Adverse birth outcomes and risk of MTCT for dolutegravir versus efavirenz in 5 randomised trials of 1074 pregnant women

P040

Simiso Sokhela[1], Francois Venter[1], Bronwyn Bosch[1], Godspower Akpomiemie[1], Angela Tembo[1], Toby Pepperrell[2], Bryony Simmons[3], Lloyd B. Mulenga[4], Alexandra Calmy[5], Tamara Tovar Sanchez[6], Eric Delaporte[6], Charles Kouanfack[7], Mireille Mpoudi-Etame[8], Carmen Perez Casas[9], Saye Khoo[10], Helen Reynolds[10], Andrew Hill[10]

1.University of the Witwatersrand Faculty of Health Sciences, Johannesburg, South Africa 2.University of Edinburgh, School of Medicine and Veterinary Medicine, Edinburgh, UK 3.London School of Economics and Political Science, LSE Health, London, UK 4.University Teaching Hospital, Lusaka, Zambia 5.Genva University Hospitals, Division of Infectious Diseases, HIV-AIDS Unit, Geneva, Switzerland 6.University of Montpellier, TransVIHMI, Montpellier, France 7.Faculty of Medicine and Pharmaceutical Sciences, University of Dschang, Dschang, Cameroon; Day Stay Hospital, Central Hospital of Yaoundé, Henri-Dunant, Yaoundé, Cameroon; ANRS Cameroon site, Central Hospital of Yaoundé, Henri-Dunant, Yaoundé, Cameroon 8.Regional Military Hospital Number 1, Yaoundé, Cameroon 9.Unitaid, Global Health Campus, Le Grand-Saconnex, Switzerland 10.University of Liverpool, Department of Pharmacology and Therapeutics, Liverpool, UK

BACKGROUND

- First-line treatment with DTG leads to rapid suppression of HIV RNA which might lower the risk of mother-to-child HIV transmission (MTCT)
- Worldwide millions of women are taking DTG
- Hence, safety in pregnancy requires careful evaluation in RCTs
- Treatment associated obesity is linked to a wide range of adverse birth outcomes in women[1]

METHODS

- Data on adverse birth outcomes was included from 5 RCTs: DolPHIN-1, DolPHIN-2, ADVANCE, NAMSAL and IMPAACT-2010
- These trials compared DTG with EFV as first-line treatment
- Data for the outcomes of neonatal deaths, stillbirths and MTCT were extracted from each trial
- The meta-analysis was conducted using RevMan Software
- The odds ratio (OR) for each endpoint was calculated using the Mantel-Haenszel test (Random-effects model).

