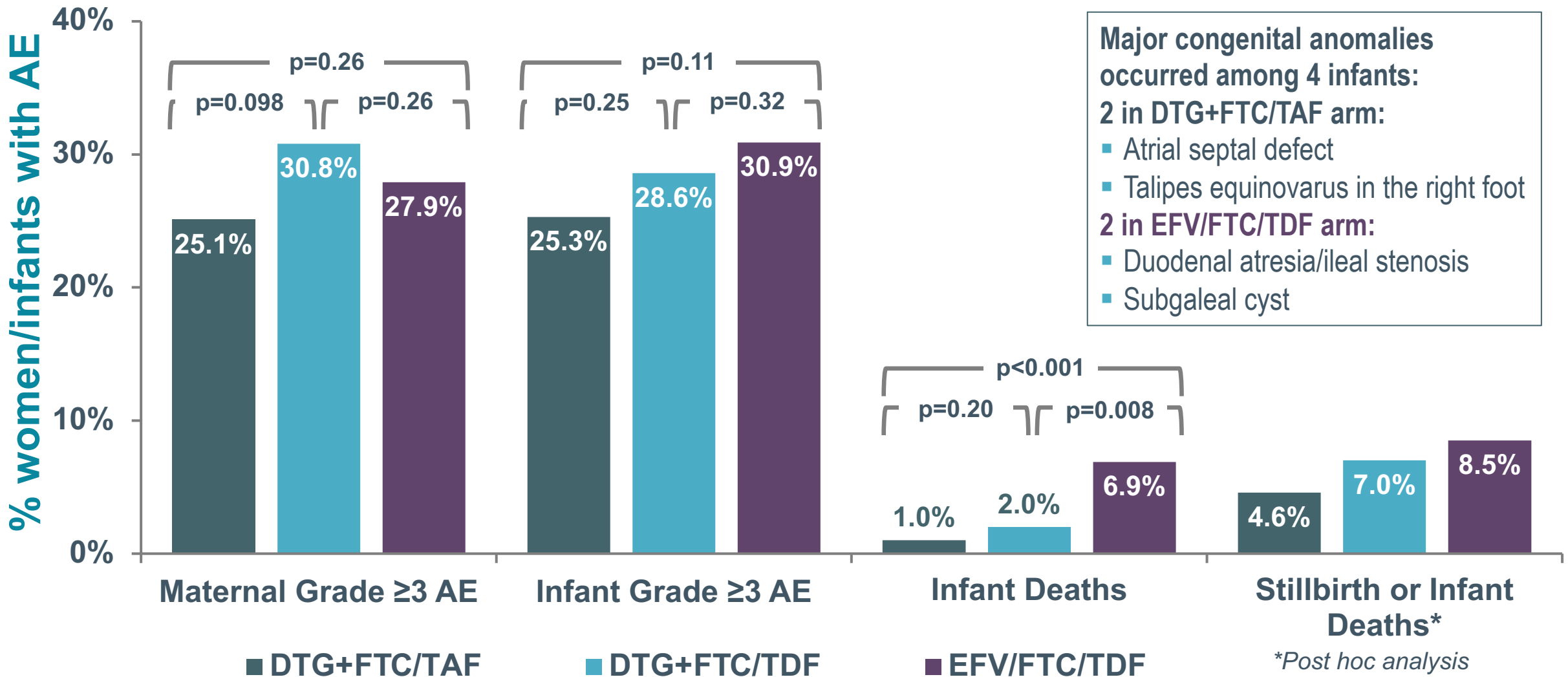


# Maternal Baseline Characteristics

	<b>DTG+FTC/TAF (N = 217)</b>	<b>DTG+FTC/TDF (N = 215)</b>	<b>EFV/FTC/TDF (N = 211)</b>	<b>Total (N = 643)</b>
<b>Age (median years)</b>	26.8	26.0	26.6	26.6
<b>Enrolled in Africa</b>	187 (86%)	189 (88%)	188 (89%)	564 (88%)
<b>Gestational age (median weeks)</b>	22.1	21.3	22.1	21.9
<b>CD4 count (median cells/mm<sup>3</sup>)</b>	467	481	439	466
<b>HIV-1 RNA (median copies/mL)</b>	781	715	1357	903
<b>HIV-1 RNA &lt;50</b>	36 (16%)	37 (17%)	27 (13%)	100 (16%)
<b>ART in pregnancy prior to entry</b>	176 (81%)	180 (84%)	176 (83%)	532 (83%)
<b>Median days on ART</b>	6	6	6	6
<b>BMI* (kg/m<sup>2</sup>), median (Q1, Q3)</b>	25.1 (22.5, 29.4)	24.5 (22.0, 28.1)	24.2 (21.5, 28.0)	24.7 (22.0, 28.4)

