Cervical Cancer: How can we overcome our history?

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Disclosures:

• Advisory Board participation: GSK/Tesaro, Merck, AstraZeneca
• Consultant: Deep6AI
Cervical cancer- a brief history of screening

- 1927: Papanicolaou and Bures note detection of cancer and dysplasia in cervical cells
- 1928: Papanicolaou presents data at "The Third Race Betterment Conference"
- 1941: Papanicolaou and Traut publish "Pap test"
The Shero behind the pap smear

Mrs. Andromahi Papanicolaou
- Worked with her husband in pathology laboratory at Cornell
- Underwent daily Pap smears for 20 years
Cervical cancer- a brief history of screening

1927 Papanicolaou and Bures note detection of cancer and dysplasia in cervical cells

1928 Papanicolaou presents data at “The Third Race Betterment Conference”

1941 Papanicolaou and Traut publish “Pap test”

1950s Pap testing starts in US

1976 zur Hausen determines HPV likely cause of cervical cancer

1995 HPV 16 and 18 are sequenced and concluded as causal agents for cervical cancer

2000s Liquid based cytology begins

2006 Gardasil HPV vaccine introduced

2014 HPV test FDA approved
Cervical cancer incidence was reduced by screening

14.81 per 100,000 in 1975

6.67 per 100,000 in 2018

Cervical cancer mortality did not decrease

SEER 9 5-Year Relative Survival Percent from 1975–2013, All Races, Females. Modeled trend lines were calculated from the underlying rates using the Joinpoint Survival Model Software.
Stage of disease dictates cure

**5-Year Relative Survival**

- **Localized**: 91.9%
- **Regional**: 58.2%
- **Distant**: 17.6%
- **Unknown**: 52.4%

**Percent of Cases by Stage**

- **Localized (44%)**
- **Regional (36%)**
- **Distant (16%)**
- **Unknown (4%)**

SEER 18 2011–2017, All Races, Females by SEER Summary Stage 2000
### Rate of New Cases per 100,000 Persons by Race/Ethnicity: Cervical Cancer

<table>
<thead>
<tr>
<th>Sex-specific cancer type</th>
<th>MALE</th>
<th>FEMALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races</td>
<td>7.5</td>
<td>7.1</td>
</tr>
<tr>
<td>White</td>
<td>7.3</td>
<td>7.0</td>
</tr>
<tr>
<td>Black</td>
<td>8.6</td>
<td>8.4</td>
</tr>
<tr>
<td>Asian / Pacific Islander</td>
<td>6.4</td>
<td>6.3</td>
</tr>
<tr>
<td>American Indian / Alaska Native</td>
<td>7.6</td>
<td>7.0</td>
</tr>
<tr>
<td>Hispanic</td>
<td>9.3</td>
<td>9.0</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>7.1</td>
<td>7.0</td>
</tr>
</tbody>
</table>

SEER 21 2014-2018, Age-Adjusted
### Death Rate per 100,000 Persons by Race/Ethnicity: Cervical Cancer

<table>
<thead>
<tr>
<th>Sex-specific cancer type</th>
<th>MALE</th>
<th>FEMALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Races</td>
<td>2.2</td>
<td>2.0</td>
</tr>
<tr>
<td>White</td>
<td>2.1</td>
<td>2.1</td>
</tr>
<tr>
<td>Black</td>
<td>3.3</td>
<td>3.2</td>
</tr>
<tr>
<td>Asian / Pacific Islander</td>
<td>1.7</td>
<td>1.5</td>
</tr>
<tr>
<td>American Indian / Alaska Native</td>
<td>2.4</td>
<td>2.3</td>
</tr>
<tr>
<td>Hispanic</td>
<td>2.6</td>
<td>2.4</td>
</tr>
<tr>
<td>Non-Hispanic</td>
<td>2.2</td>
<td>2.0</td>
</tr>
</tbody>
</table>

U.S. 2014–2018, Age-Adjusted
Treatment for advanced stage disease remains palliative.

