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

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Disclosures

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- **Consultant/Advisory board**: Allergan, Bayer Healthcare, Cooper Surgical, and Merck
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Dr. Jensen
- **Advisory board**: AbbVie, Bayer Healthcare, Merck, Population Council, and Sebela
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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/Ethynyl 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
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

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%

<table>
<thead>
<tr>
<th>Screened N=3319</th>
<th>Did not enroll n=1041</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled n=2278</td>
<td></td>
</tr>
<tr>
<td>Analyzed for efficacy n=2265</td>
<td></td>
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</tbody>
</table>

- Discontinued early n (%)
  - Pregnancy: 54 (2.4)
  - Adverse event: 276 (12.2)
  - Lost to follow-up: 214 (9.4)
  - Withdrew consent: 193 (8.5)
  - Eligibility: 146 (6.4)
  - Compliance: 45 (2.0)
  - Repeated Expulsions: 33 (1.5)
  - Other: 1 (0.04)

- Completed the study n (%)  
  - 13 cycles: 1303 (57.5)
  - <13 cycles: 941 (41.6)
  - >13 cycles: 362 (16.0)

\(^1\)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 studies¹,²

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

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

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

- Were satisfied or very satisfied
- Found it easy to use
- Has recommended it to family/friends
- Would pay to use it in future
- Believes the CVS is better than other contraceptive methods

Percent of Participants

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
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

Donors