*Median duration of antepartum follow-up: 17.4 weeks; \*Pre-pregnancy BMI was not available*

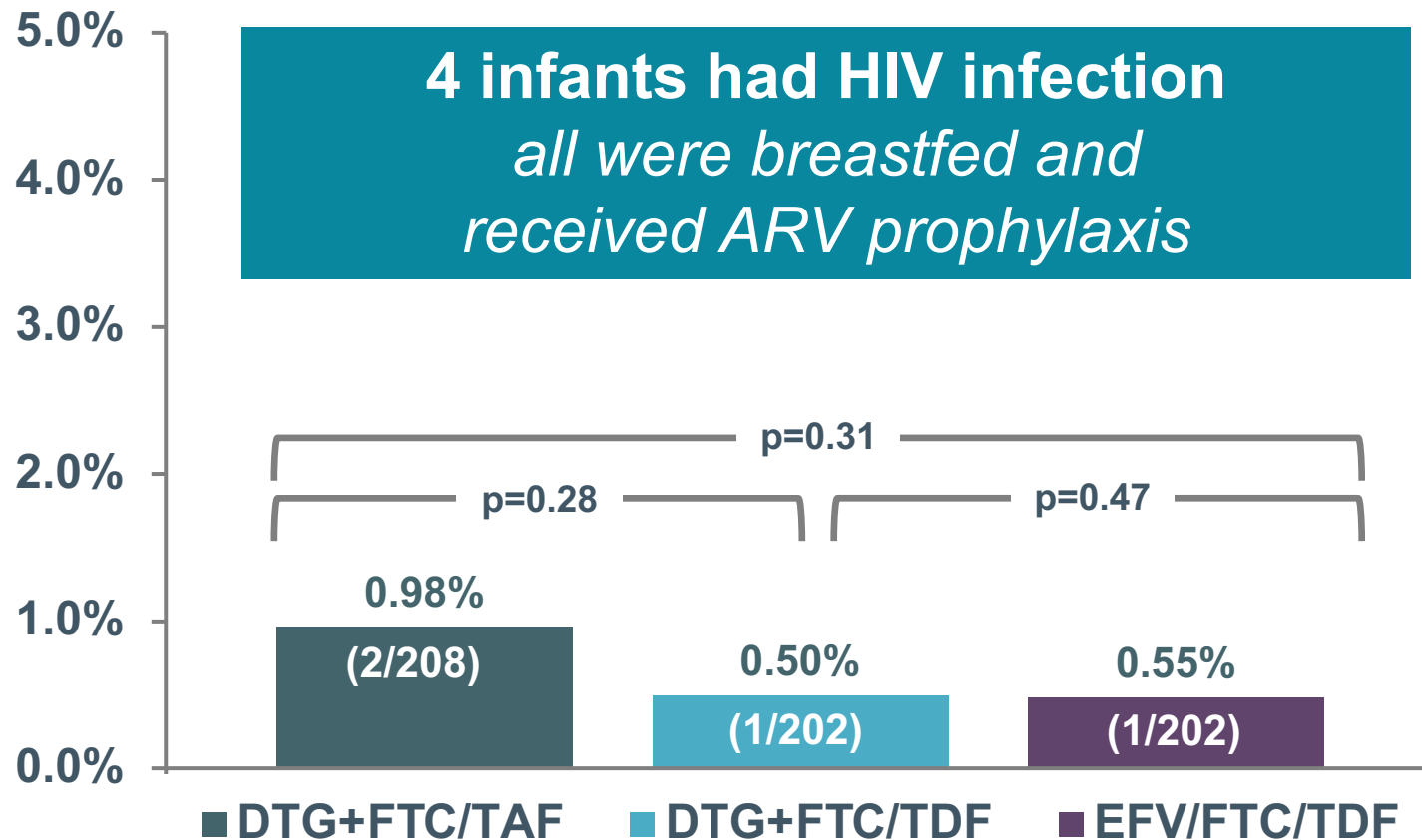
# Results: Maternal and Infant Grade 3 or Higher Adverse Events by Arm Through 50 Weeks Postpartum





