Efficacy of the 1-Year Segesterone Acetate/Ethinyl Estradiol Contraceptive Vaginal System

Carolyn L Westhoff, MD[1]; Philip Darney, MD[2]; Jeffrey T Jensen, MD[3]; Luis Bahamondes, MD[4]; Dan Apter, MD, PhD[5]; Ruth B Merkatz, PhD[6]

[1]Columbia University Irving Medical Center, New York, NY, USA
[2]University of California, San Francisco General Hospital, San Francisco, CA, USA
[3]Oregon Health & Science University, Portland, OR, USA
[4]University of Campinas, Campinas, Brazil
[5]VL-Medi Clinical Research Center, Helsinki, Finland
[6]Population Council, New York, NY, USA

Disclosures

Dr. Westhoff

- **Consultant/Advisory board:** Allergan, Bayer Healthcare, Cooper Surgical, and Merck
- **Research support:** Agile Therapeutics, Estetra SPRL, Leon Farma, and Medicines 360

Dr. Jensen

- **Advisory board:** AbbVie, Bayer Healthcare, Merck, Population Council, and Sebela
- **Research support:** AbbVie, Bayer Healthcare, Dare Bioscience, Estetra SPRL, Medicines 360, Merck, NIH, and NICHD

Dr. Apter

- **Research support:** WHO

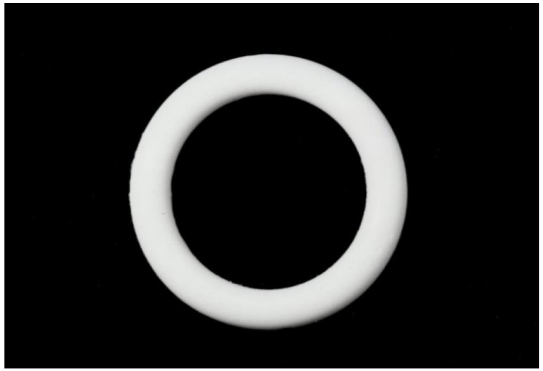
Dr. Merkatz

- **Works with** Population Council, an international, non-profit research organization

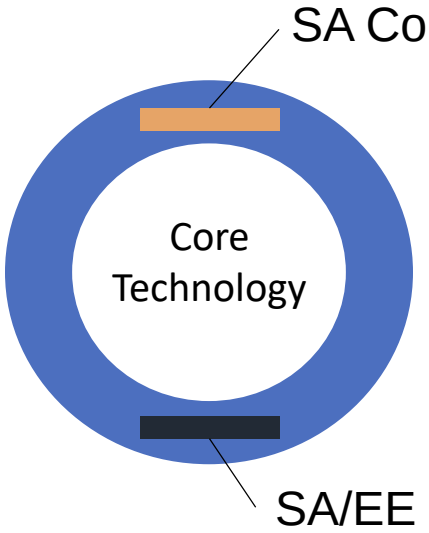
Drs. Darney and Bahamondes

- No conflicts of interest

Segesterone Acetate/Ethinyl Estradiol (SA/EE) 1-Year Contraceptive Vaginal System (CVS)



Delivers average of SA 0.15 mg/EE 0.013 mg/day
13 cycles: 3 weeks on/1 week off



8.4 mm (3/8”) cross section

58 mm (2 1/4”) diameter

EE: ethinyl estradiol; SA: segesterone acetate

Objectives

- To evaluate the contraceptive efficacy of the SA/EE CVS in two phase 3, multicenter, 1-year, open-label trials
- To evaluate the acceptability data of the CVS assessed in one of these phase 3 trials

CVS: contraceptive vaginal system; EE: ethinyl estradiol; SA: segesterone acetate

Two Phase 3 Pivotal Trials: Clinical Sites

- 300A (CCN006) conducted by NICHD CCTN
  - 15 study sites in the US
- 300B supported by Population Council, USAID & WHO
  - 12 international study sites
    - 3 in Latin America (Brazil, Chile, Dominican Republic)
    - 3 in Europe (Finland, Hungary, Sweden)
    - 1 in Australia
    - 5 in US (Bronx, Columbus, Chicago, Los Angeles, San Francisco)
  - Assessed acceptability of the CVS

NICHD: National Institute of Child Health and Human Development; USAID: United States Agency for International Development; WHO: World Health Organization.

