Vaccination in Cancer Prevention: Cervical Cancer is Largely Preventable, But is Increasing Globally

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The views expressed are my own and do not necessarily reflect those of NCI/NIH
Disclosures

• National Institutes of Health (NIH) has patents on papillomavirus L1 virus-like particle (VLP) vaccine technology. I am an inventor.

• NIH has licensed L1 VLP technology to Merck and GlaxoSmithKline, the two companies with commercial versions of the vaccine.

• Licensees of other NIH technologies of which I am an inventor: GlaxoSmithKline, Sanofi, Shanta Biotech, Cytos Biotech, Aura Biosciences, Etna Biotech, Acambis, PanVax
Hepatitis B Virus vaccination can reduce liver cancer risk, but high impact takes many years

- Universal HPV vaccination at birth begun in Taiwan in 1986
- Very long interval between infection and development of cancer

From Chang et al, Gastroenterology 2016
The paradox of cervical cancer: a largely preventable cancer that globally is still common

- A cancer that disproportionally affects women from poor countries & poor women
- Current high quality cervical cancer screening and HPV vaccination need to become more cost-effective for their widespread dissemination to less developed regions of the world
Cervical cancer mortality rates will continue to increase in less developed regions of the world.

Less developed regions: Where ~90% of worldwide cervical cancer deaths occur; where cervical cancer accounts for ~10% of female cancer deaths; where cervical cancer represents ~90% of HPV-associated cancer.

Projections developed from Globocan 2012.
Global control of cervical cancer and other HPV-associated cancers should soon be feasible

- Research for vaccination and screening is likely to lead to changes in standard of care with increased cost-effectiveness in the near future
- Once that point has been reached, resources are needed to widely implement the interventions; there may be sufficient global commitment to marshal these resources
High efficacy of HPV L1 VLP vaccines against new cervical precancer and genital warts by vaccine-targeted types in randomized trials

In women with no genital HPV infection detected in at the start of each trial

<table>
<thead>
<tr>
<th>End Point</th>
<th>Sex</th>
<th>Age</th>
<th>Vaccine</th>
<th>Targeted HPV Types</th>
<th>Efficacy (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Precancer</td>
<td>Female</td>
<td>15-26</td>
<td>Quadrivalent / Gardasil</td>
<td>HPV 6, 11, 16, 18</td>
<td>100% (85.5-100)</td>
</tr>
<tr>
<td>Genital Warts</td>
<td>Female</td>
<td>15-26</td>
<td>Quadrivalent / Gardasil</td>
<td>HPV 6, 11, 16, 18</td>
<td>96.4% (91.4-98.4)</td>
</tr>
<tr>
<td>Precancer</td>
<td>Female</td>
<td>15-25</td>
<td>Bivalent / Cervarix</td>
<td>HPV 16, 18</td>
<td>100% (90.5-100)</td>
</tr>
<tr>
<td>Precancer</td>
<td>Female</td>
<td>16-26</td>
<td>Nonavalent / Gardasil-9</td>
<td>HPV 6, 11, 16, 18, 31, 33, 45, 52, 58</td>
<td>97.1% (83.5-99.9)</td>
</tr>
</tbody>
</table>

Precancer = Cervical Intraepithelial Neoplasia Grade 3
Lehtinen Lancet Oncol 2011; Munoz JNCI 2010; Huh Lancet 2017

First successful vaccines against a local sexually transmitted infection
2016: 9-valent vaccine approved for 2 doses for 9-14 year olds
Herd Immunity: Decreased incidence of genital warts in heterosexual Australian men following female HPV vaccine implementation in 2007

Trends in U.S. Vaccination Rates: Ages 13-17 Years

The Costa Rica Vaccine Trial: Prevalent HPV infection 11 years after bivalent HPV vaccination: One dose is not inferior to three doses (post-hoc analysis)

From Aimee Kreimer et al, unpublished data
Stable HPV seropositivity for 11 years

100% of HPV-vaccinated women remained HPV16 seropositive 11 years after HPV vaccination

From Aimee Kreimer et al, unpublished data
Summary and Conclusions

• Basic research led to identification of HPV as the cause of several cancers and to development of the HPV vaccines
  – The vaccines can confer high protection and herd immunity

• Increased vaccine uptake in US is needed to achieve personal protection for more individuals and greater herd immunity

• Control of cervical cancer and other HPV-associated cancers as worldwide public health problems may soon be feasible