# Results: Infant HIV Infection through Week 50 After Birth

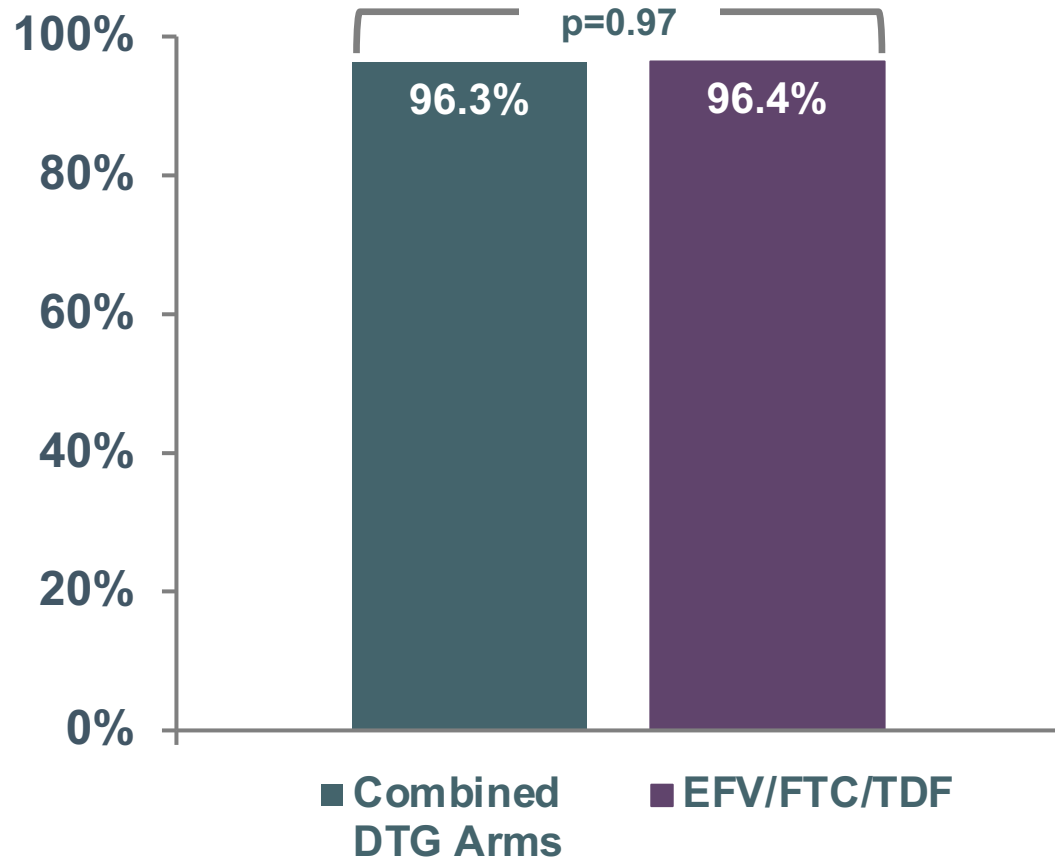
Estimated prob. of infant HIV infection (n/N)



- 2 had first HIV positive test within 14 days after birth
  - ✓ 1 in **DTG+FTC/TAF** arm with maternal HIV RNA >9,000 copies/mL at all visits through delivery
  - ✓ 1 in **DTG+FTC/TDF** arm with highest maternal through delivery HIV RNA = 42 copies/mL
- 1 in **DTG+FTC/TAF** arm with first positive test at 6 weeks, with maternal HIV RNA <40 copies/mL from 8 weeks on study onward
- 1 in **EFV/FTC/TDF** arm with first positive test at 50 weeks after birth, with maternal HIV RNA >40 copies/mL through 26 weeks postpartum