Phase 3 Trials: Efficacy Assessments

Primary endpoint

- Pearl Index (PI) for women ≤35 years of age
  - Estimates the number of pregnancies per 100-woman years of product use
  - Number of pregnancies/number of on-treatment cycles X 1300
  - Excludes cycles with adjunctive contraception

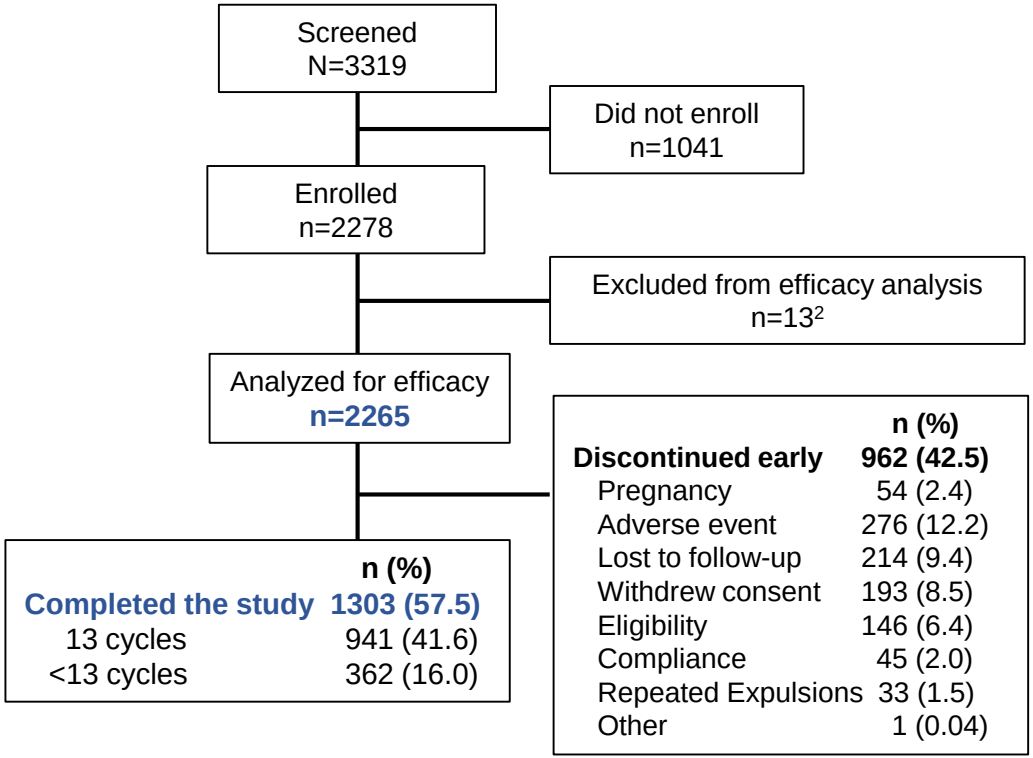
Secondary outcomes

- PI for subgroups
- Intent-to-treat (ITT) Kaplan-Meier life-table analyses

Women (18–40 yrs) followed a 21/7-day in/out schedule up to 13 cycles and were instructed to keep the CVS in continuously for 21 days per cycle

Subject Disposition and Demographics

- Mean age: 26.7 y
- Mean BMI: 24 kg/m^2
- Race[1]
  - White: 77%
  - Black/African American: 19%
  - Asian: 5%
  - Unknown: 5.0%
  - American Indian: 1.2%
  - Native Hawaiian: 0.7%



[1]Multiple races allowed per subject. [2]Includes 12 subjects who enrolled at more than one site and one subject who did not contribute any cycles for analysis.

