

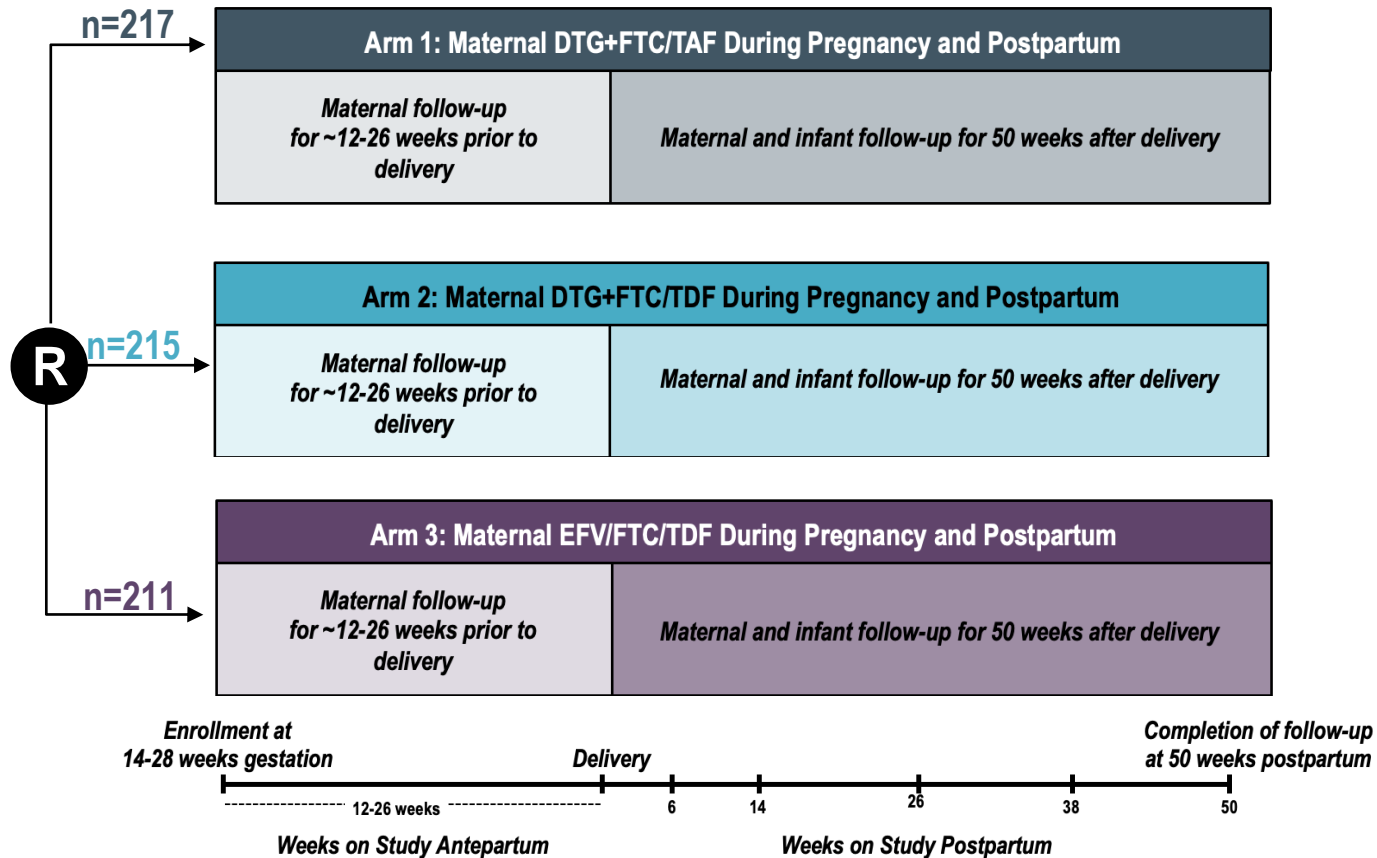
Update on IMPAACT 2010/VESTED Findings

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Protocol Co-chair
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ANNUAL MEETING
2022

Randomized Open-Label Trial of the Virologic Efficacy and Safety of Three ART Regimens Started in Pregnancy



