CERVICAL CANCER
A GLOBAL PERSPECTIVE

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ACOG, Fundación Instituto Valenciano de Oncología
GCIG Chair

Cervical Cancer Education Symposium.
Mexico, Jan 2017
Gynecological Cancer

- Gynecological Cancers represent around 15% of all cancers

- Trends in incidence:
  - Endometrial Cancer 6% (slightly increase)
  - Ovarian Cancer 4% (stable)
  - Cervical cancer 3% (stable in Western world, increasing in Developing countries)
  - Vulva, vagina and others: 1.2% (increasing)
• “... 65% of cancer deaths occurred in lower income countries.”

• A prototype of this distinct distribution:

  Cervical Cancer:

  In Developing Countries it is the leading cause of cancer death
A Prototype: Estimated Cervical Cancer Mortality Worldwide

Estimated Age-Standardised rates per 100,000

Globocan 2012 - WHO
Cervical Cancer in the United States

Incidence Rate is 12,000 and Mortality Rate 4,000 per year

Presented by: Gottfried E. Konecny, M.D.
Cervical Cancer in the World

Incidence rate is 530,000 and Mortality Rate 275,000 per year

Presented by: Gottfried E. Konecny, M.D.
Cervical Cancer in Latin America

- Life expectancy - Average age at death = Number of years of life lost by each death
- Number of years of life lost by each death \(\times\) total number of deaths per period = Number of years of life potentially lost.

- A loss of 633,000 potential years of life in Latin America

<table>
<thead>
<tr>
<th>Countries</th>
<th>Number of deaths</th>
<th>Life expectancy (LE)</th>
<th>Potential years of life lost (PYLL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td>2127</td>
<td>80</td>
<td>53175</td>
</tr>
<tr>
<td>Bolivia</td>
<td>845</td>
<td>69</td>
<td>11830</td>
</tr>
<tr>
<td>Brazil</td>
<td>8414</td>
<td>77</td>
<td>185,108</td>
</tr>
<tr>
<td>Chile</td>
<td>734</td>
<td>82</td>
<td>19818</td>
</tr>
<tr>
<td>Colombia</td>
<td>1986</td>
<td>78</td>
<td>45678</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>116</td>
<td>82</td>
<td>3132</td>
</tr>
<tr>
<td>Cuba</td>
<td>569</td>
<td>81</td>
<td>14704</td>
</tr>
<tr>
<td>Ecuador</td>
<td>1026</td>
<td>79</td>
<td>24624</td>
</tr>
<tr>
<td>El Salvador</td>
<td>388</td>
<td>77</td>
<td>8536</td>
</tr>
<tr>
<td>Guatemala</td>
<td>672</td>
<td>75</td>
<td>13440</td>
</tr>
<tr>
<td>Haiti</td>
<td>575</td>
<td>65</td>
<td>5750</td>
</tr>
<tr>
<td>Honduras</td>
<td>417</td>
<td>76</td>
<td>8757</td>
</tr>
<tr>
<td>Mexico</td>
<td>4769</td>
<td>80</td>
<td>119,225</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>424</td>
<td>78</td>
<td>9752</td>
</tr>
<tr>
<td>Panama</td>
<td>134</td>
<td>80</td>
<td>3350</td>
</tr>
<tr>
<td>Paraguay</td>
<td>439</td>
<td>74</td>
<td>8341</td>
</tr>
<tr>
<td>Peru</td>
<td>1715</td>
<td>77</td>
<td>37730</td>
</tr>
<tr>
<td>Puerto Rico</td>
<td>84</td>
<td>82</td>
<td>2268</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>600</td>
<td>76</td>
<td>12600</td>
</tr>
<tr>
<td>Uruguay</td>
<td>175</td>
<td>80</td>
<td>4375</td>
</tr>
<tr>
<td>Venezuela</td>
<td>1798</td>
<td>78</td>
<td>41147</td>
</tr>
<tr>
<td>Total</td>
<td>27998</td>
<td></td>
<td>633,430</td>
</tr>
</tbody>
</table>

Source: Deaths, according to GLOBOCAN 2012.

