

**Web Appendix & Supplemental Materials**

**Supplemental Table 1: Metabolic Outcomes in Major Trials Evaluating Two-Drug ART Regimens**

Studies in ART Naive PLWHIV																																																									
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GEMINI-1 & 2 <sup>16,17</sup>	DTG/3TC	DTG + TDF/3TC	Mean change in lipids from baseline (week 48):	Mean change in renal markers from baseline (week 48):	Mean change in bone turn-over markers from baseline (week 48):	Mean change in weight from baseline (week 144):																																																			
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DTG + NRTI

SWORD 1 & 2 <sup>24-26, 79,80</sup>	DTG + RPV	Current/ standard ART Therapy (cART)  At 52 weeks, these participants were switched to DTG + RPV (late switch group)	Mean change in lipids from baseline (week 48):	Mean change in renal biomarkers from baseline (week 48) <sup>1</sup> :	Mean change in bone turn-over markers from baseline (week 48):																																																			
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\*\* Significance of P<0.01

<sup>1</sup> No change in median eGFR by serum cystatin C, regardless of previous TDF exposure in early-switch group; late-switch group showed a transient 7% reduction at week 100 followed by a return to late-switch baseline values at week 148

**Abbreviations:** DTG Dolutegravir, 3TC Lamivudine, TDF Tenofovir Disoproxil Fumarate, TAF Tenofovir alafenamide, FTC *emtricitabine*, mmol/L Millimoles per liter, TC total cholesterol, HDL high-density lipoprotein cholesterol, LDL low-density lipoprotein cholesterol, TRIG triglyceride, eGFR estimated glomerular filtration rate, SCr serum creatinine, Cr creatinine, LPV lopinavir, r ritonavir, ABC abacavir, ATV atazanavir, BMI body mass index, RT reverse transcriptase, NRTI nucleoside reverse transcriptase inhibitors, BMD bone mineral density, NRTI nucleoside reverse transcriptase inhibitors, DEXA dual-energy X-ray absorptiometry