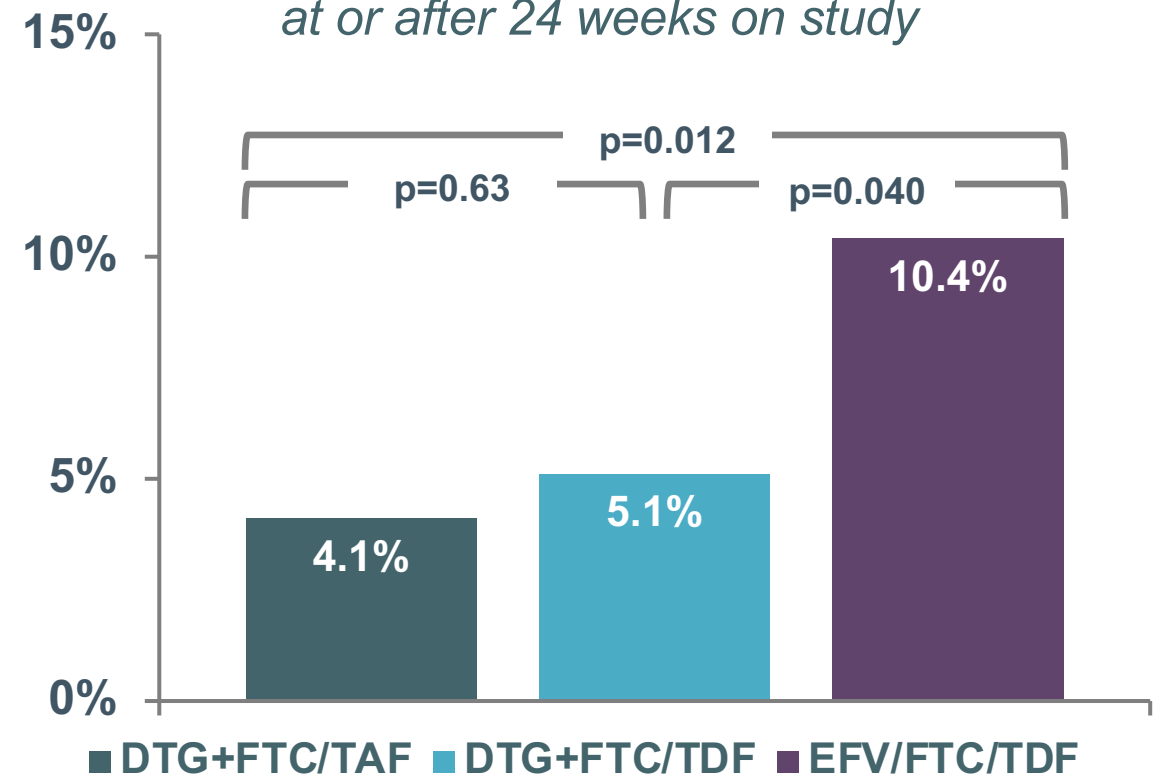
# Results: Maternal Virologic Outcomes

**Maternal HIV-1 RNA Suppression  
at week 50 postpartum**



*Per ITT analysis*

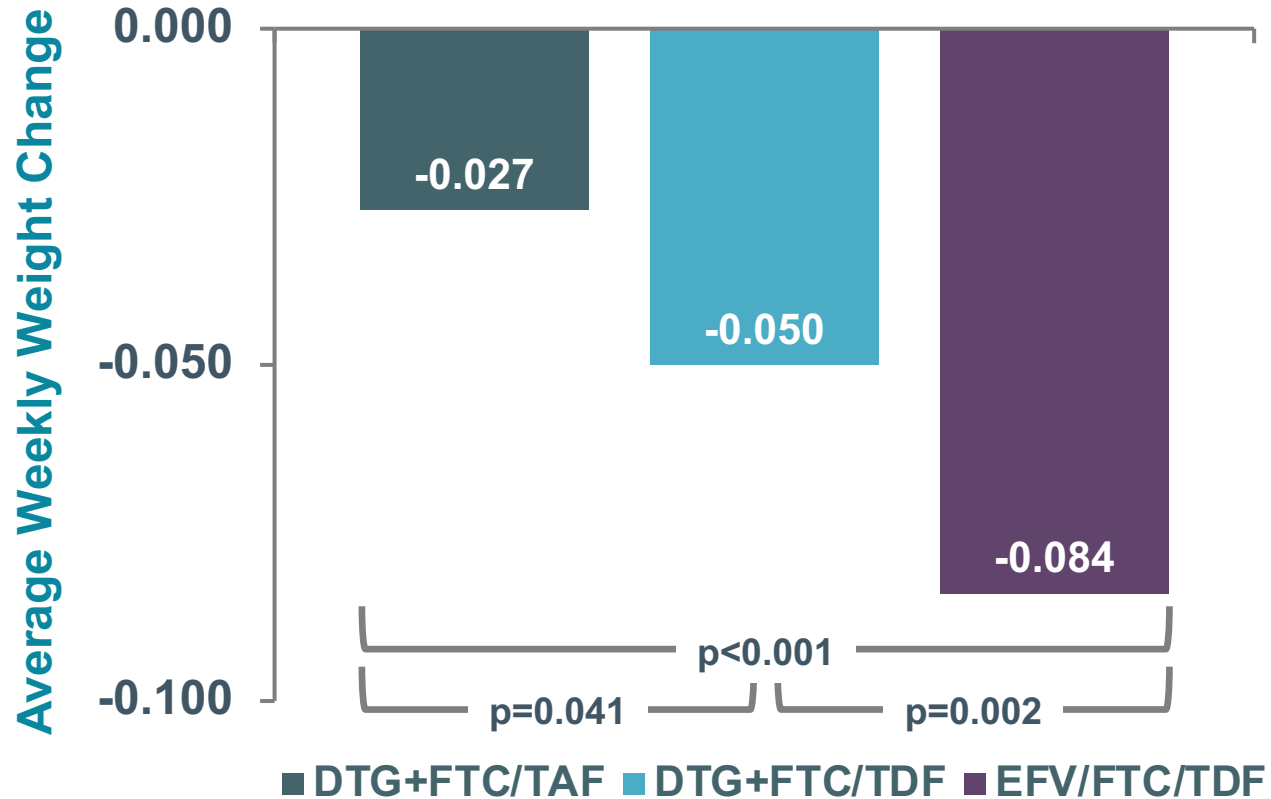
**Maternal Virologic Failure  
2 successive HIV RNA  $\geq$  200 copies/mL  
at or after 24 weeks on study**



