Safety and Efficacy of DTG vs EFV and TDF vs TAF in Pregnancy: IMPAACT 2010 TRIAL

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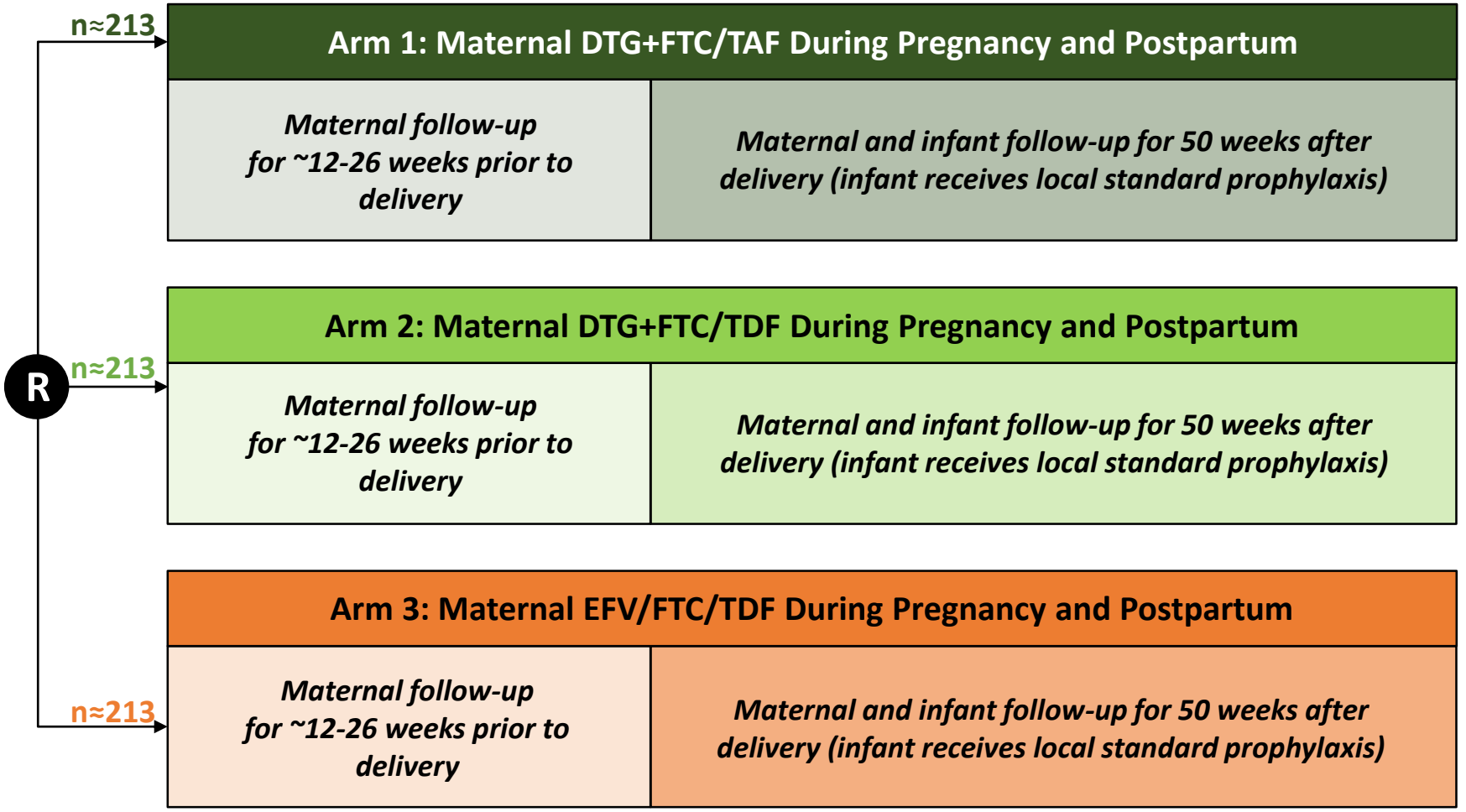
IMPAACT
International Maternal Pediatric Adolescent AIDS Clinical Trials Network

