The study team questionnaire resulted in higher severity
The 79/216 (37%), 93/213 (44%), and 101/211 (48%) MI pairs experienced at least one of the ranked
Mother
Arm B
Odds ratios (ORs) were computed for the composite
1.6
The risk
When more severe outcomes were given more weight,
Ordinal ORs resulted in
5%
SDMC) and UM1AI106716
Clinical trials often summarize risks and benefits in
Questionnaire included a hypothetical 2
Severity Weight
18
1.0
Healthcare Ltd,
2.5%
2.5%
Study team members
| Twitter: @IMPAACTNetwork
Standard ORs consistently favored the DTG arms over the EFV/FTC/TDF arm, and the
DTG+FTC/TAF provided the best overall
risk-benefit trade-off.

### METHODS
- 643 pregnant women living with HIV in 9 countries were randomized in 2018-2019 to one of three antiretroviral treatment arms: dolutegravir (DTG)-emtricitabine (FTC)/tenofovir alafenamide (TAF); DTG+FTC/tenofovir disoproxil fumarate (TDF); or efavirenz (EFV)/FTC/TDF.
- Key inclusion criteria included: ≥ 18 years of age, confirmed HIV-1 infection, ART-naive at screening, no evidence of multiple gestation or fetal anomaly, gestational age of 14-28 weeks.
- Mother-infant (MI) pair adverse outcomes were grouped in a pre-specified secondary outcome according to the most severe outcome experienced: 1) infant death, 2) spontaneous abortion or stillbirth, 3) infant HIV infection (benefit via reduction), 4) very preterm delivery (<32 weeks), 5) major congenital anomaly, 6) preterm delivery (<37 weeks), 7) small for gestational age (<10th percentile, SGA), 8) infant hospitalization, and 9) infant grade 3 or 4 adverse event.
- Non-protocol-specified analyses weighted the ranked outcome according to the study team’s belief of their severity based on a tipping point strategy.
- Questionnaire included a hypothetical 2-arm study in which infant death rate was 2.5% higher in one arm.
- Study team members blinded to the ranked outcome were asked to provide endpoint rates that would result in the 2 arms having a similar profile (Table 1).
- Odds ratios (ORs) were computed for the composite outcomes at each level of the ranked outcome plus more severe events.
- Weighted and unweighted ordinal ORs were computed to provide a summary OR across all event types.

### RESULTS
- 79/216 (37%), 93/213 (44%), and 101/211 (48%) MI pairs experienced at least one of the ranked outcomes in the DTG+FTC/TAF, DTG+FTC/TDF, and EFV/FTC/TDF arms, respectively.
- Standard ORs consistently favored the DTG arms over the EFV/FTC/TDF arm, and the DTG+FTC/TAF arm over the DTG+FTC/TDF arm (Figure 1).
- Ordinal ORs resulted in a better risk-benefit trade-off for DTG+FTC/TAF compared to EFV/FTC/TDF (OR=0.60, 95% confidence interval [CI]:0.42, 0.88).
- The study team questionnaire resulted in higher severity weights for more extreme outcomes.
- In the severity-weighted analysis, DTG+FTC/TAF had even better benefit-trade-off relative to DTG+FTC/TDF (OR=0.64, 95% CI:0.49, 0.84) and DTG/FTC/TDF (OR=0.28, 95% CI:0.21, 0.36).

### CONCLUSIONS
- The risk-benefit trade-off was clearer with the weighted ranked outcome that includes many outcomes, compared to previously reported separate analyses.
- DTG+FTC/TAF provided the best overall risk-benefit trade-off.

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