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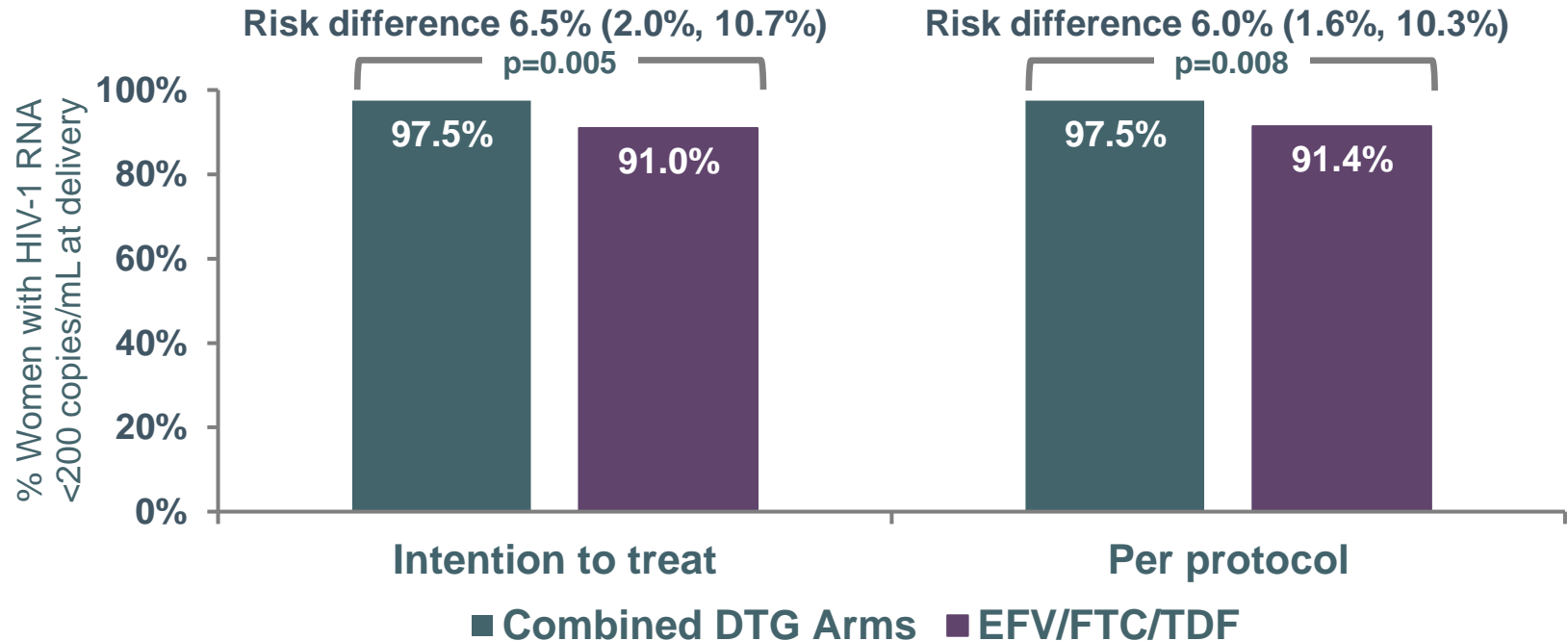
Summary of key findings to date

- ▶ Virologic efficacy was better with DTG compared to EFV
 - ▶ Virologic suppression at delivery significantly more likely in DTG arms
 - ▶ Virologic suppression similar across arms at week 50 postpartum **but** virologic failure and resistance significantly more likely in EFV arm
- ▶ Pregnancy outcomes were significantly better with DTG+TAF
 - ▶ Infant demise was significantly more likely in the EFV arm
- ▶ Insufficient maternal weight gain during pregnancy and poor infant growth were more likely in the EFV arm
 - ▶ Insufficient weight gain was associated with adverse pregnancy outcome
- ▶ Other maternal and infant adverse events similar across arms

Virologic suppression at delivery was significantly higher in the DTG arms compared with the EFV arm