Background and Rationale

- WHO now recommends dolutegravir (DTG)-based antiretroviral treatment (ART) globally, given favorable efficacy, toxicity, resistance, and cost profiles
- Countries are transitioning from efavirenz (EFV)- to DTG-based first-line ART
  - Tenofovir alafenamide fumarate (TAF) is a recommended first-line agent for adults in the US
- ***It is essential to obtain pregnancy safety and efficacy data for agents that are expected to be widely used by women during pregnancy, such as DTG and TAF***
- We designed a Phase III, three-arm randomized open-label trial to compare the safety and virologic efficacy of three regimens started by women living with HIV (WLHIV) during pregnancy

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

Study Objectives: Virologic Efficacy

Whether treatment initiated during pregnancy with a DTG-containing regimen (DTG arms combined) is non-inferior to EFV/FTC/TDF with regard to HIV-1 RNA <200 copies/mL at delivery (primary)

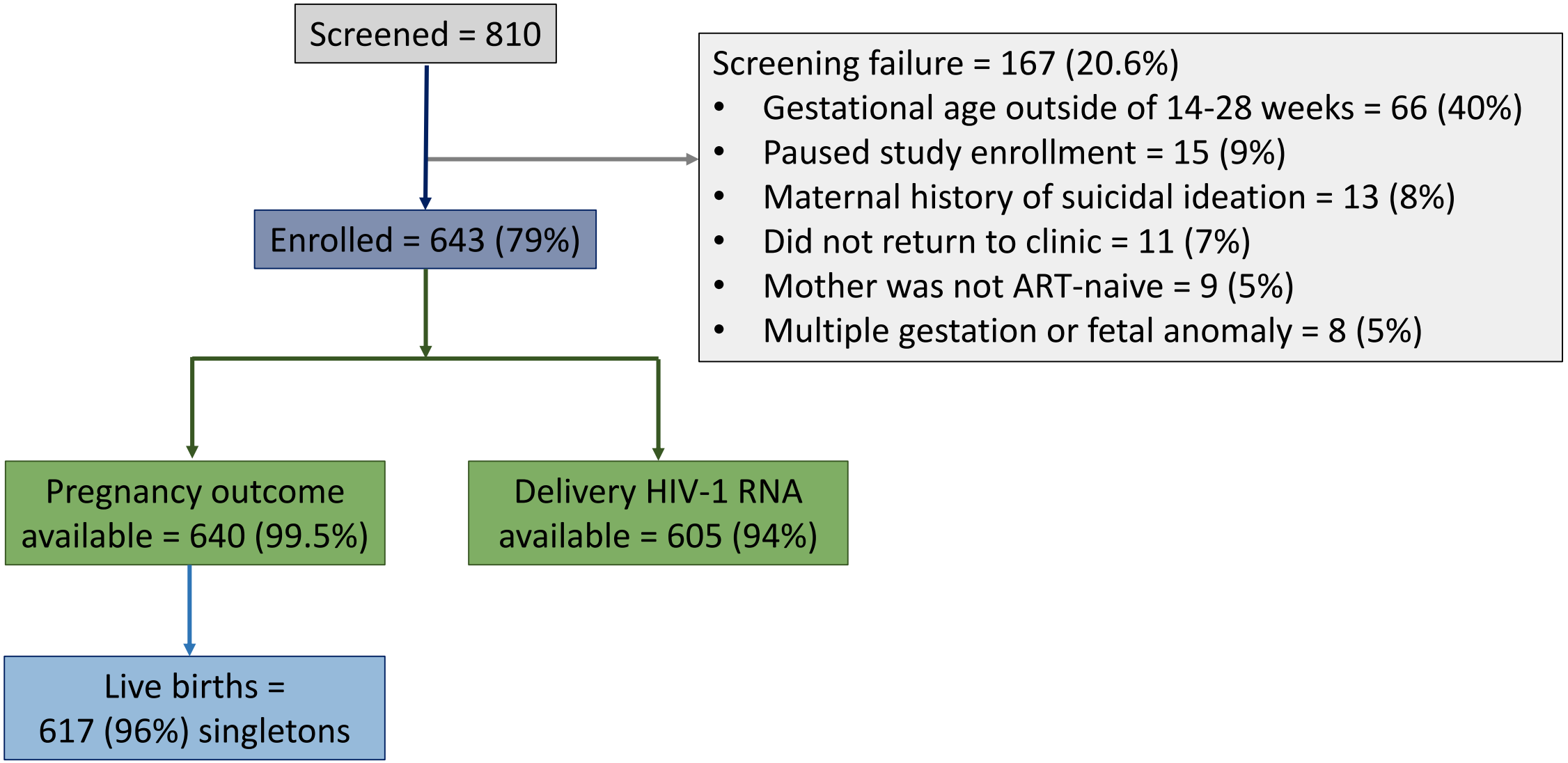
- -10% non-inferiority margin in favor of EFV for virologic efficacy
- Assessed superiority after establishing non-inferiority

