Recent findings from the NCI Costa Rica HPV-16/18 Vaccine Trial

Aimée R. Kreimer, Ph.D.
Investigator
Infections and Immunoepidemiology Branch
Division of Cancer Epidemiology and Genetics
National Cancer Institute

kreimera@mail.nih.gov
Cervical Cancer

• Worldwide incidence and mortality
  – 500,000 new cases per year
  – 250,000 deaths per year

• Incidence and survival rates vary by geographical region
  – 85% occur in developing nations

• HPV is a necessary cause of cervical cancer
HPV-associated cancers: US

Incidence increasing over time

Percent of Cancer Cases

Cervix
Anus
Penis
Vagina
Vulva
Tonsil
Oral Cavity
## Estimated burden of HPV-associated cancers

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>WORLDWIDE</th>
<th></th>
<th>UNITED STATES</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females</td>
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<td>Cervix</td>
<td>530,000</td>
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# Two prophylactic HPV Vaccines

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<th>Manufacturer</th>
<th>HPV Types Included in Vaccine</th>
<th>US FDA Licensure</th>
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<tr>
<td><strong>Glaxo Smith Kline</strong></td>
<td>HPV 16, HPV 18</td>
<td>70% of Cervical Cancer</td>
</tr>
<tr>
<td>Cervarix</td>
<td></td>
<td>Females ages 10-25 for the prevention of cervical disease</td>
</tr>
<tr>
<td><strong>Merck</strong></td>
<td>HPV 16, HPV 18, HPV 6, HPV 11</td>
<td>90% of Genital Warts</td>
</tr>
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<td>Gardasil</td>
<td></td>
<td>Females ages 9-26 for the prevention of cervical, vulvar, vaginal, and anal disease</td>
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<td>Males ages 9-26 for the prevention of genital warts and anal disease</td>
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Use of the vaccine

- Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention
- HPV vaccine recommended for:
  - Females- ages 11-12; range: 9 to 26 years
  - Males- ages 11-12 with the quadrivalent vaccine;
    - Recommended range: 9 to 21 years
    - Permissive range: 22 to 26 years
Both HPV vaccines prevent cervical HPV infections among uninfected young women.

Findings from our vaccine trial confirm reports from commercial trials

NCI findings from the Costa Rica Vaccine Trial

1. No therapeutic efficacy of the prophylactic HPV vaccine

2. Vaccine safety profile is comparable to other licensed vaccines
   - Not recommended during pregnancy

3. High vaccine efficacy for HPV16/18 as well as non-vaccine HPV types
   - Vaccine impact highest when vaccination is given at younger ages, prior to sexual initiation

Recent Findings from NCI

1. Vaccine efficacy of fewer than 3 doses
2. Vaccine efficacy at other anatomic sites
Costa Rica Vaccine Trial

*Design of the Trial*

HPV Vaccine: Virus-like particle
Costa Rica Vaccine Trial
A community-based, randomized trial

7,466 Women 18-25 yo
Enrolled (06/04 – 12/05)

CENSUS

Hepatitis A Vaccine
- Vaccine Dose 1
- Vaccine Dose 2
- Vaccine Dose 3

HPV-16/18 Vaccine
- Vaccine Dose 1
- Vaccine Dose 2
- Vaccine Dose 3

6 Months

COMPLETED
Costa Rica Vaccine Trial

7,466 Women
18-25 years old

- Hepatitis A Vaccine
- HPV-16/18 Vaccine

• Annual follow-up visits for 4 years
• Cervical samples collected at all visits
• Anal and oral specimens collected at 4 year visit
Long-term follow-up of the Costa Rica Vaccine Trial

- 7,466 Women
  - 18-25 years old

**Completed**
- Hepatitis A Vaccine
- HPV-16/18 Vaccine

**On-going**
- 10 total years of follow-up
  - 6 years
  - 4 years
Proof-of-Principle Evaluation of the Efficacy of Fewer Than Three Doses of a Bivalent HPV16/18 Vaccine


**Conclusion**

Four years after vaccination of women who appeared to be uninfected, this nonrandomized analysis suggests that two doses of the HPV16/18 vaccine, and maybe even one dose, are as protective as three doses.

J Natl Cancer Inst 2011;103:1–8
# Vaccine efficacy by doses received

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<th># of Doses</th>
<th>Arm</th>
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<th># of persistent HPV16/18 infections</th>
<th>HPV16/18 VE (95%CI)</th>
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<tr>
<td>3</td>
<td>Control</td>
<td>3010</td>
<td>133</td>
<td>80.9% (71.1% to 87.7%)</td>
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<td>2</td>
<td>Control</td>
<td>380</td>
<td>17</td>
<td>84.1% (50.2% to 96.3%)</td>
</tr>
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<td>188</td>
<td>10</td>
<td>100% (66.5% to 100%)</td>
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<tr>
<td></td>
<td>HPV</td>
<td>196</td>
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Conclusions

• After 4 years, the HPV vaccine provides high efficacy regardless of the number of doses received

• A simpler, more affordable vaccination schedule might be feasible
Important Questions Remain

– Will these results apply to other populations?
– Will these results apply to other vaccine formulations?
– What is the minimum antibody level required for protection?
– What is the duration of protection for <3 doses?
Vaccine efficacy at other anatomic sites

HPV Vaccine: Virus-like particle
Efficacy of a bivalent HPV 16/18 vaccine against anal HPV 16/18 infection among young women: a nested analysis within the Costa Rica Vaccine Trial


Interpretation The AS04-adjuvanted vaccine affords strong protection against anal HPV infection, particularly among women more likely to be HPV naive at enrolment.
Vaccine efficacy among women without HPV

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<td></td>
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Kreimer AR et al *Lancet Oncology* September 2011
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<td>81</td>
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Conclusions

• HPV vaccine strongly protects against anal HPV16/18 infections in women
• Protection is comparable to that observed at the cervix
• Women who receive the HPV vaccine will have less anal HPV infection
Upcoming research and future directions

1. Oral HPV16/18 vaccine efficacy
2. Long-term impact of vaccination
   - Duration of protection
   - Screening
   - Safety
3. Immunological markers of protection
4. Natural history of HPV infection in a vaccinated cohort
Summary of recent findings

1. Confirmed that the bivalent HPV vaccine is highly effective in the prevention of cervical HPV infection
2. Raised the possibility that only two, or maybe even a single dose, of the HPV vaccine may be necessary
3. Demonstrated the vaccine protects at an additional anatomic site where HPV is known to cause cancer
Acknowledgements

NCI, US

- Allan Hildesheim (IIB)
- Hormuzd Katki (BB)
- Doug Lowy (CCR)
- Ligia Pinto (IIB-SAIC)
- Mahboobeh Safaeian (IIB)
- Mark Schiffman (CGB)
- John Schiller (CCR)
- Mark Sherman (HREB)
- Diane Solomon (DCP)
- Sholom Wacholder (BB)

Proyecto Epidemiologico Guanacaste, Costa Rica

- Paula Gonzalez
- Rolando Herrero
- Silvia Jimenez
- Carolina Porras
- Ana Cecilia Rodriguez

Other Groups

- Julie Buckland (IMS)
- Jean Cyr (IMS)
- Mary Sidawy (Georgetown)
- Wim Quint (DDL)
- LJ van Doorn (DDL)