Pearl Index (PI)

- Primary PI was 2.98 (95% CI 2.13–4.06) per 100 women-years in women ≤35 years (n=2111; 17,427 cycles)
  - Younger age correlated to higher contraceptive failure, which is consistent with findings from other contraceptive studies[1,2]

Subgroup analysis by age	n	Pearl Index (95% CI)
18-19	140	8.15 (3.50–15.8)
20-24	842	4.22 (2.69–6.24)
25-29	744	1.65 (0.75–3.07)
30-35	385	1.20 (0.30–3.12)
≥36	154	0.99 (0.06–4.34)

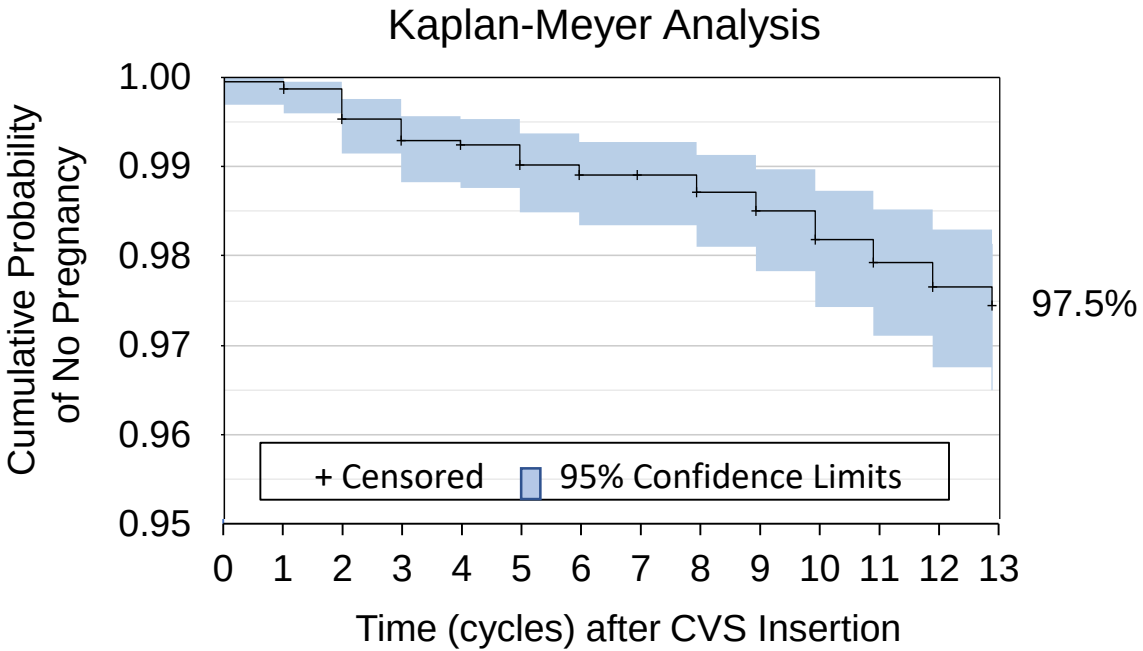
1. Winner B, et al. *N Engl J Med* 2012;366:1998-2007. 2. Kazerooni R, et al. *Ann Pharmacother* 2015;49:1284-1290.

Secondary Endpoint: Pearl Index by Subgroup

- When analyzed by subgroups, the PI was significantly different by age, CVS removal, parity, race, ethnicity and site, but not BMI

ITT Subgroup Analysis, n=2265	Characteristics	n	Pearl Index (95% CI)
CVS Removal	<2 hours (followed use instructions) >2 hours (documented removals)	1706 421	**2.10 (1.37–3.06)** **5.89 (3.46–9.27)**
Parity	0 ≥1	1472 793	1.48 (0.83–2.40) **5.43 (3.63–7.74)**
Race	White African American Mixed race	1613 319 333	**1.77 (1.09–2.68)** **7.12 (3.70–12.2)** **5.19 (2.70–8.90)**
Ethnicity	Non-Hispanic Hispanic	1614 651	1.41 (0.79–2.28) **6.04 (4.04–8.62)**