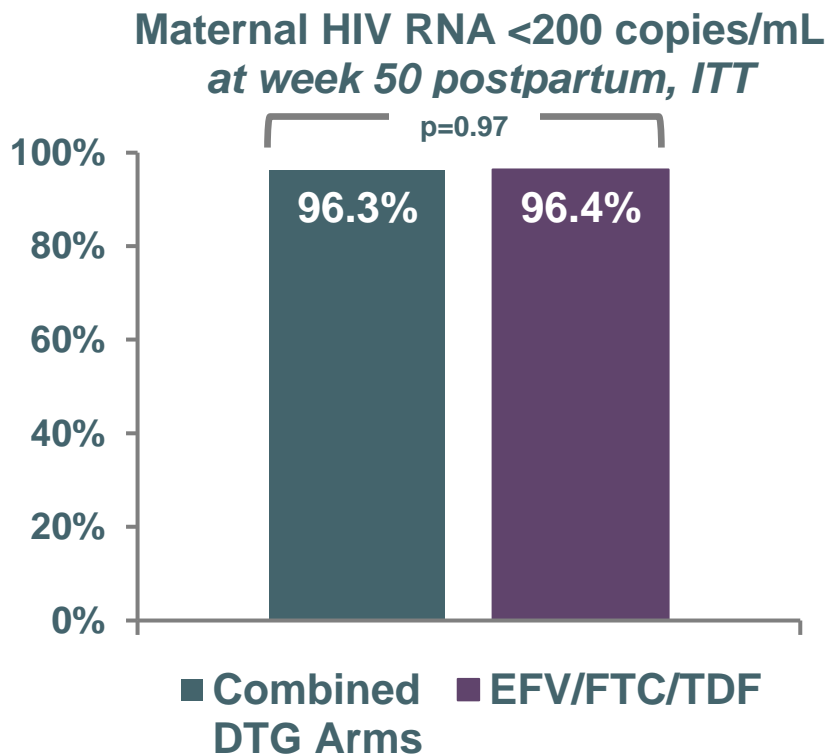
Proportion of women with HIV-1 RNA <200 copies/mL at delivery visit:

Combined DTG-ART arms vs EFV/FTC/TDF arm

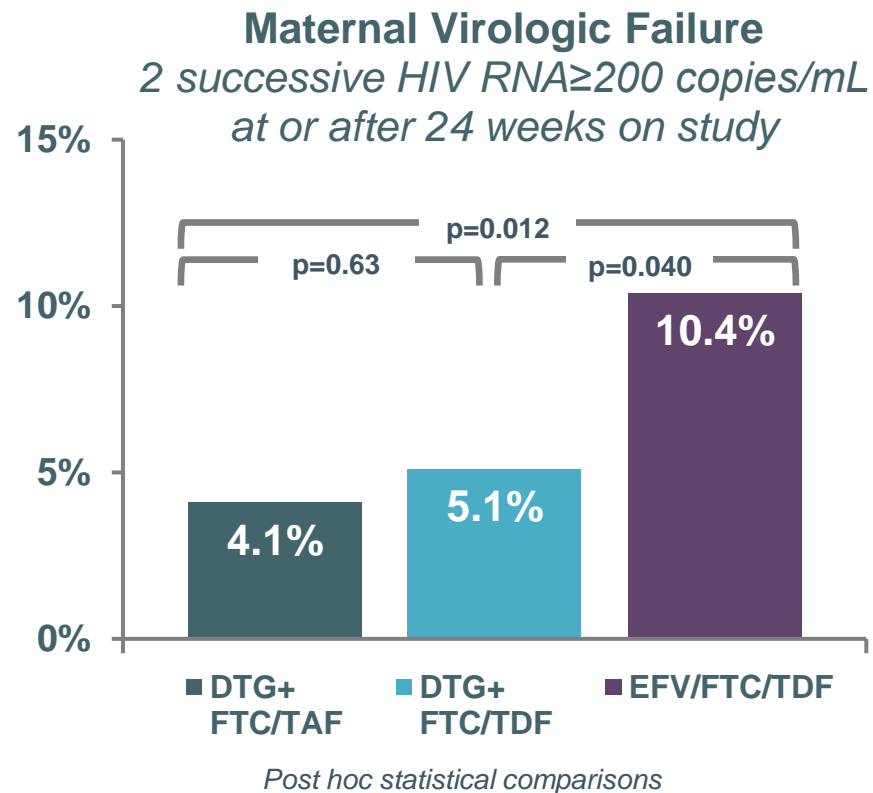


DTG arms had shorter time to viral suppression: log-rank p-value <0.001

Viral suppression was similar in the combined DTG-arms and **EFV-arm** at week 50 postpartum

