# Evidence for safe use of doravirine with hormonal contraceptives in African women living with HIV

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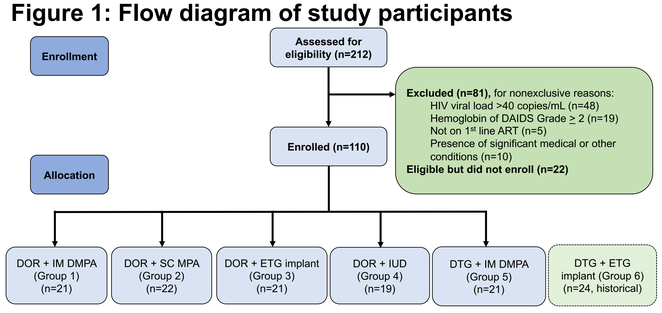
## BACKGROUND

- Prior to scale-up of new antiretroviral therapy (ART), exploring drug-drug interactions between ART and hormonal contraception is crucial
- EPIC is a parallel group pharmacokinetic study to examine drug-drug interactions between doravirine (DOR)-containing ART (DOR+3TC+TDF) and hormonal contraceptives (intramuscular [IM] or subcutaneous [SC] MPA, etonogestrel [ETG] implant) among women living with HIV in Johannesburg, South Africa

## METHODS

- Enrolled 110 participants, November 2021- February 2024
- Viral load (VL) ≤40 copies/mL, ≥6-week oral DOR lead-in
- Participants selected contraceptive groups (**Figure 1**)

**Figure 1: Flow diagram of study participants**




- Compared IM DMPA and ETG implant groups (**Table 1**)
- We report: 1) MPA and ETG concentrations (measured using validated LC-MS/MS assays and analyzed with log-transformed concentrations with geometric mean ratios at each visit), 2) safety (number & severity of adverse events [AE]), and 3) tolerability (patient satisfaction & adherence)

**Table 1: Baseline characteristics of women living with HIV, EPIC, Nov. 2021-Feb 2024**

| Characteristic, n (%) or median (IQR) | DOR + IM DMPA (Group 1) (n=21) | DOR + ETG implant (Group 3) (n=21) | DTG + IM DPMA (Group 5) (n=21) | DTG + ETG implant[1] (Group 6) (n=24) |
|---|---|---|---|---|
| **Age, years** | 35 (29, 38) | 37 (28, 40) | 39 (34, 41) | 35 (33, 37) |
| **Parity** | 2 (1, 3) | 3 (2, 3) | 2 (1, 3) | 3 (2, 3) |
| **Married** | 2 (9) | 2 (10) | 2 (8) | 11 (46) |
| **Educational level** | | | | |
| Primary | 0 | 0 | 0 | 14 (58) |
| Secondary | 22 (96) | 18 (86) | 24 (100) | 9 (38) |
| Higher | 1 (4) | 3 (14) | 0 | 1 (4) |
| **Ethnicity** | | | | |
| Zulu | 7 (30) | 8 (38) | 7 (29) | 0 |
| Sotho | 5 (22) | 6 (29) | 9 (38) | 0 |
| Xhosa | 2 (9) | 3 (14) | 1 (4) | 0 |
| Luo | 0 | 0 | 0 | 23 (96) |
| Other | 9 (39) | 4 (19) | 6 (25) | 0 |
| **BMI kg/m²** | 25 (21, 28) | 22 (20, 25) | 21 (19, 25) | 24 (2, 26) |
| **Duration on ART before study enrollment (years)** | 5 (3, 12) | 9 (6, 10) | 7 (6, 11) | 9 (8, 11) |

BMI=body mass index; ART=antiretroviral therapy; [1]A historical control group from PARVI study conducted in Kisumu, Kenya

DOR-containing ART **does not** reduce ***contraceptive hormone concentrations***, appears ***safe*** **and** ***tolerable*** among women concomitantly using contraceptives

## RESULTS

- Of 208 women screened, 110 (53%) enrolled, 104 (95%) completed study follow-up (**Table 1**):
  - Common reasons for ineligibility included lack of HIV viral suppression (n=48, 59%) and/or haemoglobin abnormality of grade 2 or higher (n=19; 23%)
  - Most were aged 28 years or older, had secondary or higher education level, not formally employed or married, and had been on ART for at least two years
- Age and body mass index-adjusted GMRs/visit were similar between groups (**Figures 2-3, Table 2**)
- Safety: of all AEs reported to date (n=269), 25 (9%) were attributable to DOR, of which headaches (n=9, 2%), nausea/vomiting (n=4, 1%), or change in appetite (n=4, 1%) were most frequent
  - All DOR-attributable AEs occurred at grade 1, except for 4 AEs at grade 2
- Tolerability: among DOR groups, only 1 participant reported any DOR dissatisfaction, and 88% of participants had >76% adherence by pill count
- Efficacy: 72/81 (89%) of exiting participants in the DOR groups with VL maintained viral suppression