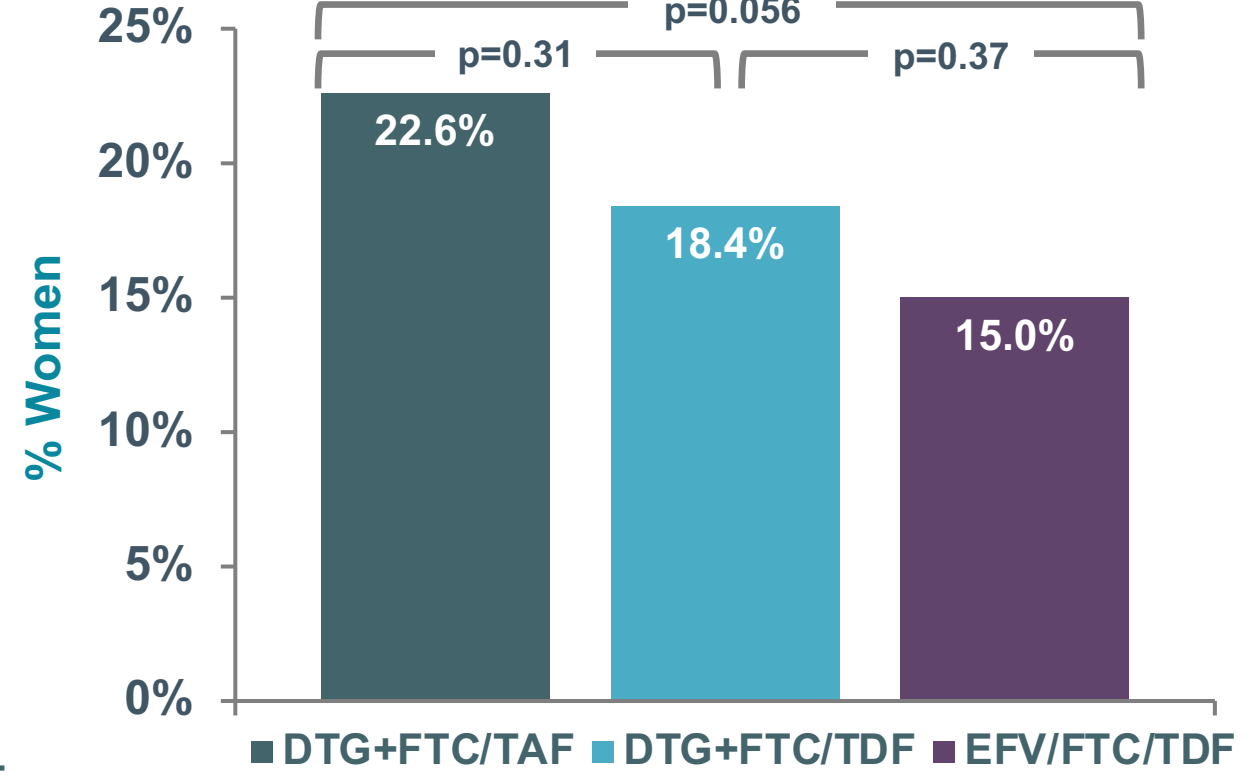
*Post hoc statistical comparisons*

# Results: Maternal Weight

**Average Weekly Maternal Weight Change**  
Enrollment through Week 50 Postpartum



**Maternal Obesity at Week 50**  
( $BMI \geq 30 \text{ kg/m}^2$ )



*Post hoc statistical comparisons*

# Conclusions

- ▶ Rates of maternal and infant grade  $\geq 3$  AEs were similar across arms from enrollment to Week 50 postpartum
  - Infant mortality was higher (though stillbirths somewhat less frequent) in the EFV arm
- ▶ The proportion of women with virologic suppression at week 50 postpartum was similarly high in the combined DTG 3-drug ART arms vs. the EFV arm
  - More women experienced virologic failure (and switched antiretrovirals due to virologic failure) in the EFV arm
- ▶ The rate of weight loss was significantly higher in the EFV arm and lowest in the DTG+FTC/TAF arm, which had the highest prevalence of obesity at week 50 postpartum
- ▶ Results from this study provide additional reassuring data for use of DTG and TAF during pregnancy and postpartum

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# Questions and Discussion

# Extra Slides



# Maternal AEs ≥3 through 50 weeks postpartum

	<b>DTG+FTC/TAF (N = 217)</b>	<b>DTG+FTC/TDF (N = 215)</b>	<b>EFV/FTC/TDF (N = 211)</b>
<b>Infections</b>	5 (2.3%)	5 (2.3%)	9 (4.3%)
<b>Laboratory abnormalities</b>	16 (7.3%)	33 (15.3%)	23 (10.9%)
<b>Low hemoglobin (most grade 3)</b>	8	20	15
