The WISDOM survey: Physicians’ Level of Comfort Prescribing Treatment for Vulvar and Vaginal Atrophy (VVA) Symptoms in Women with a Predisposition or History of Breast Cancer

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Disclosures

• **Advisory board:** AMAG Pharmaceuticals, Palatin Technologies and Valeant Pharmaceuticals

• **Speaker’s bureau:** Valeant Pharmaceuticals
VVA in Breast Cancer Survivors

- More than 60% of postmenopausal breast cancer patients experience symptoms of VVA including vaginal dryness and dyspareunia\textsuperscript{1,2}
- VVA symptoms are the most poorly addressed side effects of adjuvant endocrine therapy including aromatase inhibitors\textsuperscript{3}
- Local estrogen therapy is an approved treatment of VVA in menopausal women
- A major concern of prescribing vaginal estrogens in breast cancer survivors is the potential risk of systemic absorption and potential breast effects\textsuperscript{3}

VVA: vulvar and vaginal atrophy.
Local Estrogen Therapy for Breast Cancer Survivors with VVA

- Local or systemic menopausal estrogen therapies for treating VVA are currently contraindicated for women with known, suspected, or a history of breast cancer.
- Pharmacokinetic studies have found very low to non-existent systemic absorption of some low-dose, local, vaginal estrogen therapies\textsuperscript{1-4}
- NAMS, ACOG, and IMS support using vaginal estrogens in women with a history of estrogen-dependent breast cancer who are unresponsive to non-hormonal therapies\textsuperscript{5-7}


# Estradiol Parameters for Vaginal vs Oral Estrogens

<table>
<thead>
<tr>
<th>Route</th>
<th>Products</th>
<th>Dose</th>
<th>Sampling Time (d)</th>
<th>AUC$_{0-24}$ (pg*h/mL)</th>
<th>C$_{avg}$ (pg/mL)</th>
<th>C$_{max}$ (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaginal</td>
<td>Premarin® Cream</td>
<td>0.3 mg CEE$^1$</td>
<td>7</td>
<td>231 ± 285 369 ± 28</td>
<td>9.6</td>
<td>12.8 ± 16.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.625 mg CEE$^2$</td>
<td>7</td>
<td>6.2</td>
<td>15.4</td>
<td>26.4</td>
</tr>
<tr>
<td></td>
<td>Vagifem®³</td>
<td>10 µg estradiol</td>
<td>14</td>
<td>157 ± 439</td>
<td>6.6</td>
<td>15.8 ± 35.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25 µg estradiol</td>
<td>14</td>
<td>110 ± 55 172 ± 80</td>
<td>4.6 ± 2.3</td>
<td>7.3 ± 2.4</td>
</tr>
<tr>
<td></td>
<td>TX-004HR⁴</td>
<td>4 µg estradiol</td>
<td>14</td>
<td>87 ± 43 110 ± 55</td>
<td>3.6 ± 1.8</td>
<td>4.8 ± 2.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>10 µg estradiol</td>
<td>14</td>
<td>110 ± 55 172 ± 80</td>
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<td>7.3 ± 2.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>25 µg estradiol</td>
<td>14</td>
<td>172 ± 80</td>
<td>7.1 ± 3.3</td>
<td>15.7 ± 7.6</td>
</tr>
<tr>
<td></td>
<td>Placebo⁴</td>
<td>14</td>
<td></td>
<td>104 ± 66</td>
<td>4.3 ± 2.8</td>
<td>5.5 ± 3.4</td>
</tr>
<tr>
<td>Oral</td>
<td>Estrace®⁵</td>
<td>2.0 mg estradiol</td>
<td>11</td>
<td>2642 ± 1156</td>
<td>110 ± 50</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Premarin®⁶</td>
<td>0.3 mg CEE</td>
<td>7</td>
<td>325 ± 499</td>
<td>13.5</td>
<td>19.4 ± 24.7</td>
</tr>
</tbody>
</table>

Data expressed as mean ± SD, when possible.

CEE: conjugated equine estrogens

Breast Cancer Risk With Vaginal Estrogens

- In the WHI-Observational Study (1993-2005), the risk of invasive breast cancer in women with or without an intact uterus was not significantly different between vaginal estrogen users and nonusers.

<table>
<thead>
<tr>
<th>Breast cancer</th>
<th>n</th>
<th>VE use N events (rate*)</th>
<th>No VE use N events (rate*)</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>45,663</td>
<td>40 (3.6)</td>
<td>1185 (4.1)</td>
<td>0.91 (0.64–1.29)</td>
</tr>
<tr>
<td>Intact uterus†</td>
<td>32,433</td>
<td>26 (3.2)</td>
<td>858 (4.0)</td>
<td>0.79 (0.51–1.22)</td>
</tr>
<tr>
<td>Hysterectomy†</td>
<td>14,133</td>
<td>14 (4.7)</td>
<td>327 (4.2)</td>
<td>1.23 (0.68–2.21)</td>
</tr>
</tbody>
</table>

*Rate/1000 person-year; †Numbers don’t add up, due to the time varying nature of hysterectomy status: 903 change from no hysterectomy to hysterectomy and are counted in both cells.
CI: confidence interval; HR: hazard ratio; VE: vaginal estrogens.