Study Objectives: Safety

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

- **Adverse pregnancy composite outcome** (primary): occurrence of preterm delivery (PTD) <37 weeks, small for gestational age (SGA) <10th centile, stillbirth (SB) ≥20 weeks, or spontaneous abortion (SAB) <20 weeks
- **Maternal grade 3 or higher adverse events** through 50 weeks postpartum *(this analysis includes follow-up through 14 days postpartum)*
- **Infant grade 3 or higher adverse events** through 50 weeks postpartum *(this analysis includes follow-up through 28 days after birth)*
- **Infant neonatal death** (≤28 days) *(post-hoc)*

Enrollment and Retention



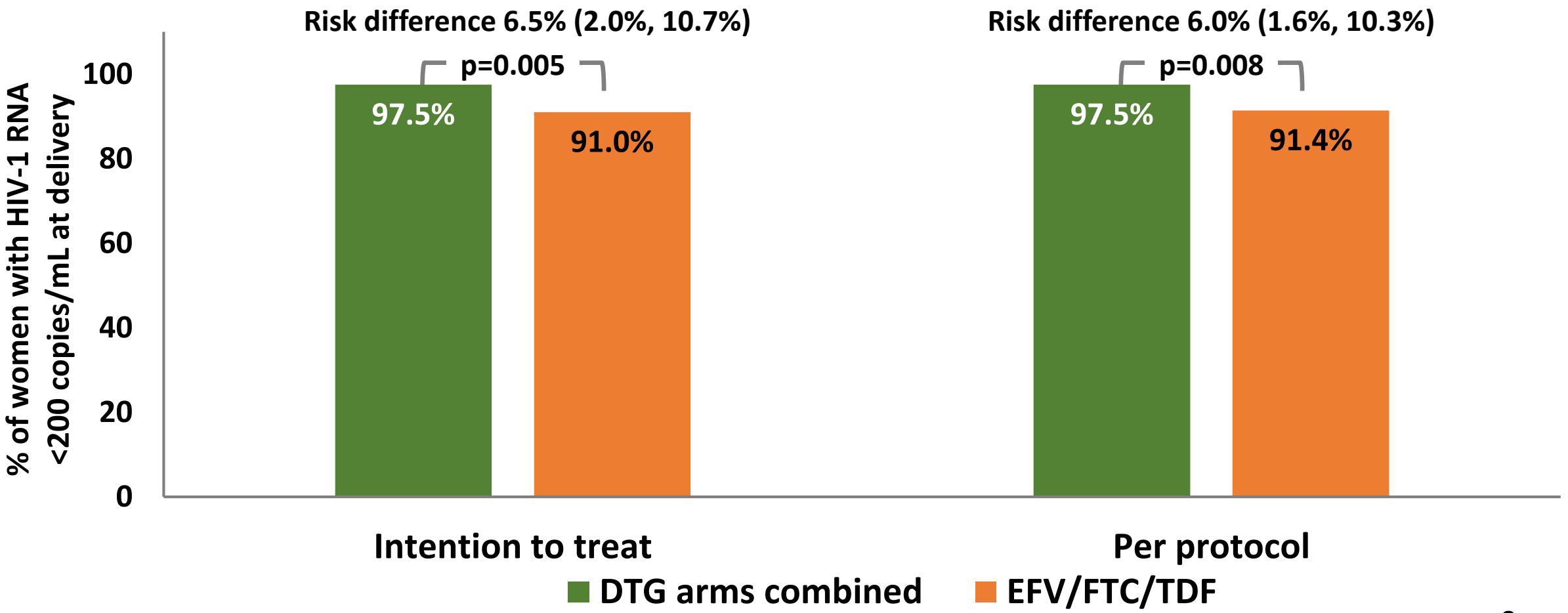