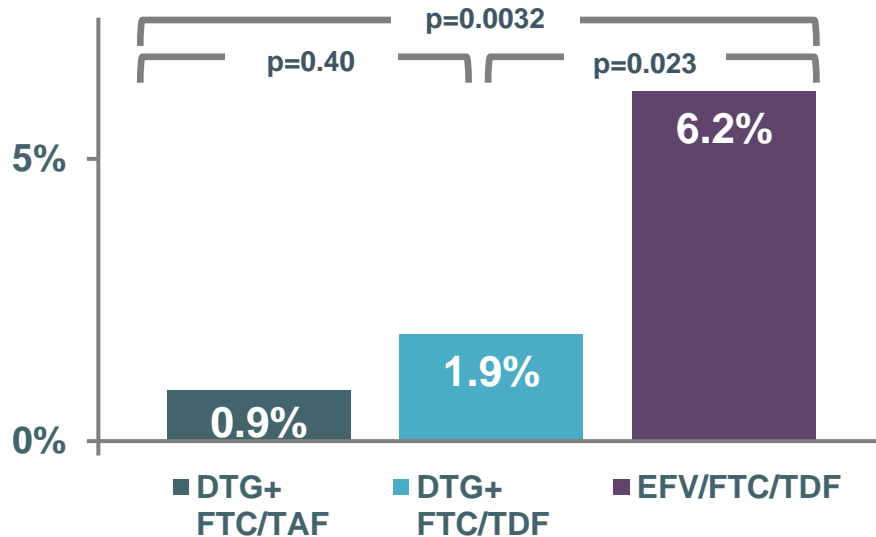


BUT cumulative virologic failure more frequent in **EFV arm** than the combined DTG-arms



HIV drug resistance at virologic failure was significantly lower in the DTG arms compared with the EFV arm

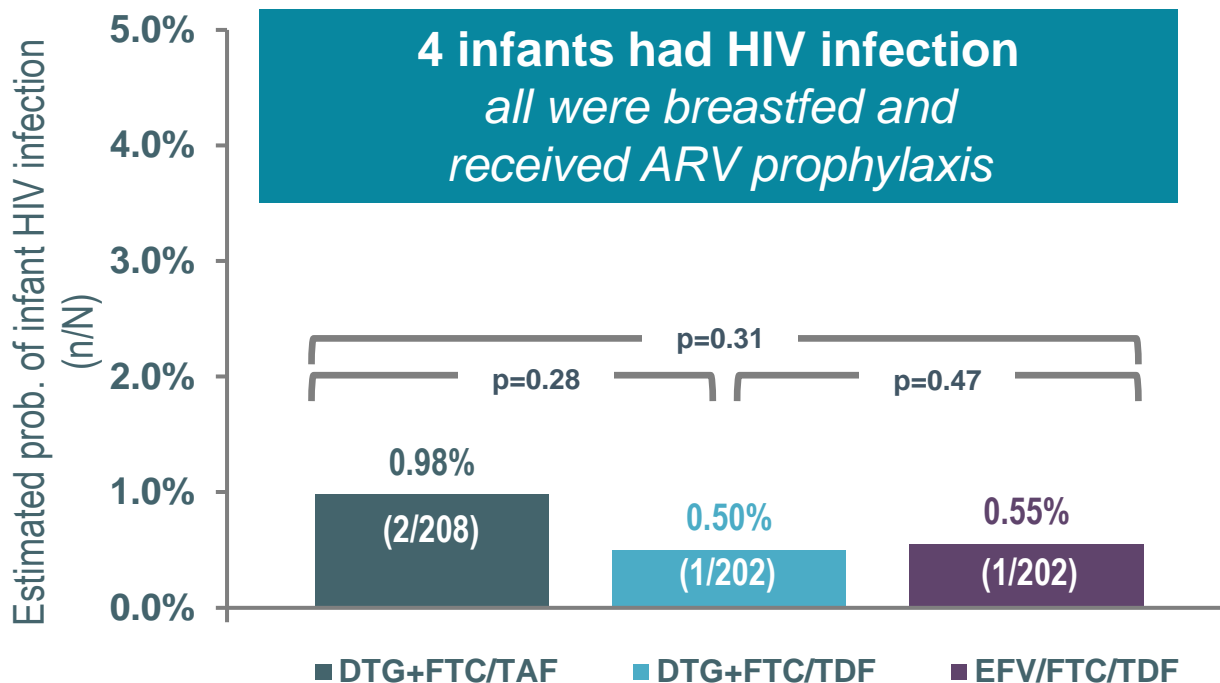
Proportion of women with HIV drug resistance at virologic failure