Objective

• To evaluate physicians’ behaviors and attitudes regarding VVA treatment in menopausal women
  • The WISDOM survey
  • This report focuses on treating women with or without a history of breast cancer
Survey Topics

• Number of patients seen in a month, stratified by age
• Number of menopausal women with VVA or VMS symptoms
• Treatments used for VVA
• Beliefs on local estrogen therapy use
• Use of vaginal estrogen in women with breast cancer history or predisposition
Overview of Patients

- In a typical month, OB/GYNs and PCPs see 111 and 99 menopausal women, respectively.
  - Of these, 61 (55%) and 44 (44%) had VVA symptoms, respectively.

*VVA symptoms such as painful intercourse (dyspareunia), vaginal dryness, vaginal itching and burning and/or bleeding with intercourse.
†VMS symptoms such as hot flashes and/or night sweats.
Treatments for VVA

- Prescription therapy was the most common VVA treatment
  - More OB/GYNs than PCPS preferred to treat VVA with prescription therapy
  - OB/GYNs wrote more scripts per month than PCPs (44 vs 35)

<table>
<thead>
<tr>
<th>Treatment recommended to patients with VVA</th>
<th>OB/GYNs (n=369)</th>
<th>PCPs (n=275)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prescription Therapy*</td>
<td>53%</td>
<td>43%</td>
</tr>
<tr>
<td>OTC products only†</td>
<td>23%</td>
<td>25%</td>
</tr>
<tr>
<td>Behavioral/lifestyle management only‡</td>
<td>9%</td>
<td>12%</td>
</tr>
<tr>
<td>Vaginal laser therapy only</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>No treatment</td>
<td>13%</td>
<td>15%</td>
</tr>
</tbody>
</table>

*With or without any other type of treatment; †Vaginal lubricants and moisturizers; ‡Increased sex, vaginal dilation, other. OTC: Over the counter.
Local Vaginal Estrogen Use

- Most felt comfortable using localized estrogen therapy for menopausal women

"I feel comfortable using localized estrogen therapy for menopausal women"

<table>
<thead>
<tr>
<th>Agree/Strongly agree</th>
<th>Neutral</th>
<th>Disagree/Strongly disagree</th>
</tr>
</thead>
<tbody>
<tr>
<td>OB/GYNs (n=369)</td>
<td>PCPs (n=275)</td>
<td></td>
</tr>
</tbody>
</table>

- Agree/Strongly agree: 87% for OB/GYNs, 65% for PCPs
- Neutral: 4% for OB/GYNs, 16% for PCPs
- Disagree/Strongly disagree: 9% for OB/GYNs, 19% for PCPs
Local Vaginal Estrogen vs Other Therapies

• Most physicians prefer using localized estrogen therapy over other therapies

“I prefer the use of localized estrogen therapies over other therapies”
No Personal History of Breast Cancer

- Most physicians were comfortable prescribing therapy to treat VVA among women with no personal history or predisposition to breast cancer.

“How comfortable are you in using existing prescription therapy* to treat VVA in women with no personal history or predisposition to breast cancer?”

*Vaginal or oral ET, Osphena, Estring, DHEA, or other existing VVA products.
OB/GYNs seem to be more comfortable than PCPs prescribing existing therapy to women with a personal history of breast cancer. But only 34% of OB/GYNs are comfortable doing so.

"How comfortable are you in using existing prescription therapy* to treat VVA in women with a personal history of breast cancer?"

*Vaginal or oral ET, Osphena, Estring, DHEA, or other existing VVA products.
Predisposition to Breast Cancer

- OB/GYNs are more comfortable than PCPs prescribing therapy to women with a predisposition to breast cancer, such as a family history or a BRCA mutation.
  - But only 49% of OB/GYNs are comfortable doing so.

"How comfortable are you in using existing prescription therapy* to treat VVA in women with a predisposition to breast cancer†?"

*Vaginal or oral ET, Osphena, Estring, DHEA, or other existing VVA products.
†Family history, BRCA mutations, etc.
Conclusions

- Most OB/GYNs and PCPs are comfortable prescribing vaginal estrogen therapy for VVA, and prefer it over other products.
- However, a relatively low percentage of OB/GYNs and PCPs are comfortable prescribing VVA therapies to women with a history of or a predisposition to breast cancer.
  - Twice as many OB/GYNs felt comfortable prescribing therapy to women with a personal history or a predisposition to breast cancer than PCPs.
- Physician comfort level is low despite:
  - Medical-society support for using vaginal estrogen therapy in women with a history of estrogen-dependent breast cancer who were unresponsive to non-hormonal therapies.
  - Studies showing very low to negligible systemic absorption of estradiol with some vaginal products.