<b>Low estimated CrCl (all grade 3)</b>	4	7	3
<b>Elevated AST</b>	1	4	2
<b>Gestational hypertension</b>	5 (2.3%)	5 (2.3%)	7 (3.3%)
<b>Pre-eclampsia</b>	4 (1.8%)	2 (0.9%)	2 (0.9%)
<b>Gestational diabetes</b>	0	1 (0.5%)	0
<b>Estimated delivery CrCl , week 50 (mean [SD] mL/min)</b>	124 (42)	118 (35)	131 (36)

# Infant AEs Grades $\geq 3$ through 50 weeks after birth

	<b>DTG+FTC/TAF (N = 208)</b>	<b>DTG+FTC/TDF (N = 202)</b>	<b>EFV/FTC/TDF (N = 207)</b>
<b>Major congenital anomaly</b>	2 (1.0%)	0	2 (1.0%)
<b>Any (Grade <math>\geq 2</math>) reported congenital/genetic anomaly</b>	6 (2.9%)	5 (2.5%)	4 (1.9%)
<b>Laboratory abnormalities*</b>	27 (12.9%)	25 (12.4%)	29 (14.0%)
<b>Infections</b>	10 (4.8%)	17 (8.4%)	19 (9.1%)
<b>Respiratory disorders</b>	11 (5.3%)	7 (3.5%)	13 (6.3%)
<b>Nervous system disorders</b>	4 (1.9%)	1 (0.5%)	7 (3.4%)
<b>Stillbirths or infant deaths (combined)</b>	10 (4.8%)	15 (7.4%)	18 (8.7%)

\* Most frequent abnormalities: Neutrophil count decreased, Hemoglobin decreased, and increased blood creatinine level

# Reasons for early ART regimen switches or stops

	<b>DTG+FTC/TAF N=208</b>	<b>DTG+FTC/TDF N=202</b>	<b>EFV/FTC/TDF N= 207</b>
<b>Virologic failure or drug resistance</b>	0	0	14
<b>Adverse events</b>	4	2	3
<b>Postpartum fertility choices</b>	11	10	0
<b>Other reasons*</b>	18	13	8
<b>Total</b>	<b>33</b>	<b>25</b>	<b>26</b>

\*Other; most frequent reasons were withdrew consent, relocated, noncompliance