Maternal Baseline Characteristics

	DTG+FTC/TAF (N = 217)	DTG+FTC/TDF (N = 215)	EFV/FTC/TDF (N = 211)	Total (N = 643)
Age (median years)	26.8	26.0	26.6	26.6
Enrolled in Africa	187 (86%)	189 (88%)	188 (89%)	564 (88%)
Gestational age (median weeks)	22.1	21.3	22.1	21.9
CD4 count (median cells/mm^3)	467	481	439	466
HIV-1 RNA (median copies/mL)	781	715	1357	903
HIV-1 RNA <50	36 (17%)	37 (17%)	27 (13%)	100 (16%)
ART in pregnancy prior to entry	176 (81%)	180 (84%)	176 (83%)	532 (83%)
Median days on ART	6	6	6	6

Median duration of antepartum follow-up: 17.4 weeks

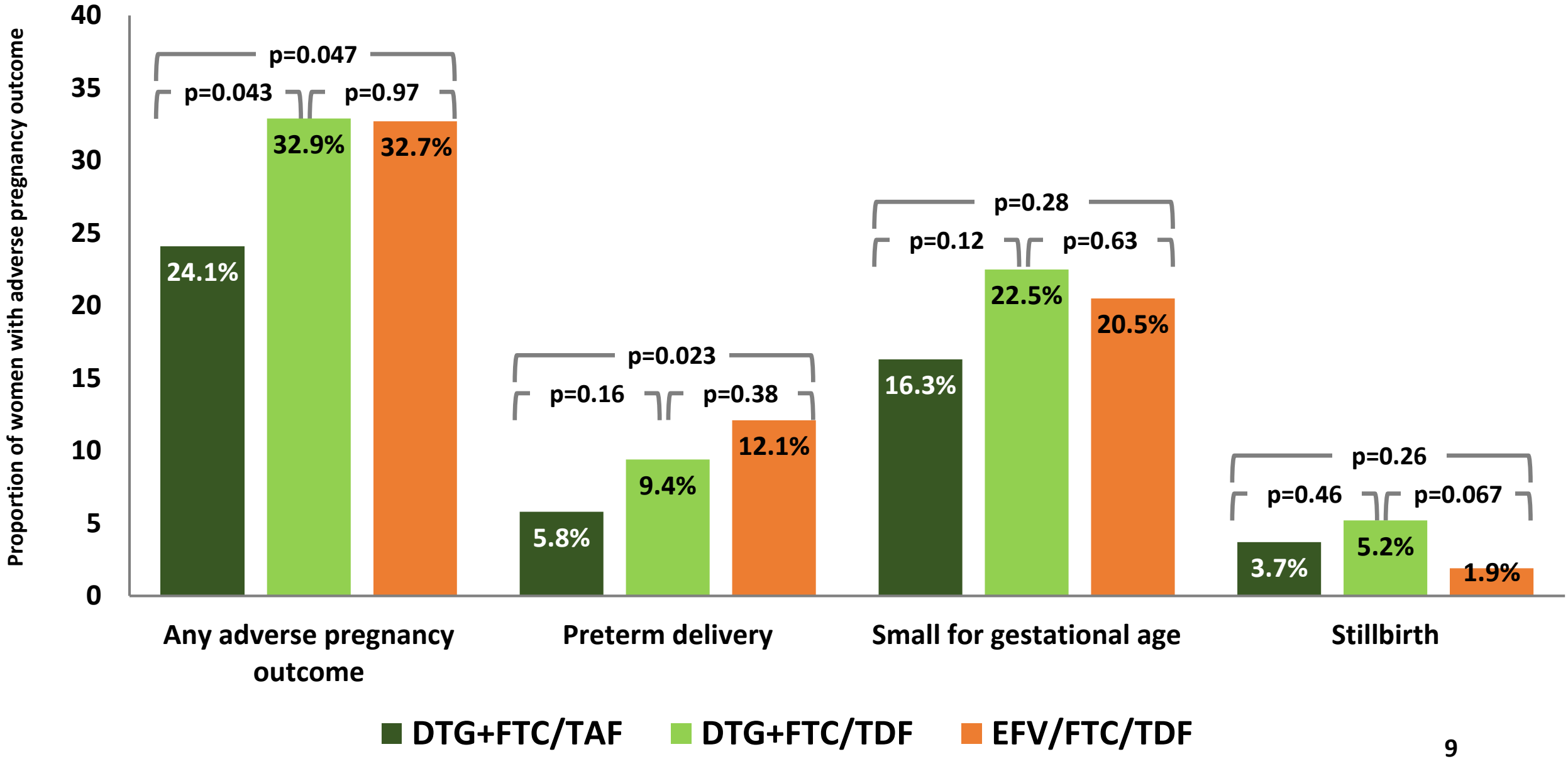
Virologic Suppression at Delivery was Significantly Higher in the DTG Arms Compared with EFV Arm