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Chemotherapy</th>
<th>N</th>
<th>RR</th>
<th>CR</th>
<th>PR</th>
<th>PFS (mos)</th>
<th>OS (mos)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOG 43</td>
<td>CP 50mg/m2 D1</td>
<td>150</td>
<td>20.7%</td>
<td>10%</td>
<td>10.7%</td>
<td>3.7</td>
<td>7.1</td>
</tr>
<tr>
<td>GOG 43</td>
<td>CP 100mg/m2 D1</td>
<td>166</td>
<td>31.4%*</td>
<td>12.7%</td>
<td>18.7%</td>
<td>4.6</td>
<td>7.0</td>
</tr>
<tr>
<td>GOG 43</td>
<td>CP 20mg/m2 D1-5</td>
<td>128</td>
<td>25%</td>
<td>8.6%</td>
<td>16.4%</td>
<td>3.9</td>
<td>6.1</td>
</tr>
<tr>
<td>GOG 110</td>
<td>CP + I</td>
<td>140</td>
<td>17.8%</td>
<td>6.4%</td>
<td>11.4%</td>
<td>3.2</td>
<td>8.0</td>
</tr>
<tr>
<td>GOG 149</td>
<td>CP + I + B</td>
<td>141</td>
<td>31.2%</td>
<td>NR</td>
<td>NR</td>
<td>5.1</td>
<td>8.4</td>
</tr>
<tr>
<td>GOG 169</td>
<td>CP + P</td>
<td>134</td>
<td>19%</td>
<td>6%</td>
<td>13%</td>
<td>2.8</td>
<td>8.8</td>
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<tr>
<td>GOG 179</td>
<td>CP + T</td>
<td>146</td>
<td>13%</td>
<td>2.9%</td>
<td>10.1%</td>
<td>2.9</td>
<td>6.5</td>
</tr>
<tr>
<td>GOG 204</td>
<td>CP + T</td>
<td>111</td>
<td>23.4%</td>
<td>1.8%</td>
<td>21.6%</td>
<td>4.6</td>
<td>10.3</td>
</tr>
<tr>
<td>GOG 204</td>
<td>CP + G</td>
<td>112</td>
<td>22.3%</td>
<td>0.9%</td>
<td>21.4%</td>
<td>4.7</td>
<td>10.3</td>
</tr>
<tr>
<td>GOG 204</td>
<td>CP + V</td>
<td>108</td>
<td>25.9%</td>
<td>7.4%</td>
<td>18.5%</td>
<td>4.0</td>
<td>10.0</td>
</tr>
<tr>
<td>GOG 240</td>
<td>CP + P + Bev</td>
<td>115</td>
<td>50%</td>
<td>16%</td>
<td>35%</td>
<td>8.2*</td>
<td>17.5*</td>
</tr>
<tr>
<td>GOG 240</td>
<td>CP + P</td>
<td>114</td>
<td>46%</td>
<td>10%</td>
<td>36%</td>
<td>6.0*</td>
<td>15.0</td>
</tr>
<tr>
<td>T+P + Bev</td>
<td></td>
<td>112</td>
<td>48%</td>
<td>12%</td>
<td>37%</td>
<td>16.2</td>
<td></td>
</tr>
<tr>
<td>T+P</td>
<td></td>
<td>111</td>
<td>25%</td>
<td>5%</td>
<td>20%</td>
<td>12.0</td>
<td></td>
</tr>
</tbody>
</table>
Novel agents in cervical cancer suggest improvement is possible

• Cemiplimab improved OS compared to investigators choice chemotherapy in recurrent cervical cancer (EMPOWER-Cervical1/GOG-3016/ENGOT-cx9)
  • 12 months vs. 8.5 months (HR 0.69 ( 95% CI 0.56-0.84)

• Tisotumab vedotin – recurrent cervical cancer (innovaTV 204/GOG-3023/ENGOT-cx6)
  • ORR 24%, median duration of response 8.4 months

• Pembrolizumab +platinum/paclitaxel +/-bevacizumab in advanced stage chemo naïve cervical cancer (KEYNOTE-826 trial)
  • Met its primary PFS and OS endpoints (Merck press release)
How can we address both equity and therapy?

