

Endometrial Safety with a 1-Year Segesterone Acetate/Ethinyl Estradiol Contraceptive Vaginal System

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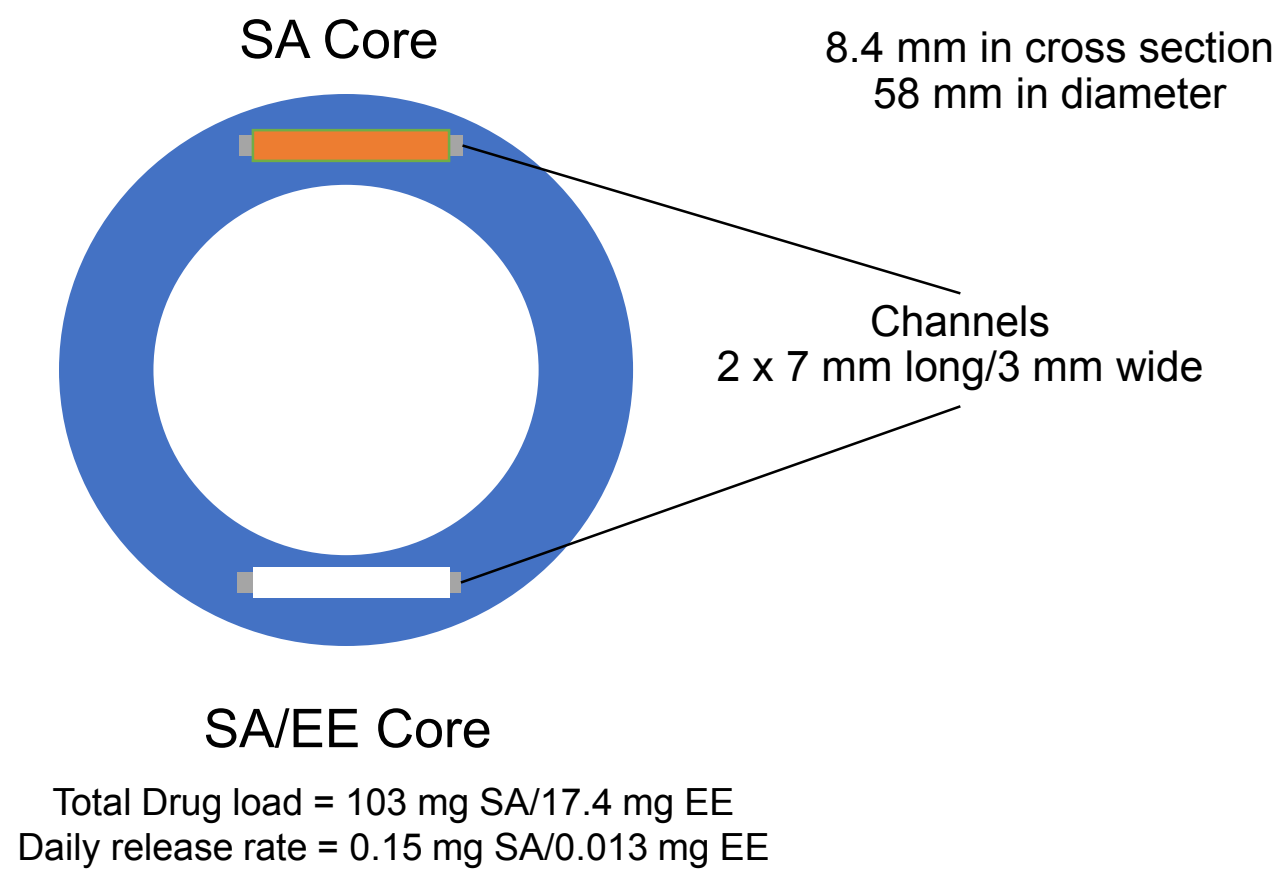
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Background

- A new contraceptive vaginal system (CVS) used for up to 13 cycles
 - Releases daily mean of segesterone acetate (SA) 0.15 mg and ethinyl estradiol (EE) 0.013 mg (**Figure 1**)
- Endometrial histology ranges from atrophic to proliferative or secretory with combined hormonal contraceptives¹⁻⁴

Figure 1. Segesterone acetate/ethinyl estradiol contraceptive vaginal system (SA/EE CVS)



Objective

To demonstrate the endometrial safety profile of the SA/EE CVS after 13 cycles of use