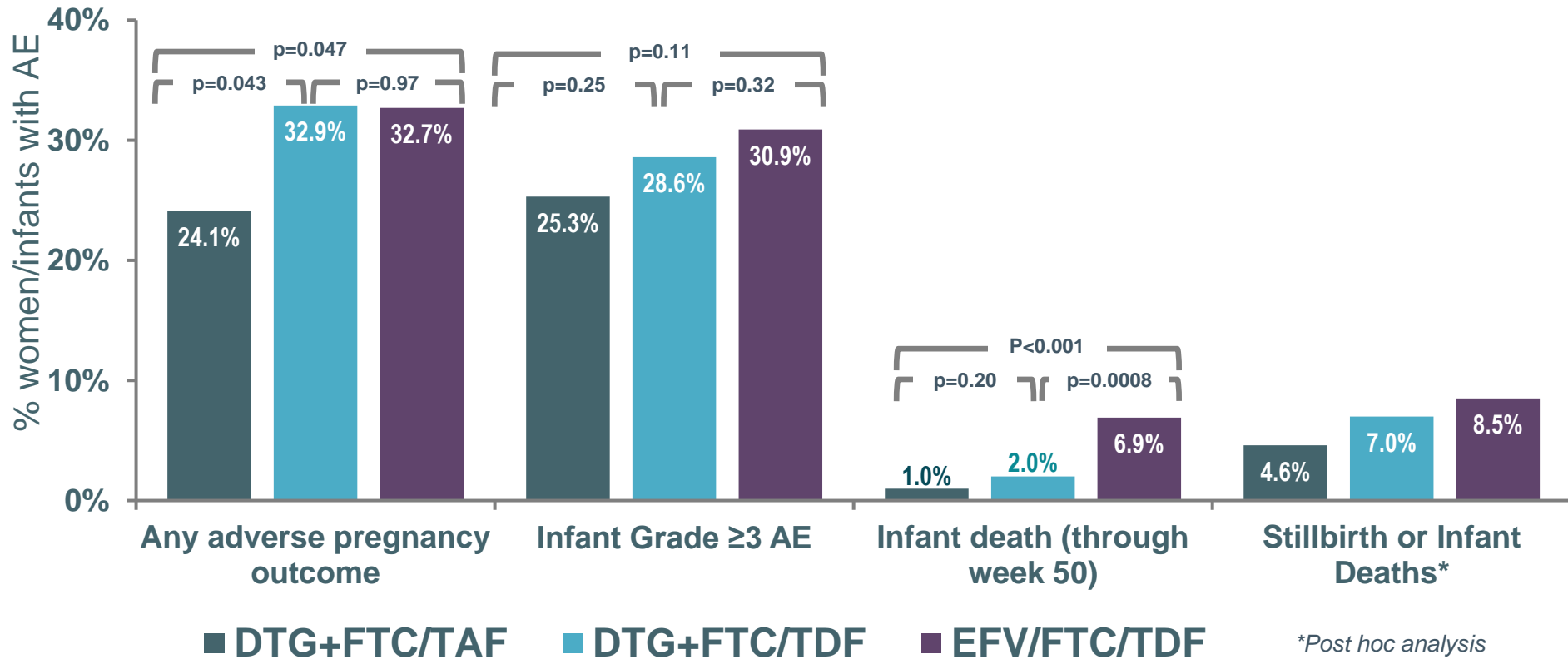
Women who experienced virologic failure had high prevalence of pre-ART resistance

DTG arms	5/6 (1 in TAF and 4 in TDF)
EFV arm	10/13

There were few infants diagnosed with HIV during the study and no apparent differences between arms

