

Pregnancy Incidence and Outcomes Among Women Using the Dapivirine Vaginal Ring

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Background

- Monthly use of the dapivirine vaginal ring has been shown to be safe and effective for HIV-1 prevention
- Dapivirine is a novel NNRTI but data are limited on the safety of dapivirine use during pregnancy
- Understanding the safety of exposure during pregnancy is important for the potential roll-out of the dapivirine ring for HIV-1 prevention
- In MTN-020/ASPIRE, use of a highly effective contraceptive method was a criterion for study participation and highly effective methods were offered to study participants; however, pregnancies occurred, resulting in short-term exposure to study product during the periconception period

Objective: To compare pregnancy incidence and outcomes by study arm among women who participated in MTN-020/ASPIRE

Methods

Study design

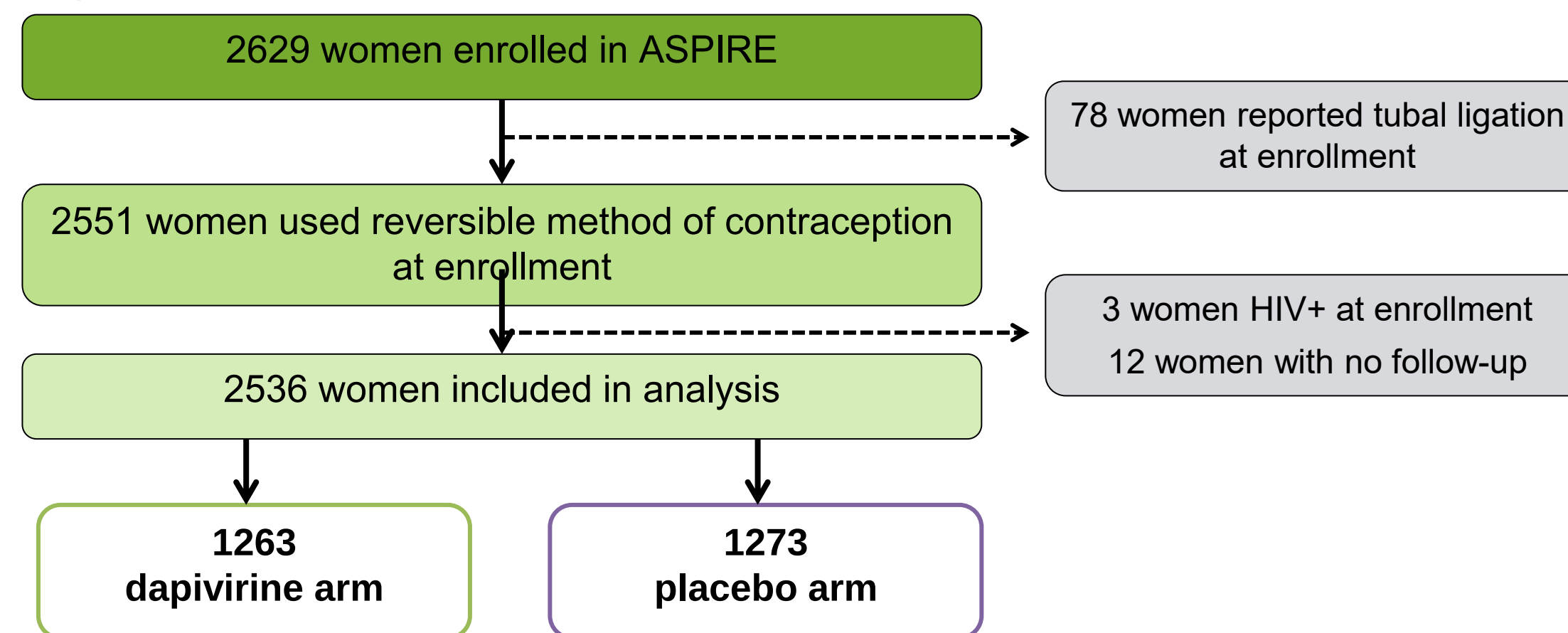
- ASPIRE was a randomised, double-blind, placebo-controlled phase III safety and effectiveness study of the dapivirine vaginal ring for HIV-1 prevention
- Sexually active women aged 18-45 from Malawi, South Africa, Uganda, and Zimbabwe were enrolled
- Urine pregnancy tests were performed monthly and, if positive, study product was withheld during pregnancy and breastfeeding
- Pregnancy outcomes and potential infant congenital anomalies were determined by participant report and medical record review

Statistical analysis

- Pregnancy incidence by arm was calculated and compared using an Andersen-Gill proportional hazards model with censoring at HIV infection
 - Women who reported a bilateral tubal ligation at enrollment, were found to be HIV infected at enrollment, and who did not return for follow-up were excluded from analysis
- Descriptive statistics were used to summarize pregnancy and infant outcomes by arm

Results

Figure 1. Analysis Population



- 169 women became pregnant during follow-up, resulting in 179 incident pregnancies and 180 pregnancy outcomes (1 set of twins)
- No difference in pregnancy incidence by study arm was observed (**Table 1**) (Hazard ratio = 0.93; 95% CI 0.68-1.26)

Table 1. Pregnancy incidence by study arm

	Dapivirine	Placebo	Total
# of pregnancies/p-yrs	86/2,162	93/2,172	179/4,334
Pregnancy incidence (per 100 p-yrs)	4.0 (3.1-5.1)	4.3 (3.4-5.5)	4.1 (3.5-4.9)

Table 2. Select participant characteristics at enrollment

	Became pregnant during follow-up N=169	Did not become pregnant during follow-up N= 2367
Median age in years (range)	23 (21, 27)	26 (22, 31)
Married	65 (38%)	962 (40%)
Secondary education or greater	94 (56%)	1,093 (46%)
Number of live births	2 (1, 2)	2 (1, 3)

Table 3. Pregnancy outcomes by arm

	Dapivirine N=86	Placebo N=94
Full term live birth	52 (60%)	53 (56%)
Preterm birth	0 (0%)	9 (10%)
Stillbirth/Intrauterine fetal demise	2 (2%)	2 (2%)
Spontaneous abortion	18 (21%)	21 (22%)
Therapeutic/elective abortion	13 (15%)	8 (9%)
Ectopic pregnancy	1 (1%)	1 (1%)

- The distribution of pregnancy outcomes appears similar by study arm (**Table 3**)
- No difference noted in frequency or pattern of potential congenital anomalies by arm (**Table 4**)

Table 4. Congenital anomalies by arm¹

	Dapivirine N=48	Placebo N=59
Any anomaly	4 (8%)	4 (7%)
Physical defect	1 (2%)	3 (5%)
Cranio-facial	1 (2%)	0
Other	2 (4%)	1 (2%)

¹Data available for 107 of 114 live births

Conclusions

- Pregnancy rates did not differ between women randomized to dapivirine ring versus placebo ring
- Pregnancy outcomes and the frequency of site-identified congenital anomalies were also similar by arm
- Dapivirine use in the periconception period does not appear to be associated with adverse effects on pregnancy
- Additional studies are needed to further assess the safety of the dapivirine ring use throughout pregnancy

References

Beaten JM et al: Use of a vaginal ring containing dapivirine for HIV prevention in women. N Engl J Med 2016; 375: 2121-32
Nel et al: Safety and efficacy of a dapivirine vaginal ring for HIV prevention in women. N Engl J Med 2016; 375: 2133-43