Methods

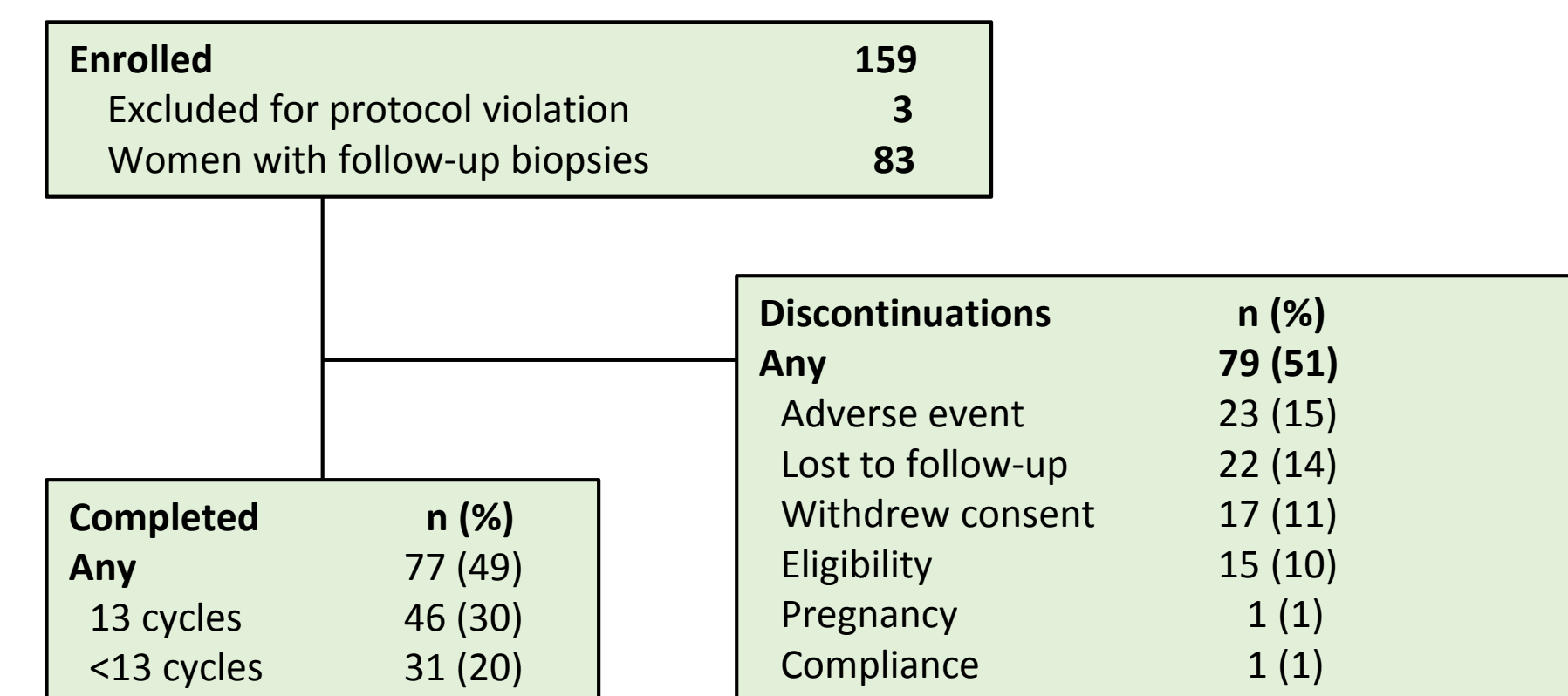
- Phase 3, multicenter, open-label study enrolled 1135 18-40 year old women to evaluate efficacy and safety of a single SA/EE CVS used on a 21-day in/7-day out regimen for up to 13 cycles
- Women could elect to join an endometrial safety substudy at 6 sites
 - All had baseline endometrial biopsies
 - First 25 women reaching cycle 6 had repeat biopsies
 - Remaining had biopsies at cycles 12-13 or at early termination
- Biopsies evaluated by three blinded pathologists
 - Women with endometrial hyperplasia or carcinoma at baseline were excluded
 - If diagnoses by pathologists differed, the most severe was used
 - A shift table was generated for results from baseline to second evaluation at cycle 6 or cycles 12-13