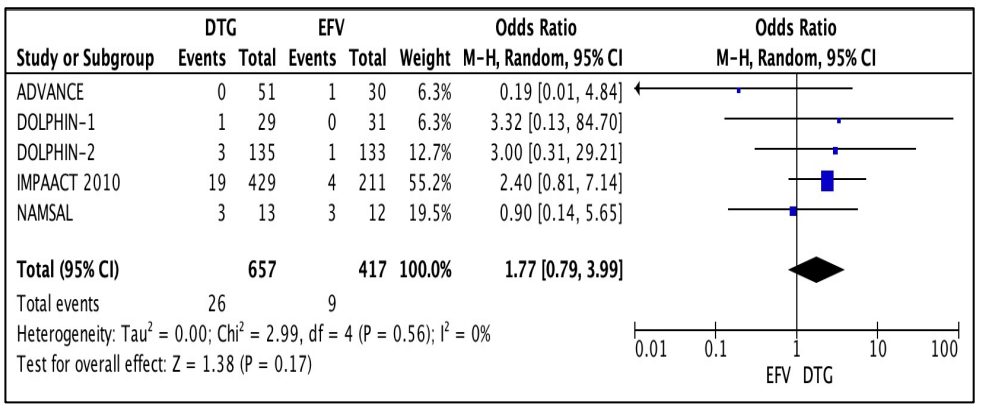

Figure 1: Forest plot for stillbirths

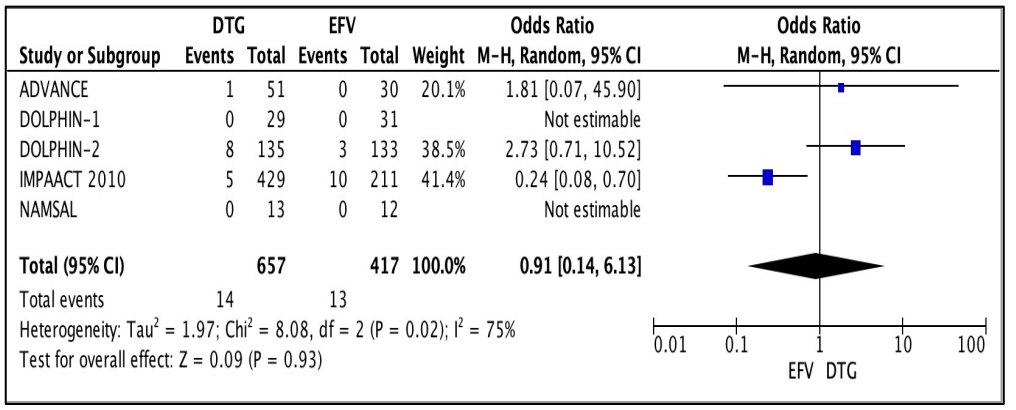

Figure 2: Forest plot for neonatal deaths

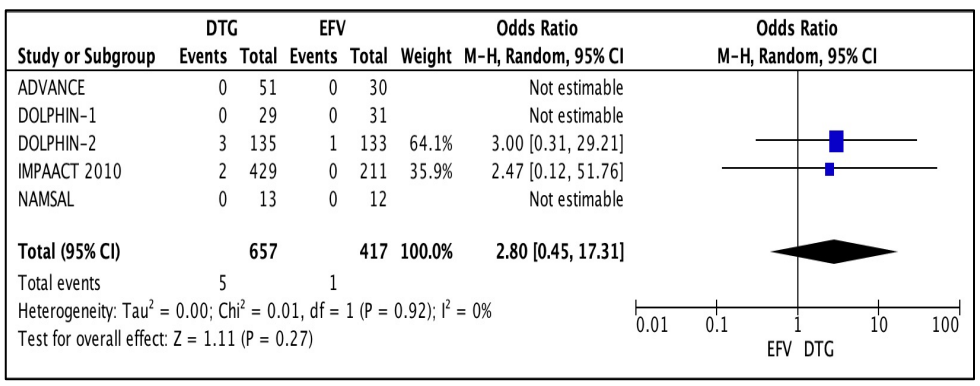

Figure 3: Forest plot for MTCT

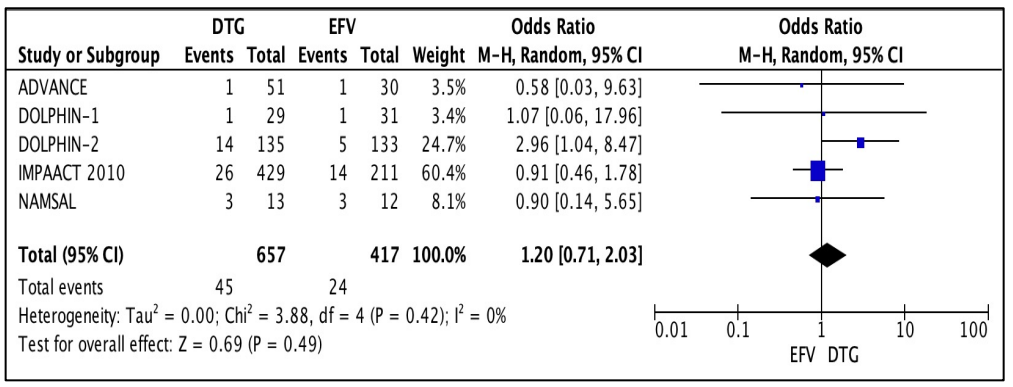

Figure 4: Forest plot for combined sum of stillbirths, neonatal deaths and MTCT

RESULTS

- DolPHIN-1 and DolPHIN-2 trials were conducted in South Africa and Uganda, ADVANCE in South Africa, NAMSAL in Cameroon and IMPAACT-2010 internationally.
- DolPHIN-1, DolPHIN-2 and IMPAACT-2010 were conducted in women already pregnant at screening. ADVANCE and NAMSAL were conducted in women who were not already pregnant at baseline
- On combining the sum of stillbirths, MTCT and neonatal deaths there were 45 events in the DTG arm and 24 in the EFV arm (OR=1.20, P-value=0.49) (Figure 5).
- No cases of Neural Tube Defects (NTDs) were observed among infants born in any of the trials
- In ADVANCE, the risk of developing clinical obesity was significantly higher for women taking DTG/FTC/TAF for 4 years (42%) versus DTG/FTC/TDF (27%) or EFV/FTC/TAF (20%)