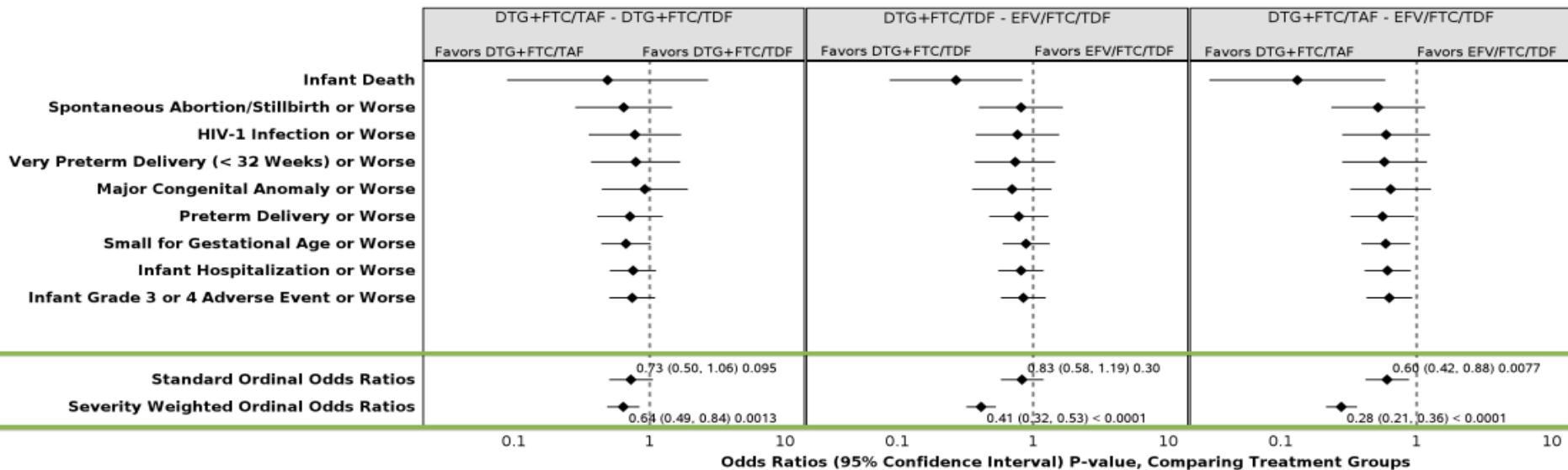


Key Maternal and Infant Safety Outcomes through 50 Weeks Postpartum



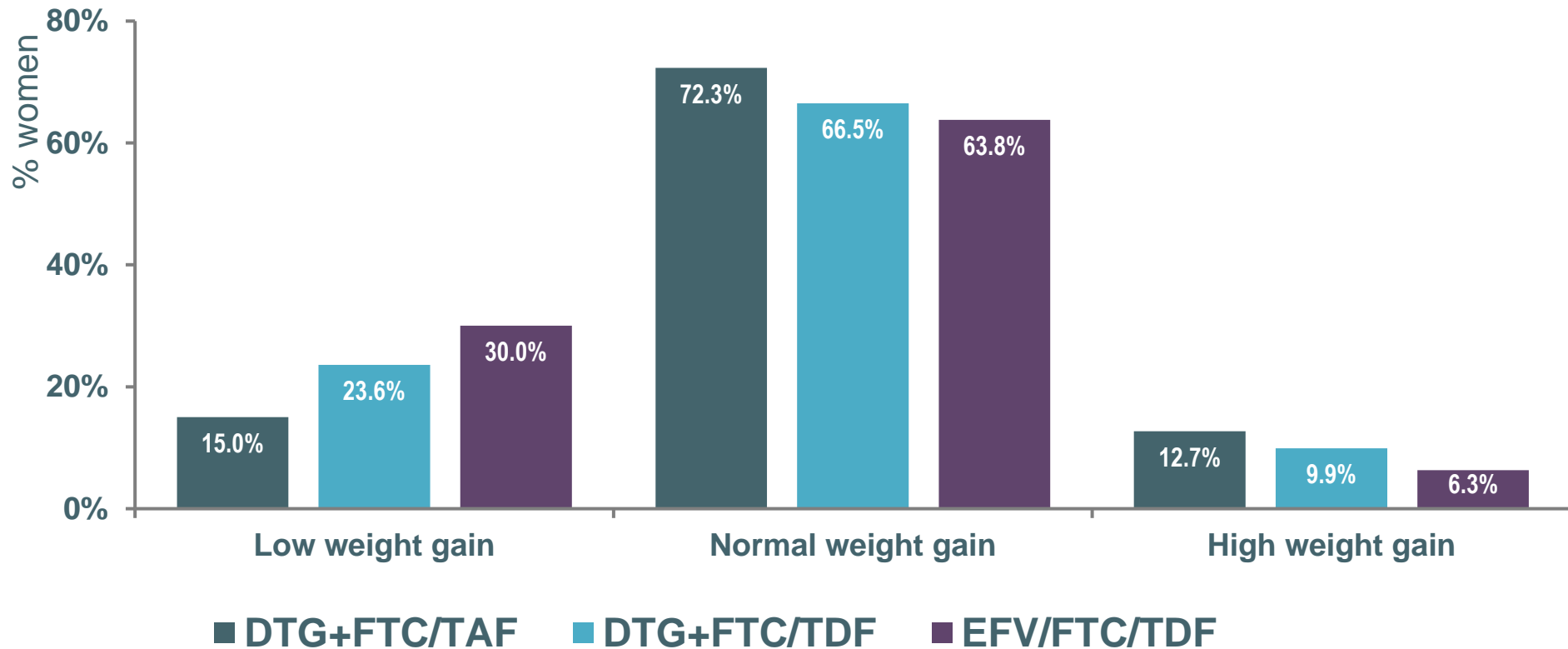
DTG+FTC/TAF had the best risk-benefit trade-off, even better than in the primary analysis, in a desirability-of-outcome-ranking (DOOR) analysis

