Clinical Trials in Cervical Cancer – Can they be all we want them to be?

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- Grants – NCI - UG1 CA23330, P50 CA 098252
- Contracted Research – Agenus, Seattle Genetics, Rubius Therapeutics
- Scientific Advisory Board – Seattle Genetics
Cervical Cancer – A Global Problem

- 604,127 (3.1%) cases
- 341,831 (3.4%) deaths
Four Decades of Cervical Cancer in the US – Why we are here today

Legend (Race/Ethnicity)
- Red: All Races (includes Hispanic)
- Blue uptriangle: Black (includes Hispanic)
- Green downward triangle: White (includes Hispanic)

Source: SEER.Cancer.gov
Access to care – Where are the majority of patients?

Number of New Cancers in the United States, 2018
Cervix, All Ages, All Races and Ethnicities, Female
NCI Designated Comprehensive Centers / NCCN Sites
Locally Advanced Cervical Cancer

• Whole pelvic radiation and brachytherapy was the standard of care
• Then 1999 came along....
• FIVE Practice changing publications referenced by the FDA
  GOG 85 (SWOG 8695), GOG 109 (SWOG/RTOG), GOG 120, GOG 123, and RTOG 90-01

NCI Urges Chemo-RT Combination for Invasive Cervical Cancer

March 31, 1999
Oncology NEWS International, Oncology NEWS International Vol 8 No 4, Volume 8, Issue 4

BETHESDA, Md-The National Cancer Institute (NCI) has recommended that oncologists use a combination of chemotherapy and radiation instead of radiation alone to treat invasive cervical cancer.
Again, how often does this happen?

NCI Urges Chemo-RT Combination for Invasive Cervical Cancer

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BETHESDA, Md-The National Cancer Institute (NCI) has recommended that oncologists use a combination of chemotherapy and radiation instead of radiation alone to treat invasive cervical cancer.
**NCCN Cervical Cancer Guidelines – NCI Investment**

<table>
<thead>
<tr>
<th>Clinical Stage (CERV-1)</th>
<th>*GOG 278*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage IA1 (no LVSI), Stage IA1 (with LVSI) and Stage IA2, Stage IB1 and Select IB2 (Fertility Sparing) (CERV-2)</td>
<td>*GOG 92, 109 → 263*, 274*</td>
</tr>
<tr>
<td>Stage IB1, IB2 and Stage IIA1 (Non-Fertility Sparing) (CERV-3)</td>
<td>*GOG 85, 120, 123, 165, 191, 219, 9929, GY006*, GY017*</td>
</tr>
<tr>
<td>Stage IB3 and Stage IIA2 (Non-Fertility Sparing) (CERV-4)</td>
<td>*GOG 43, 110, 149, 169, 179, 204, 240, 265</td>
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<tr>
<td>Stage IB3, Stage IIA2, and Stages IIB, III, and IVA (CERV-5)</td>
<td>*Ongoing</td>
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**Principles of Pathology (CERV-A)** \*GOG 49*

**Principles of Imaging (CERV-B)** \*GOG 233*

**Principles of Evaluation and Surgical Staging (CERV-C)**

**Principles of Radiation Therapy (CERV-D)**

**Sedlis Criteria for External Pelvic Radiation After Radical Hysterectomy In Node-Negative, Margin-Negative, Parametria-Negative Cases (CERV-E)**

**Systemic Therapy Regimens for Cervical Cancer (CERV-F)**

**Staging (ST-1)**

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9  Abu-Rustum NR et al.  *J Natl Compr Canc Netw* 2020
52.7% of ALL patients received standard of care treatment for LACC (SEER 2007-2015)
Older age, public insurance, and Black race were associated with decreased rates of brachytherapy
When comparing Black and White patients 5-year OS was 44.2% vs. 50.9% (p <0.0001)
In patients whose received brachytherapy there was no survival difference
Observations on Cervical Cancer in Alabama
Cervical Cancer in Alabama

Highest incidence counties
1. Dekalb 13.1 (NE)
2. Dale 15.1 (SE)
3. Etowah 15.6 (NE)
4. Walker 15.6 (UCen)
5. Dallas 18.6 (LCen)
Does distance from a CCC Matter?

92.3 vs. 72.1 mos

Barrington DA et al. Gynecol Oncol 2016
Does distance from a CCC Matter?

Barrington DA et al. *Gynecol Oncol* 2016

99.4 vs. 65.5 mos
Advanced Stage Cervical Cancer - Race, Geography and Socioeconomic Factors

• Retrospective cohort from 2005-2015
• Variables
  Race/Ethnicity
  Geography – Rural, Urban, Black Belt
  Distance to ACOG provider
  Insurance

<table>
<thead>
<tr>
<th>Variables</th>
<th>Crude OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt; 65 y vs. ≤50 y</td>
<td>1.95b</td>
<td>1.34–2.84</td>
</tr>
<tr>
<td>Black vs. white</td>
<td>1.46c</td>
<td>1.09–1.94</td>
</tr>
<tr>
<td>Rural vs. urban</td>
<td>1.19</td>
<td>0.91–1.56</td>
</tr>
<tr>
<td>Shorter distance to provider</td>
<td>0.99</td>
<td>0.98–1.01</td>
</tr>
<tr>
<td>Uninsureda</td>
<td>1.40</td>
<td>0.93–2.10</td>
</tr>
<tr>
<td>Public insurancec</td>
<td>1.80b</td>
<td>1.35–2.4</td>
</tr>
<tr>
<td>Higher income</td>
<td>0.93</td>
<td>0.85–1.03</td>
</tr>
</tbody>
</table>

Source: Center for Business and Economic Research, The University of Alabama

Powell TC et al. J Low Genit Tract Dis 2018
FDA grants accelerated approval to tisotumab vedotin-tftv for recurrent or metastatic cervical cancer

Efficacy and safety of tisotumab vedotin in previously treated recurrent or metastatic cervical cancer (innovaTV 204/GOG-3023/ENGOT-cx6): a multicentre, open-label, single-arm, phase 2 study

Robert L Coleman, Domenica Lorusso, Christine Gennigens, Antonio González-Martín, Leslie Randall, David Cibula, Bente Lund, Linn Woelber, Sandro Pignata, Frederic Forget, Andrés Redondo, Signe Diness Vindeløv, Menghui Chen, Jeffrey R Harris, Margaret Smith, Leonardo Viana Nicacio, Melinda S L Teng, Annouschka Laenen, Reshma Rangwala, Luis Manso, Mansoor Mirza, Bradley J Monk, Ignace Vergote, on behalf of the innovaTV 204/GOG-3023/ENGOT-cx6 Collaborators*
FDA approves pembrolizumab combination for the first-line treatment of cervical cancer

Pembrolizumab for Persistent, Recurrent, or Metastatic Cervical Cancer

Conclusions

• NCI sponsored research has had a substantial impact on women with cervical cancer
• Novel approaches may be needed in different geographical regions
• More recent paradigm shifting trials have been performed outside of the NCI
• While therapeutic advances remain important, novel approaches to improve primary vaccination and screening should not be forgotten
Improving cervical cancer clinical trials

• Need representative populations enrolled
  — Re-evaluate minimum of different racial & ethnic groups?
• Pursue additional research support for enrollment of underrepresented minorities
  — Bonus credit similar to LAPS versus non–LAPS sites
• “Real world” designs?
Thank you!