**Figure 2: MPA concentrations by ART group**

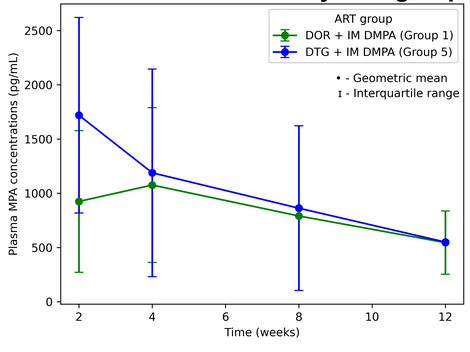



**Figure 3: ETG concentrations by ART group**

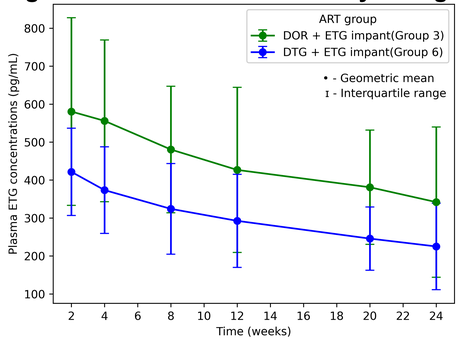



**Table 2: Hormone concentrations per study weeks after contraceptive method start, EPIC, Nov. 2021-Feb 2024**

| | Study weeks[1] | DOR-containing ART, median (range) | DTG-containing ART, median (range) | Unadjusted GMR[2] (90% CI) | Adjusted GMR[3] (90% CI) |
|---|---|---|---|---|---|
| MPA analysis | | **DOR + IM DMPA (Group 1, n=21)** | **DTG + IM DMPA (Group 5, n=21)** | | |
| | 2 | 1246.0 (2.0-2852.0) | 1761.0 (577-3610.0) | 0.76 (0.59, 0.97) | 0.85 (0.65, 1.11) |
| | 4 | 1046.5 (514.0-3913.0) | 1283.0 (384.0-4098.0) | 0.95 (0.83, 1.08) | 0.98 (0.86, 1.13) |
| | 8 | 805.0 (222.0-2310.0) | 984.0 (148.0-2136.0) | 0.96 (0.84, 1.11) | 1.04 (0.91, 1.19) |
| | 12 | 535.0 (295.0-1439.0) | 601.5 (13.0-3569.0) | 1.01 (0.82, 1.24) | 1.02 (0.82, 1.28) |
| ETG analysis | | **DOR + ETG implant (Group 3, n=21)** | **DTG + ETG implant (Group 6, n=24)** | | |
| | 2 | 589.0 (193.0-954.0) | 435.5 (93.0-600.0) | 1.15 (1.09, 1.21) | 1.16 (1.07, 1.26) |
| | 4 | 550.0 (157.0-4014.0) | 355.0 (256.0-788.0) | 1.19 (1.10, 1.29) | 1.21 (1.11, 1.33) |
| | 8 | 518.5 (163.0-2827.0) | 306.5 (226.0-518.0) | 1.19 (1.08, 1.30) | 1.20 (1.08, 1.32) |
| | 12 | 475.0 (85.0-953.0) | 258.0 (183.0-563.0) | 1.18 (1.05, 1.21) | 1.18 (1.07, 1.31) |
| | 20 | 390.0 (196.0-819.0) | 240.5 (138.0-562.0) | 1.21 (1.19,1.23) | 1.22 (1.13, 1.32) |
| | 24 | 378.0 (111.0-521.0) | 221.0 (91.0-456.0) | 1.20 (1.19, 1.20) | 1.21 (1.12, 1.31) |

ART=antiretroviral therapy; DOR=doravirine; DTG=dolutegravir; GMR=geometric mean ration; CI=confidence interval; BMI=body mass index.
Note: Lower limit of quantification (LLQ) for MPA or ETG is 20 pg/mL and for DOR or DTG is 20 ng/mL
[1]Weeks since initiation of the contraceptive method.
[2]Unadjusted linear mixed model comparing the GMR between the contraceptive + DOR group to the contraceptive + DTG group, with 90% CI
[3]Adjusted linear mixed model accounting for age and BMI

## CONCLUSIONS

- Detected no significant effects of DOR-containing ART on MPA or ETG contraceptives
- DOR-containing ART appears safe and tolerable
- These data support the viability of this option for those living in resource-limited settings who are intolerant of or unable to take DTG-containing ART

## ADDITIONAL KEY INFORMATION

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