FIGURE 1. By-Arm Odds Ratio Comparisons for the Composite and Ordinal Outcome Measures



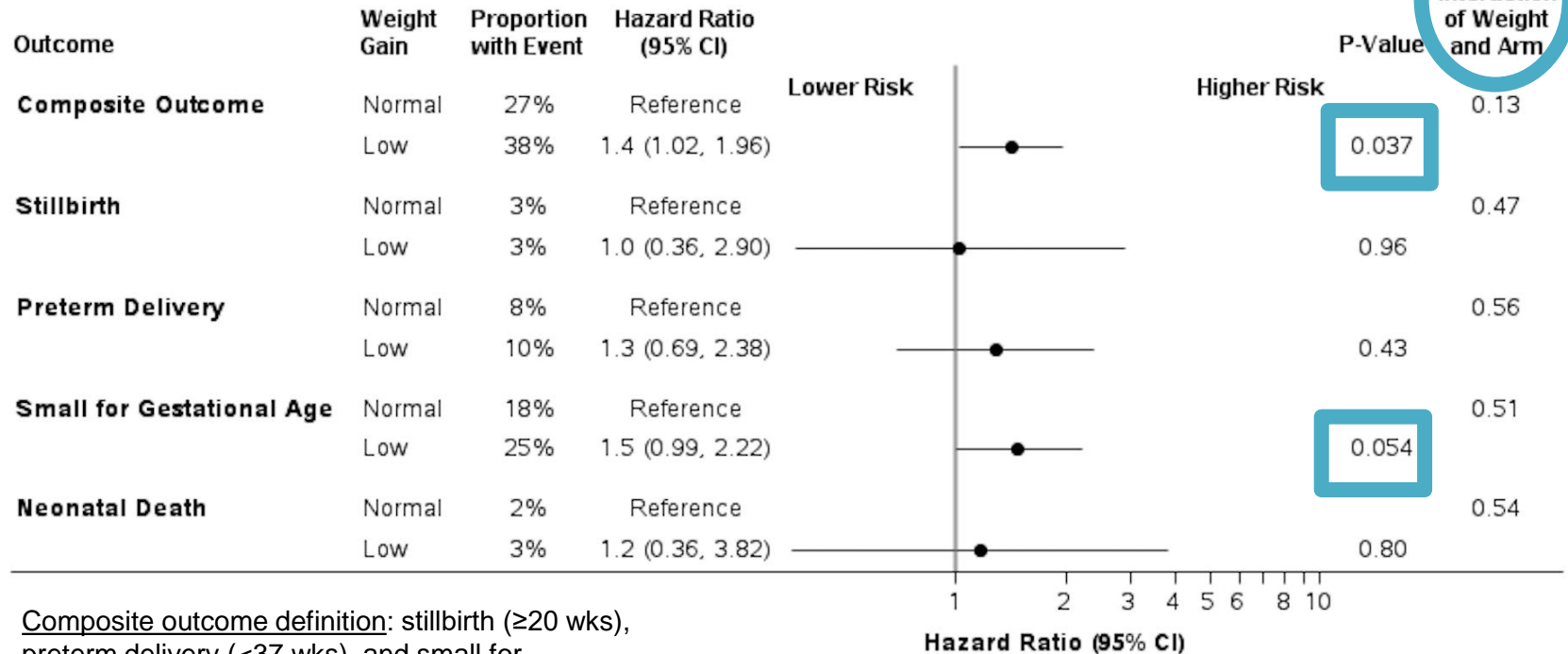
Proportions of women with low (insufficient), normal, and high (excess) antepartum weight gain

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Significant association between greater average pregnancy weekly weight gain and lower risk of any adverse pregnancy outcome