Visit [this link](http://www.who.int/.../PYLL) for more information.
Gynaecological Tumors
Cervical Cancer

- Second most common cancer among women worldwide.
- Second most common cause of cancer-related mortality in women globally.
- Human papillomavirus (HPV) infections are the cause of nearly all cervical cancers.
  - Preventable through screening and vaccination
- If not prevented → surgery for early stage disease
- If not diagnosed at early stage → radiation therapy (RT) and concomitant chemotherapy.
Cervical cancer issues

(_GCIG Brain storming, Melbourne 2014)

• **WESTERN COUNTRIES** (mainly early stages)
  – Fertility sparing/preserving
  – Sentinel node mapping
  – IMRT
  – Molecular Biology/Novel targeted therapies/predictive markers

• **DEVELOPING COUNTRIES** (mainly locally-advanced & advanced stages)
  – Pap smear screening
  – Vaccines
  – Accessibility to radiotherapy
  – Accessibility to medical treatment
GCIG
Current situation and Challenges

• Currently 29 groups are GCIG members.
  – 15 Europe
  – 7 US and Canada
  – 5 ASIA
  – 1 Australia/New Zealand
  – 1 Latin America
  – 0 Africa
Countries represented in the GCIG future?

or many others

www.gciggroup.com

>1.800 million

640 million people
GCIG
MISSION and VISION STATEMENT

• **MISSION**: to promote and facilitate high quality clinical trials in order to improve outcomes for women with gynecological cancer.

• **VISION**: Improving quality and duration of life for women with gynecologic cancers will be accomplished through a
  – focused common purpose,
  – shared expertise
  – mutual respect among members
  – with recognition and accommodation of cultural, geographic, and clinical diversities amongst and between members and patients.

www.gciggroup.com
One of the keys to improve outcomes for women with gynecological cancer is to expand research in gynecologic cancer.

- Increasing the amount of cooperative group performing clinical trials in a global network as GCIG.
Locally Advanced Stages Cervical Cancer

Key Issues

• Pap smear screening
• Vaccines
• Accessibility to radiotherapy
• Accessibility to medical treatment
Locally Advanced Stages Cervical Cancer

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Mexico, Jan 2017
Pap Smear Screening Difficulties in Developing Countries

• Costs:
  – Logistics for implementation of Cytology:
    • Infrastructure for collection; Cost of reading
    • Distribution of results (higher cost)

• Social:
  • Population (level of education, social status, access to health centers)
  • Unable to adhere to the population screening programs
  • Difficulty to identify lacks of coverage

Courtesy from Dr M Paiva Batista
Pap Smear Screening
Difficulties in Developing Countries

• Executing:
  • Quality of cytology (collecting and reading)
  • Satisfactory samples as a limiting factor
    – Lack of standardization for reading
    – False negatives: 3-30%
  • Excess of abnormal cytology generating costs and undetermined significance.

Courtesy from Dr M Paiva Batista
Locally Advanced Stages Cervical Cancer

Key Issues

• Pap smear screening
• Vaccines
• Accessibility to radiotherapy
• Accessibility to medical treatment
HPV Prevalence Among 1 Million Women With Normal Cytology

<table>
<thead>
<tr>
<th>Region</th>
<th>Adjusted HPV prevalence (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caribbean</td>
<td>35.4</td>
</tr>
<tr>
<td>Eastern Africa</td>
<td>33.6</td>
</tr>
<tr>
<td>Eastern Europe</td>
<td>21.4</td>
</tr>
<tr>
<td>Western Africa</td>
<td>19.6</td>
</tr>
<tr>
<td>Southern Africa</td>
<td>17.4</td>
</tr>
<tr>
<td>South America</td>
<td>15.3</td>
</tr>
<tr>
<td>South- Eastern Asia</td>
<td>14.0</td>
</tr>
<tr>
<td>Central America</td>
<td>13.0</td>
</tr>
<tr>
<td>WORLD</td>
<td>11.7</td>
</tr>
<tr>
<td>Eastern Asia</td>
<td>10.7</td>
</tr>
<tr>
<td>Northern Europe</td>
<td>10.0</td>
</tr>
<tr>
<td>Northern Africa</td>
<td>9.2</td>
</tr>
<tr>
<td>Western Europe</td>
<td>9.0</td>
</tr>
<tr>
<td>Southern Europe</td>
<td>8.8</td>
</tr>
<tr>
<td>Southern Asia</td>
<td>7.1</td>
</tr>
<tr>
<td>Northern America</td>
<td>4.7</td>
</tr>
<tr>
<td>Western Asia</td>
<td>1.7</td>
</tr>
</tbody>
</table>

Meta-analysis of 1,016,719 women. Adjusted HPV prevalence standardized by the regional geographical structure.