Proportion of women with HIV-1 RNA <200 copies/mL at delivery visit:
Combined DTG-ART arms vs **EFV/FTC/TDF arm**



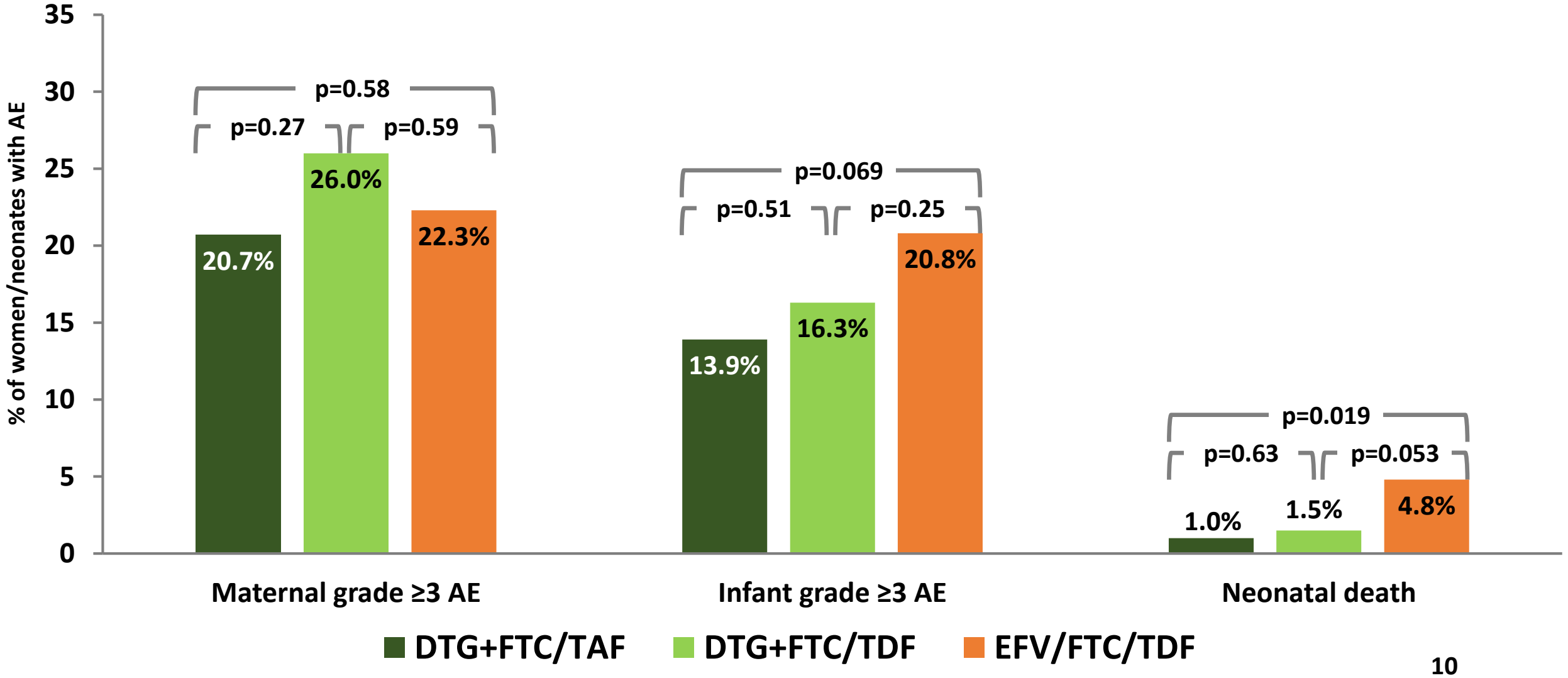
DTG arms had shorter time to viral suppression: log-rank p-value <0.001