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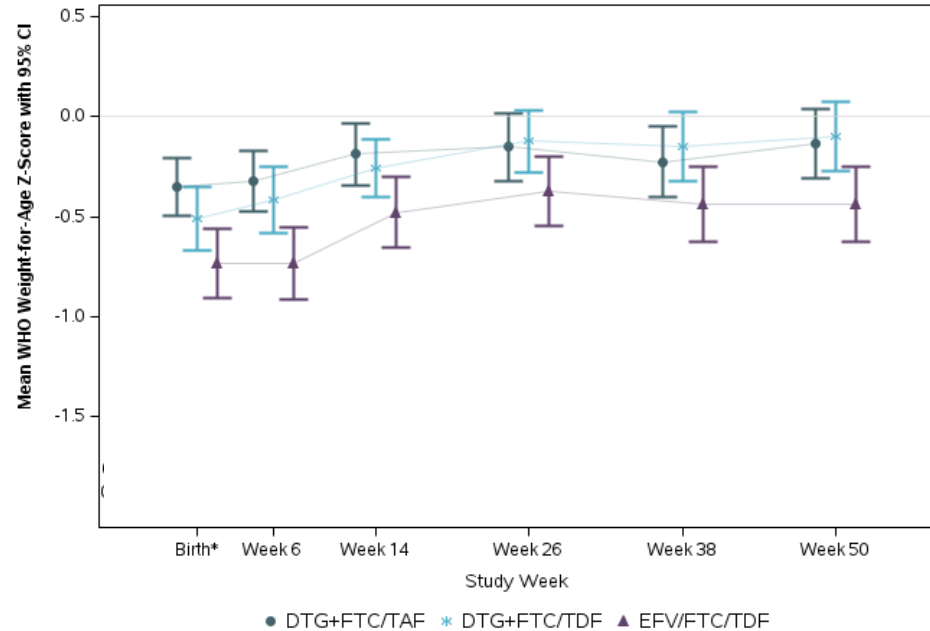


Composite outcome definition: stillbirth (≥ 20 wks), preterm delivery (< 37 wks), and small for gestational age ($< 10^{\text{th}}$ percentile)

Adjusted for gestational age stratum at baseline

Infants born to mothers who started the **EFV** arm in pregnancy were significantly smaller throughout infancy compared to infants whose mothers started on **DTG** regimens

- ▶ Infants exposed to **EFV** had lower z-scores compared to those exposed to **DTG**
 - ▶ length-for-age AND
 - ▶ weight-for-age
 - ▶ Differences present at birth, persisted through week 50
- ▶ Infants exposed to EFV had higher rates of stunting and underweight
- ▶ Infant obesity at week 50 similar between arms (2-3%)



Adverse pregnancy outcomes were very common in the 19 women who conceived on ART while on study

Outcome	ARV Treatment at Start of Pregnancy events/N (%)				
	DTG+ FTC/TAF	DTG+ FTC/TDF	EFV/FTC/TDF	Non-Study Treatment	Total
Stillbirth or Spontaneous Abortion*	1/2 (50%)	0/2 (0%)	5/12 (41.7%)	1/3 (33%)	7/19 (36.8%)
Preterm Delivery (<37 Weeks)	0/1 (0%)	0/2 (0%)	2/7 (28.6%)	1/2 (50%)	3/12 (25%)
Small for Gestational Age (<10th Percentile)	0/0 (NA)	0/1 (0%)	1/4 (25%)	0/1 (0%)	1/6 (16.7%)
Composite Adverse Outcome	1/2 (50%)	0/2 (0%)	8/12 (66.7%)	2/3 (66.7%)	11/19 (57.9%)

* One pregnancy resulting in induced abortion excluded from composite outcome analysis

Analyses underway/planned

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Analysis	Lead
Safety/Efficacy through 50 weeks postpartum	Lameck Chinula (to journal)
Infant bone and renal outcomes	Tapiwa Mbengeranwa (drafted)
Maternal bone and renal outcomes	Gaerolwe Masheto (drafted)
Changes in maternal weight, and association with outcomes	Risa Hoffman (analysis report soon)
Adverse outcomes of subsequent pregnancies	Lee Fairlie (being drafted)
Mother-to-infant transfer of antiretrovirals in pregnancy / breastmilk	Jeremiah Momper
Mother/infant ARV hair levels (and adverse outcomes, adherence)	Jillian Pintye
Maternal and infant RBC folate levels	Denise Jacobson (analysis report)
HbA1c, glucose, diabetes	Lameck Chinula
Minor resistant variants, women with VF; HIV DR, infants with HIV	Ceejay Boyce
DOOR analysis (ranked composite infant safety outcomes)	Sean Brummel
Maternal depression, anxiety	Lynda Stranix-Chibanda
Adherence to ART (and barriers, facilitators)	Rivet Amico, Lee Fairlie
NWCS 630: TAF and metabolic syndrome	Ahizechukwu Eke
DACS 722: Statistical methods for gestational age measurement	Mark Giganti

Acknowledgements

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