Results

Table 1. Patient characteristics

Characteristic	N=156 n (%)
Age, y	
18-19	5 (3.2)
20-24	56 (35.9)
25-29	55 (35.3)
30-35	28 (17.9)
≥36	12 (7.7)
BMI, kg/m²	
<20	18 (11.5)
20≤ value <25	81 (51.9)
25≤ value <27	19 (12.2)
27≤ value <29	24 (15.4)
29≤ value	14 (9.0)
Ethnicity	
Hispanic or Latina	12 (7.7)
Not Hispanic or Latina	144 (92.3)
Race (multiple races included)	
White	104 (66.7)
Black/African-American	46 (29.5)
Asian	4 (2.6)
American Indian or Native Alaskan	2 (1.3)
Native Hawaiian or Pacific Islander	1 (0.6)
Other/Unknown	4 (2.6)

Figure 2. Subject disposition



Biopsies and Histology

- 83 of 156 substudy participants had follow-up biopsies, all occurred between cycles 5 and 16 (**Table 2**)
- No cases of endometrial hyperplasia or carcinoma were found in any follow-up biopsies (**Table 3**)
- The most frequent histologic diagnoses during treatment were atrophic/inactive or secretory tissue (**Table 3**)
- No biopsies shifted from normal at baseline to hyperplasia at cycle 6 or cycles 12-13 (**Table 4**)
- One subject's biopsy shifted from hyperplasia at baseline to normal at cycle 6 (**Table 4**)

Table 2. Abnormal endometrial histology findings

Cycle	n	Normal	Abnormal			
			Hyperplasia	EIN	Polyp	Other
Baseline	156	149	2 ^a	0	0	5
Cycles 5-6	27	26	0	0	1	0
Cycles 7-11	25	25	0	0	0	0
Cycles 12-13	30	29	0	0	1	0
Cycles >13 ^b	1	1	0	0	0	0

^aOne subject was discontinued from and one subject continued in the substudy

^bOne subject used the CVS for 14 cycles and had a biopsy performed at cycle 16

EIN, endometrial intraepithelial neoplasia

Table 3. Endometrial histology by cycle

Results, n (%)	Baseline ^a (n=83)	Cycle 6 (n=24)	Cycles 12-13 (n=30)	Other (n=29)
Normal				
Insufficient or no tissue	4 (5)	0	3 (10)	1 (3)
Atrophic/inactive	6 (7)	7 (29)	8 (27)	8 (28)
Proliferative	33 (40)	4 (17)	2 (7)	6 (21)
Secretory	25 (30)	7 (29)	11 (37)	13 (45)
Menstrual	2 (2)	1 (4)	2 (7)	0
Mixed	9 (11)	4 (17)	3 (10)	1 (3)
Abnormal - hyperplasia	1 (1)	0	0	0
Other				
Endometritis	1 (1)	0	0	0
Endometrial polyp	0	1 (4)	1 (4)	0

^aAll subjects with both a baseline and follow-up biopsy

Table 4. Shifts for endometrial histology from baseline to cycles 6 and 12-13

Baseline results	On-treatment Results, n (%)							
	Insufficient or no tissue	Atrophic/inactive	Proliferative	Secretory	Menstrual	Mixed	Hyperplasia/carcinoma	Other abnormal
Cycle 6 (n=24)								
Insufficient or no tissue	0	0	0	0	0	0	0	0
Atrophic/inactive	0	2 (8)	0	0	0	0	0	0
Proliferative	0	4 (17)	3 (13)	2 (8)	1 (4)	1 (4)	0	0
Secretory	0	0	0	2 (8)	0	1 (4)	0	1 (4)
Menstrual	0	0	0	0	0	1 (4)	0	0
Mixed	0	1 (4)	1 (4)	1 (4)	0	1 (4)	0	0
Hyperplasia/carcinoma	0	0	0	1 (4)	0	0	0	0
Other	0	0	0	1 (4)	0	0	0	0
Cycles 12-13 (n=30)								
Insufficient or no tissue	0	1 (3)	0	0	0	0	0	0
Atrophic/inactive	1 (3)	1 (3)	0	0	0	0	0	0
Proliferative	2 (7)	0	2 (7)	2 (7)	2 (7)	2 (7)	0	1 (3)
Secretory	0	3 (10)	0	5 (17)	0	1 (3)	0	0
Menstrual	0	0	0	1 (3)	0	0	0	0
Mixed	0	3 (10)	0	2 (7)	0	0	0	0
Hyperplasia/carcinoma	0	0	0	0	0	0	0	0
Other	0	0	0	1 (3)	0	0	0	0

Summary and Conclusions

- No cases of endometrial hyperplasia, endometrial intraepithelial neoplasia, or carcinoma were identified with CVS use
- Women who used the SA/EE CVS for up to 13 cycles did not have any unexpected endometrial safety effects based on endometrial histology

References

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Disclosures

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