- Can we design trials for patients that will improve cervical cancer mortality for ALL those in the United States?
- We must ask ourselves the hard questions.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Category</th>
<th>Total</th>
<th>Chemotherapy Alone N (%)</th>
<th>Chemotherapy plus Bevacizumab N (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity</td>
<td>Hispanic</td>
<td>54</td>
<td>33 (15)</td>
<td>21 (9)</td>
<td>0.2316</td>
</tr>
<tr>
<td></td>
<td>Non-Hispanic</td>
<td>374</td>
<td>183 (81)</td>
<td>191 (84)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unknown/Unsp.</td>
<td>24</td>
<td>13 (6)</td>
<td>11 (5)</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td>Asian</td>
<td>19</td>
<td>11 (5)</td>
<td>8 (4)</td>
<td>0.7409</td>
</tr>
<tr>
<td></td>
<td>Black</td>
<td>60</td>
<td>30 (13)</td>
<td>30 (13)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Amer. Indian</td>
<td>5</td>
<td>2 (1)</td>
<td>3 (1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pacific Islander</td>
<td>1</td>
<td>1 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>White</td>
<td>351</td>
<td>179 (80)</td>
<td>172 (76)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unknown/Unsp.</td>
<td>16</td>
<td>6 (3)</td>
<td>10 (4)</td>
<td></td>
</tr>
</tbody>
</table>
What are the opportunities to do better?

Traditional clinical trial design

Reality
Rare Disease
• Treat it like a rare disease

Address structural racism
• Create clinical trials that address the inequities of participation

Cervical cancer affects low SES patients
• Create opportunities for patients who need tangible stuff to participate

Location matters
• Urban solutions are not the same as rural solutions
Feasibility

Structural
• Where are humans with cervical cancer?
• Where do they get their care?
• Do these centers open cervical cancer trials?
• If not, why? Cost? Lack of enrollment (insurance coverage/language/trust)?

Trial specific
• Are the inclusion criteria representative of a population that exists in sufficient quantity to study?
• Is there testing required for screening that has a significant time or requires multiple visits?
• Is there a role for a smaller or broader study?
Rare disease

• 13,800 newly diagnosed cervical cancer cases estimated in 2020.
• 4290 deaths due to cervical cancer

• Context: Myeloma cases in women estimated 14,740 in 2020
• Included on National Organization for Rare disorders.
• Cervical cancer is not.

Rare disease Magnets

- Registries
  - Large national well-annotated datasets
- Support groups-local and national and VIRTUAL
- Strategies utilizing electronic medical record data to screen populations in real time.
- Data sharing
Address structural racism

• “Diversity is silent on the subject of equity. In an anti-oppression context, therefore the issue is not diversity but rather equity. Often when people talk about diversity, they are thinking of only the non-dominant groups.” – Baltimore Racial Justice Action


Rate of New Cancers in the United States
Cervix, All Ages, All Races and Ethnicities, Female

Rate of New Cancers in the United States
Cervix, All Ages, All Races and Ethnicities, Female

US Census 2016: Black or African American alone, Percent


[https://www.census.gov/quickfacts/fact/map/US/RHI225219](https://www.census.gov/quickfacts/fact/map/US/RHI225219)
Rate of New Cancers in the United States
Cervix, All Ages, All Races and Ethnicities, Female


US Census 2016: Hispanic or Latino, percent

https://www.census.gov/quickfacts/fact/map/US/RHI725219
Rate of New Cancers in the United States
Cervix, All Ages, All Races and Ethnicities, Female

Percent in Poverty by Race
Povertyusa.org/data/2019

- White: 11.1%
- Hispanic: 19.6%
- Black: 23.0%
- Asian: 10.9%
- Native American: 24.9%
Low English fluency is a barrier to clinical trial enrollment

• In-person translation is essential for consent
  • Hospital based translator services are strongly preferred
  • Clinical trial budgets must reflect this requirement

• Patient reported outcomes need to be in the patient’s preferred language
  • *This includes online content!!*


Rate of New Cancers in the United States
Cervix, All Ages, All Races and Ethnicities, Female

Language other than English spoken at home, percent of persons age 5 years +, 2015-2019


https://www.census.gov/quickfacts/fact/map/US/POP815219
Location Matters

Incidence is higher in some places. Rural and Urban areas differ.
Rate of New Cancers in the United States
Cervix, All Ages, All Races and Ethnicities, Female

Households with a broadband Internet subscription, percent 2015-2019


https://www.census.gov/quickfacts/fact/map/US/INT100219

#burnerphones4research
Final thoughts

• Reimagine cervical cancer as a disease of patients who are historically underrepresented due to race, language, poverty and location.

• Recognize that cervical cancer is rare disease.

• Consider clinical trial designs that improve equity
  1. Allow smaller enrollment numbers per site
  2. Promote non-English fluent patients to participate
  3. Compensate patients for their travel or provide them with tech to allow for off-site monitoring
Thank you

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United States of America
Dr. Sarah Temkin
Dr. Janine Clayton
Dr. Vivian Pinn

The Office of Research on Women’s Health