DISCUSSION AND CONCLUSION

- This analysis evaluated 1074 pregnant women in 5 RCTs
- There was no significant difference between DTG and EFV in the overall risk of neonatal deaths, stillbirths or MTCT cases
- This analysis includes outcomes after first-line treatment typically up to 6 months before birth
- Outcomes for women becoming pregnant after long term treatment could be different given higher risks of clinical obesity for DTG, especially if combined with TAF/FTC

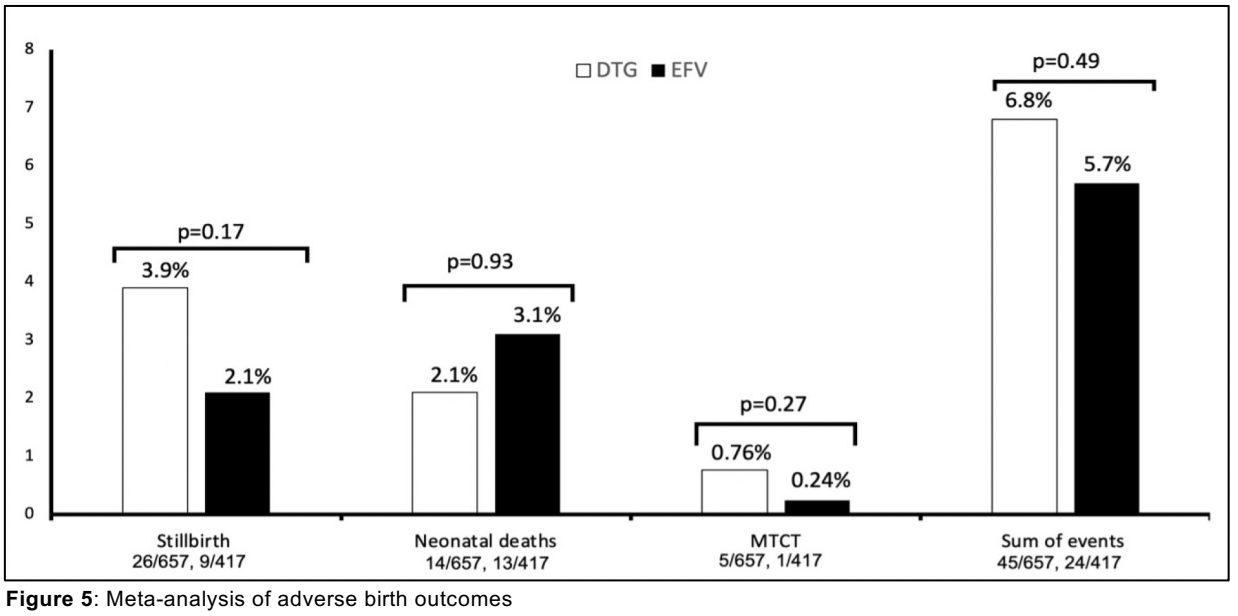

Figure 5: Meta-analysis of adverse birth outcomes

References:

1. Asif S, Baxevanidi E, Hill A, Venter WDF, Fairlie L, Masenya M, Serenata C, Sokhela S, Chandiwana N. The predicted risk of adverse pregnancy outcomes as a result of treatment-associated obesity in a hypothetical population receiving tenofovir alafenamide/emtricitabine/dolutegravir, tenofovir disoproxil fumarate/emtricitabine/dolutegravir or tenofovir disoproxil fumarate/emtricitabine/efavirenz. AIDS. 2021 Dec 15;35(Suppl 2):S117-S125. doi: 10.1097/QAD.0000000000003020. PMID: 34261099.