Cumulative Probability of Not Becoming Pregnant with CVS Use Was 97.5%*

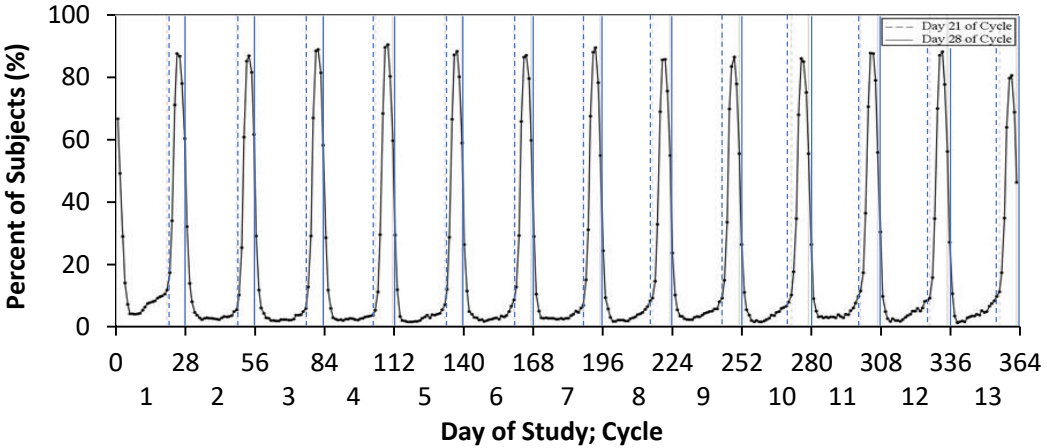


Pregnancies did not increase across cycles

*during or within 7 days of last CVS use

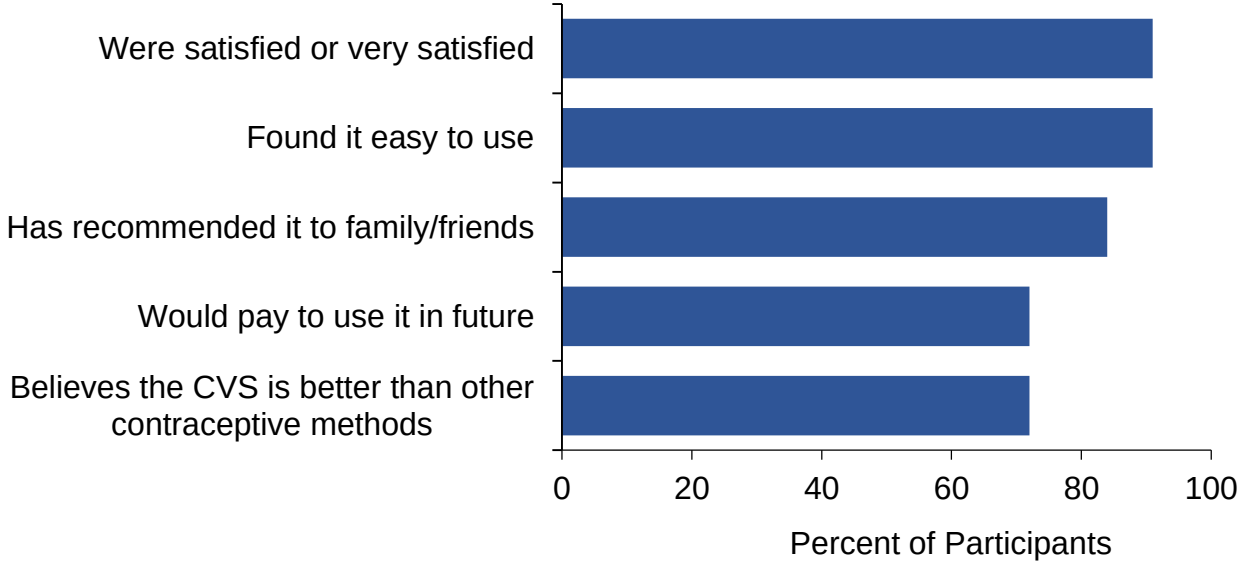
Bleeding Profile

- Mean number of scheduled bleeding was 4.6–5.2 days per cycle
  - 5%–8% of women reported absence of scheduled bleeding per cycle



- Early discontinuation due to unacceptable bleeding was 1.7%

CVS Acceptability Questionnaire



n=861

Conclusions

- SA/EE CVS (Annovera™) is an effective, convenient, easily-used novel contraceptive method
  - Approved by the US FDA August 10, 2018*
- 97.5% effective in preventing pregnancy
- High level of user satisfaction
- Under a woman's control
- Effective and convenient contraception for 1 year that may help address a worldwide contraceptive need

*TherapeuticsMD is licensed to market Annovera, SA/EE CVS in the United States

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THANK YOU

To the 3000+ women volunteers from 4 continents who helped us develop Annovera

The Investigators, sub investigators, coordinators and other dedicated staff at clinical sites

Product development scientists, statistical, data management, regulatory, legal and support staff

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