Adverse Pregnancy Outcomes by Arm

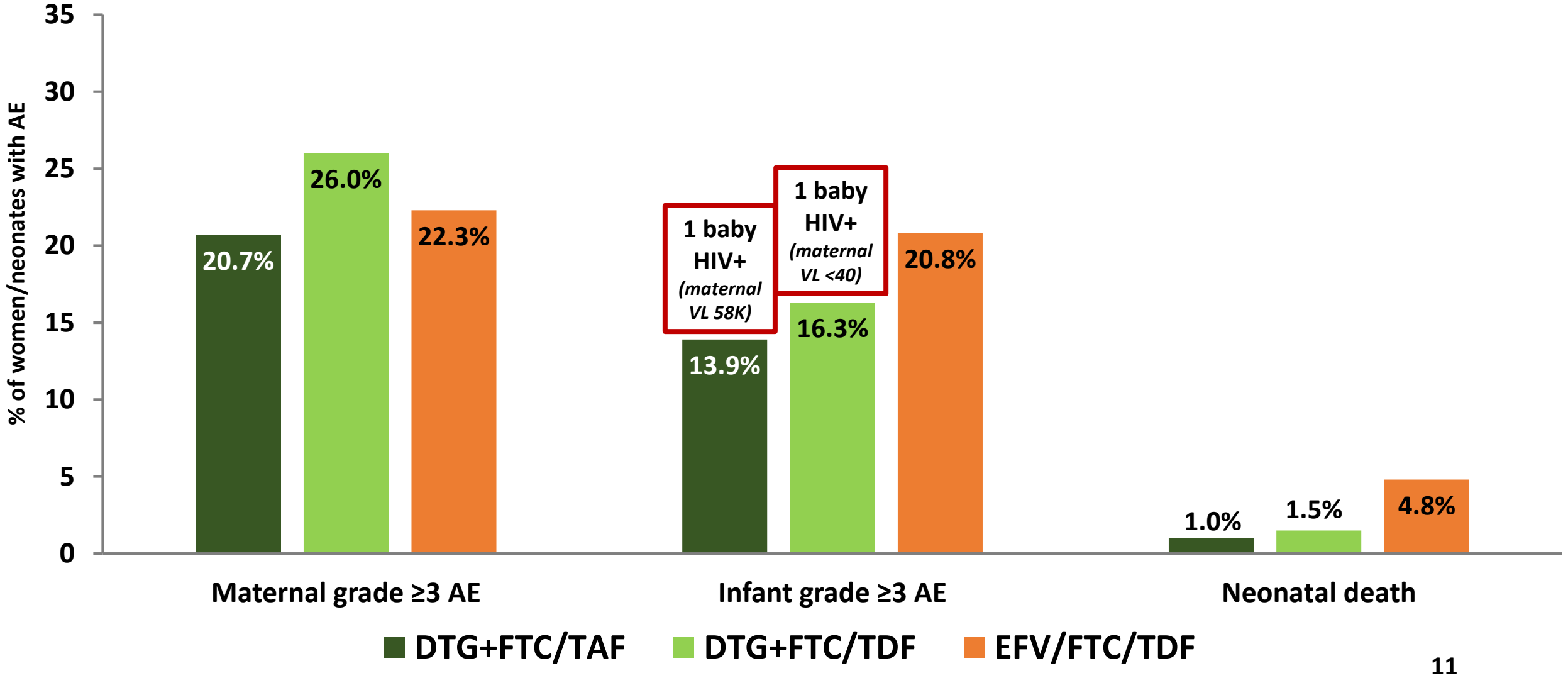


Notes: stillbirth was post-hoc analysis; and no spontaneous abortions occurred

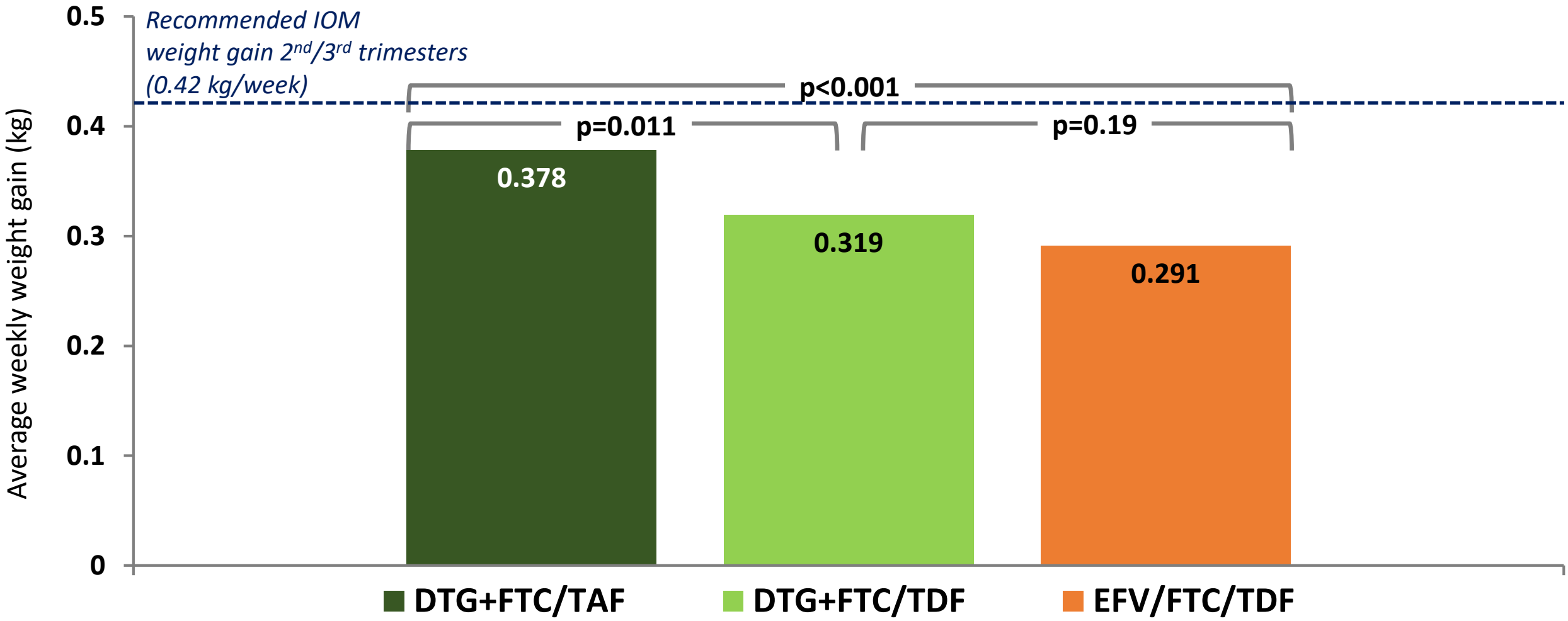
Maternal and Infant Grade 3 or Higher Adverse Events by Arm



Maternal and Infant Grade 3 or Higher Adverse Events by Arm



Average Weekly Maternal Weight Gain by Arm



Conclusions

- All three study regimens showed high efficacy, and safety that was similar to or better than that observed in other studies of ART in pregnancy
- DTG-containing ART had superior virologic efficacy at delivery compared to EFV/FTC/TDF
- DTG+FTC/TAF was associated with significantly fewer adverse pregnancy outcomes (driven by lower preterm and SGA rates) and fewer neonatal deaths than EFV/FTC/TDF
- Results affirm the WHO recommendation to use DTG in all populations, including during pregnancy, and showed that TAF may be preferable to TDF in pregnancy

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