Interim doravirine safety results from a pilot switch study for women of childbearing potential (WCBP) in South Africa

Authors: Joana Woods[1], Simiso Sokhela[1], Bronwyn Bosch[1], Godspower Akpomiemie[1]
1. Ezintsha, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Background

Women comprise almost half of those living with HIV globally, yet fewer antiretroviral treatment (ART) options are available to them particularly in low- and middle-income countries. Doravirine is a non-nucleoside reverse transcriptase inhibitor and a potential alternative for women who do not tolerate either efavirenz- or dolutegravir-based ART [1–2].

Method

A pilot open label, single-arm, single center, phase 3, switch study, recruited 100 HIV-positive ART-experienced women in South Africa, to evaluate viral suppression, tolerability, overall safety, and efficacy of DOR/3TC/TDF.

Results

In a 24-week interim analysis, participants had: a mean age of 34 (IQR 22 - 49), 100 African black females and 32% unemployed. Pre study, 54% were on efavirenz and 47% on dolutegravir-based ART, with baseline virological suppression (VL<50) at screening. No serious adverse events (AE's) were reported, with 16% of AE's possibly related to doravirine (97% of AE's were Grade 1), there were no clinically significant neuropsychiatric outcomes. Statistically significant decreases in lipid panel from baseline to week 24 (n = 94) include: Cholesterol -0.50 (IQR -0.60 to -0.39) p<0.001; Triglycerides -0.15 (-0.23 to -0.07) p<0.001; LDL -0.18 (-0.27 to -0.09) p<0.001; HDL -0.25 (-0.31 to -0.19) p<0.001. Glucose changes not significant.

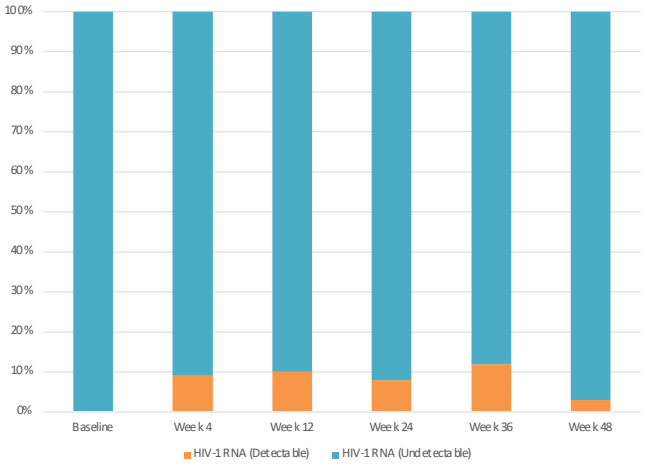

Figure 1: . Proportion of participants and HIV-1 RNA efficacy outcomes by visit

Results Cont.

Median weight gain from baseline to week 24 (n = 95) was 2 kg (IQR 0-5.4) in 82% of patients (95% CI: 74, 88). Of these, there was 3.2 kg weight gain (SD 4.4) in the efavirenz group and 1.4 kg (SD 3.7) in the dolutegravir group. Viral suppression at week 24 (n = 95): 92% HIV-1 RNA <50 copies/mL; 7% RNA 50-1000 copies/mL, 1% RNA >1000 copies/mL (at week 48 [n = 40]: 95%,3%,2% respectively). One patient developed doravirine resistance due to poor adherence. One pregnancy occurred, with good foetal outcomes.

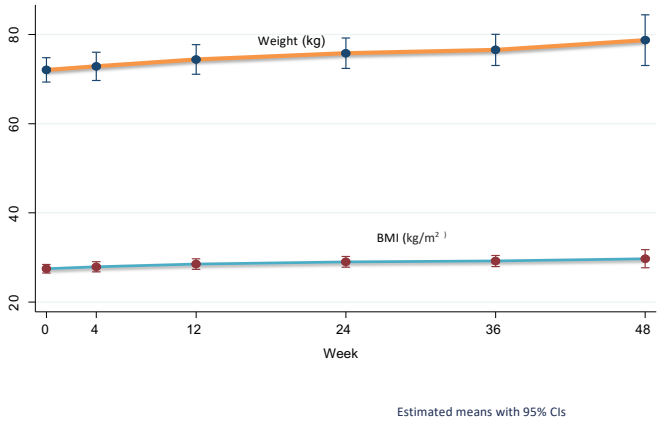

Figure 2: Mean changes in weight and body mass over study visits

Conclusion

Doravirine based regimes are an effective, tolerable alternative first line treatment in WCBP, with improved lipid profile, although potential long-term weight gain needs to be further investigated.

Regulatory approvals
We obtained ethical clearance from the University of the Witwatersrand Human Research Ethics Committee (191108), Approval was granted by the 19 Dec 2019.

Acknowledgements
We gratefully acknowledge the Gauteng Departments of Health for their partnership and support for this project. Thank you to the participants for sharing their experiences, views and recommendations. This project was supported in part by a research grant from the Investigator-Initiated Studies Program of Merck Sharp & Dohme LLC. The opinions expressed in this paper are those of the authors and do not necessarily represent those of Merck Sharp & Dohme LLC.

References:
1.Molina JM, Squires K, Sax PE, Cahn P, Lombaard J, DeJesus E, et al. Doravirine versus ritonavir-boosted darunavir in antiretroviral-naive adults with HIV-1 (DRIVE-FORWARD): 48-week results of a randomised, double-blind, phase 3, non-inferiority trial. The lancet HIV. 2018;5(5):e211-e20.
2.Orkin C, Squires KE, Molina JM, Sax PE, Wong WW, Sussmann O, et al. Doravirine/Lamivudine/Tenofovir Disoproxil Fumarate is Non-inferior to Efavirenz/Emtricitabine/Tenofovir Disoproxil Fumarate in Treatment-naive Adults With Human Immunodeficiency Virus-1 Infection: Week 48 Results of the DRIVE-AHEAD Trial. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2019;68(4):535-44

Corresponding Author:
Joana Woods
Email: jwoods@ezintsha.org.za **Website:** www.ezintsha.org