HPV Vaccination Programs to 2014/2015

64 COUNTRIES, 4 REGIONS, & 12 TERRITORIES

Locally Advanced Stages Cervical Cancer

Key Issues

• Pap smear screening
• Vaccines
• Accessibility to radiotherapy
• Accessibility to medical treatment
Number of People Served by Each Radiotherapy Center by Country

Locally Advanced Stages Cervical Cancer

Key Issues

- Pap smear screening
- Vaccines
- Accessibility to radiotherapy
- Accessibility to medical treatment
Recurrent/Metastatic Cervical Cancer

Key Issues

• Accessibility to medical treatment
• Few options to cure
• Standard of care: platinum combination (≤2013)
  Cisplatin + paclitaxel
GOG 240: OS for Chemo vs Chemo + Bev

<table>
<thead>
<tr>
<th></th>
<th>Chemotherapy (n=225)</th>
<th>Chemotherapy + Bev (n=227)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Events, n (%)</td>
<td>140 (62)</td>
<td>131 (58)</td>
</tr>
<tr>
<td>Median OS, mos</td>
<td>13.3</td>
<td>17.0</td>
</tr>
<tr>
<td>HR=0.71 (97% CI, 0.54-0.94)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P=0.0035</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median follow-up</td>
<td>20.8 mos</td>
<td></td>
</tr>
</tbody>
</table>

Presented by: Krishnansu S. Tewari, MD, FACOG, FACS
Recurrent/Metastatic Cervical Cancer

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Improved Survival with Bevacizumab in Advanced Cervical Cancer

Krishnansu S. Tewari, M.D., Michael W. Sill, Ph.D., Harry J. Long III, M.D., Richard T. Penson, M.D., Helen Huang, M.S., Lois M. Ramondetta, M.D., Lisa M. Landrum, M.D., Ana Oaknin, M.D., Thomas J. Reid, M.D., Mario M. Leitao, M.D., Helen E. Michael, M.D., and Bradley J. Monk, M.D.

N ENGL J MED 370;8 NEJM.ORG FEBRUARY 20, 2014
Progress in Survival in Advanced and Recurrent Cervical Cancer

GOG 64 Cisplatin

GOG 110 Cisplatin + Ifosfamide

GOG 149 Cisplatin + Ifosfamide + Bleomycin

GOG 179 Cisplatin + Paclitaxel + Bevacizumab

GOG 189 Cisplatin + Paclitaxel + Topotecan

Year


Months

0 2 4 6 8 10 12 14 16 18
Recurrent/Metastatic Cervical Cancer

Accessibility to medical treatment

• Few options to cure
• Standard of care: platinum combination 
  (2013)
  – Cisplatin + paclitaxel + Bevacizumab
• Clinical Practice Changing
Expectations

• The institute of Medicine, Global Task Force on Expanded Access to Cancer Care and Control in Developing Countries, the WHO:

“Stepping Stones in improving the fight against cancer in Low-, Middle-, and High-Income Countries.”

Souza et al, JCO vol34, Jan 2016
Thinking about numbers...

• In 2010:
  – Long term costs of patients with cancer and their families - US$ 2.5 trillion annually worldwide.

• The implementation of prevention, early detection, and treatment strategies:
  – Potentially save 2.4-3.7 million lives annually
  – The majority of this lives in Low- and Middle- Income countries
  – Economic benefit in excess of US$400 billion.
“Stepping stones against cancer in Low and Middle-Income countries”:

✓ Focus on prevention and risk reduction strategies
  • National Cancer Control Plan
  • Basic Health Care infrastructure and education

✓ Prevention and WHO list of essential medications
  • Prevention and early detection programs
  • Access to basic pathology and imaging services
Gynecological Tumors
Cervical Cancer
Remarks

• First world advances in both diagnosis and treatment should be applicable to developing countries.

• To establish networks to improve survival in cervical cancer is a priority.
Please look to the future