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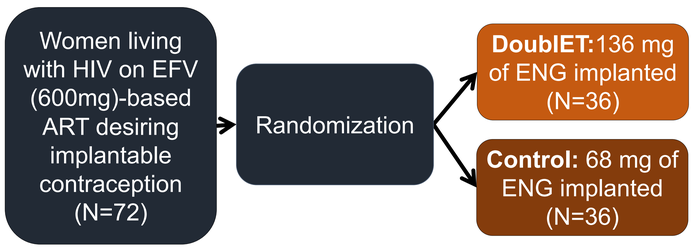
Double-Dose Etonogestrel Contraceptive Implant Overcomes Interaction with Efavirenz

Catherine A. Chappell[1], Mohammed Lamorde[2], Shadia Nakalema[2], Isabella Kyohairwe[2], Pauline Byakika-Kibwika[2], Leslie A. Meyn[1], Michelle Pham[3], Kimberly K. Scarsi[3]
[1]University of Pittsburgh Pittsburgh, PA, USA, [2]Infectious Diseases Institute, Kampala, Uganda, [3]University of Nebraska Medical Center, Omaha, NE, USA

BACKGROUND

- Concomitant use of EFV-based ART and an etonogestrel (ENG) contraceptive implant resulted in 82% lower ENG pharmacokinetics (PK) compared to women not receiving ART[1], increasing the risk of pregnancy[2].
- We hypothesized that doubling the dose of the ENG implant (DoublET group) would reduce the rate of ovulation and increase ENG PK compared to standard dose ENG (Control group) in women on EFV-based ART.

METHODS



- Key inclusion criteria: Regular menstrual periods (21-35 days) for two months and copper IUD at entry to prevent pregnancy.
- Ovulation analysis: The primary endpoint was ovulation over 48 weeks; evaluated by serum progesterone concentrations over 4 consecutive weeks at 3 (weeks 9-12), 6 (weeks 21-24) and 12 (weeks 45-48) months. Progesterone >3ng/mL were interpreted as consistent with ovulation[3].
- Ovulation rate was compared using Fisher's exact by month and generalized estimating equations over 48 weeks.
- PK analysis: Plasma was collected at day 3 and weeks 1, 4, 12, 24, 36 and 48 after implant placement.
- ENG PK was summarized as median (IQR) and compared between groups by geometric mean ratio with 90% CI.

RESULTS

Table 1 Demographic Characteristics

	DoublET (n=36)	Control (n= 36)
Age	31 (29, 34.5)	32 (28, 36)
Weight (kg)	59.25 (51.0, 69.5)	60.25 (55.0, 68.4)
Marital Status n (%)		
Single	6 (16.7%)	8 (22.2%)
Married	20 (55.5%)	23 (63.9%)
Separated	10 (27.8%)	5 (13.9%)
Prior Live Births; median (IQR)	3 (2.0, 3.25)	3 (2.75, 4.0)
CD4 count (cells/mm^3)	682 (535.5, 806.5)	654 (602.75, 917.25)

Placing **two** etonogestrel implants improved ovulation suppression and increased etonogestrel pharmacokinetics compared to one etonogestrel implant among women on efavirenz-based ART over the first year of combined use.

We recommend **doubling the dose** of etonogestrel with efavirenz-based ART to improve contraceptive effectiveness.

Figure 1: Study Flow

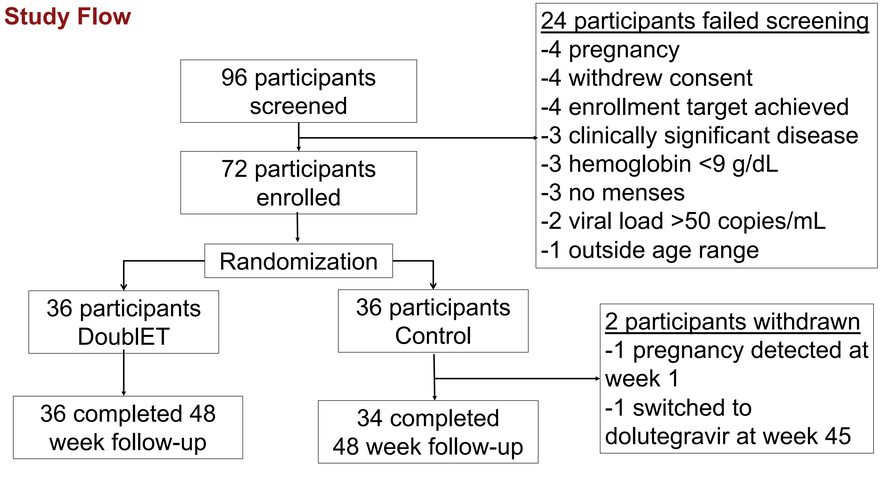
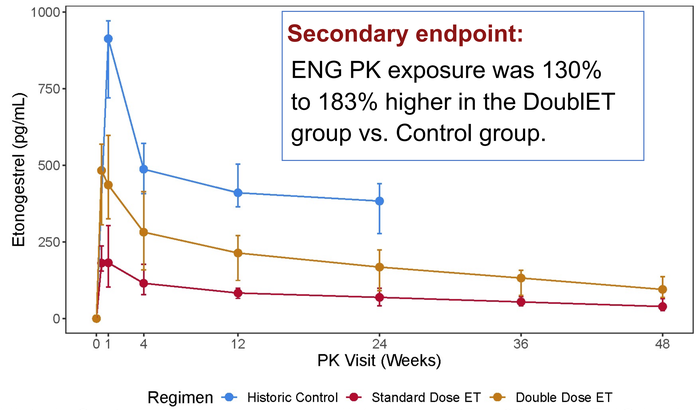


Table 2: Ovulation Number and Rate

	DoublET	Control
Month 3	0 (0%)	11 (31%)
Month 6	0 (0%)	17 (49%)
Month 12	2 (6%)	19 (56%)

Primary endpoint:
Over 48 weeks, the odds of ovulation were reduced by **97.7%** (95% CI: 90.1-99.5) in the DoublET group compared to the Control group.

Figure 2: Etonogestrel concentrations time curve*



*Historic Control: Women living with HIV not on ART + 68 mg of ENG implant[1]

Table 3: Etonogestrel Plasma Concentrations (pg/mL)

	DoublET Group: ENG 136 mg + EFV 600 mg-based ART (n=36)	Control Group: ENG 68 mg + EFV 600 mg-based ART (n=34)	GMR (90% CI) DoublET: Control
Day 3	484 (306, 570)	181 (155, 237)	2.69 (1.83, 3.32)
Week 1	439 (327, 618)	182 (102, 303)	2.74 (1.68, 3.47)
Week 4	282 (158, 414)	115 (79, 178)	2.35 (1.54, 2.93)
Week 12	214 (124, 271)	83 (66, 99)	2.49 (1.56, 3.14)
Week 24	168 (91, 224)	69 (42, 99)	2.30 (1.48, 2.89)
Week 36	132 (75, 157)	54 (42, 71)	2.40 (1.50, 3.05)
Week 48	95 (69, 137)	39 (25, 64)	2.83 (1.89, 3.53)

CONCLUSIONS

- For the first year of use, placing two ENG implants suppressed ovulation and increased ENG PK compared to one ENG implant among women on EFV-based ART.

REFERENCES

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