Innovations in Human Papillomavirus Vaccine
1. Current HPV vaccines
2. New development
3. What’s next?
PART I

CURRENT HPV VACCINES
Current HPV Vaccines

Worldwide incidence of cervical cancer

Worldwide incidence of cervical cancer per 100 000 females (all ages), age-standardized to the WHO standard population, 2005

Continuously HPV infection is dominated cause of the disease!!!

Human Papillomavirus types 16&18 (HPV16&18) — causing 70% of cervical cancer cases worldwide

WORLDWIDE HPV–16 AND –18 PREVALENCE (%) AMONG WOMEN WITH NORMAL CYTOLOGY
A META–ANALYSIS OF 42,823 WOMEN AGED ≥ 15 YEARS

Current HPV Vaccines

Human Papillomavirus Vaccine (HPV) — World’s first vaccine against cancer

- Persistent infection of certain high risk types of HPV can cause cervical cancer in women
  - More than 529,000 new cases each year worldwide
  - More than 274,000 deaths each year
  - > 85% deaths are in developing countries
  - Represents 13% of all female cancers

- HPV can also cause:
  - Anogenital cancer
  - Head and neck cancers
  - Genital warts

![Graph showing new case numbers per year for different cancers]
There are two HPV vaccines available on the market:

- Merck’s Gardasil® (HPV 6/11/16/18)
- GlaxoSmithKline’s Cervarix® (HPV 16/18)

By August 2014, 58 countries (30%) had introduced HPV vaccine in their national immunization program for girls, and in some countries also for boys.

<table>
<thead>
<tr>
<th>Vaccine</th>
<th>Company</th>
<th>Market launch</th>
<th>2012 Sales (US$)</th>
<th>2013 Sales (US$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gardasil</td>
<td>Merck</td>
<td>Jan 2006</td>
<td>1.6 billion</td>
<td>1.8 billion</td>
</tr>
<tr>
<td>Cervarix</td>
<td>GSK</td>
<td>Sep 2007</td>
<td>362 million</td>
<td>230 million</td>
</tr>
</tbody>
</table>
PART II

NEW DEVELOPMENT
Increased Valences

- From 2-valent & 4-valent to 9-valent
- Increased coverage rate from 70% to 90% (next page)
- Phase III study completed, waiting for approval by US FDA
- 3-valent and 5-valent vaccines are also been developed
9-Valent HPV Vaccine

— Stronger protect against Cervical Cancer

Global Prevalence of HPV Types in Cervical Cancer

<table>
<thead>
<tr>
<th>HPV Types</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>57.6%</td>
</tr>
<tr>
<td>+18</td>
<td>71.7%</td>
</tr>
<tr>
<td>+45</td>
<td>77.4%</td>
</tr>
<tr>
<td>+31</td>
<td>81.3%</td>
</tr>
<tr>
<td>+X</td>
<td>85.0%</td>
</tr>
<tr>
<td>+33</td>
<td>87.9%</td>
</tr>
<tr>
<td>+52</td>
<td>90.1%</td>
</tr>
<tr>
<td>+58</td>
<td>91.8%</td>
</tr>
<tr>
<td>+35</td>
<td>93.3%</td>
</tr>
<tr>
<td>+59</td>
<td>94.6%</td>
</tr>
<tr>
<td>+56</td>
<td>95.7%</td>
</tr>
</tbody>
</table>

— JON COHEN, 29 APRIL 2005 VOL 308 SCIENCE
Reduced Injection

- From 3-dose regimen to 2-dose regimen
- WHO recommended using 2-dose regimen for routine immunization
- Shortened immunization schedule make it easier to administer
- New standard for new developers to match

- HPV has been recommended for routine immunizations in 40+ countries
Results of a systematic review indicate that 2 doses of HPV vaccine in girls aged 9–14 years are non-inferior to 3 doses in terms of immunogenicity when compared to 3 doses in girls aged 9–14 years or 3 doses in women aged 15–24 years.
2-dose regiment VS. 3-dose regiment

Results of a systematic review indicate that 2 doses of HPV vaccine in girls aged 9–14 years are non-inferior to 3 doses in terms of immunogenicity when compared to 3 doses in girls aged 9–14 years or 3 doses in women aged 15–24 years.

Gardasil (Quadrivalent HPV vaccine): For girls and boys aged 9–13 years this vaccine can be administered according to a 2-dose schedule (0.5 mL at 0 and 6 months). If the second vaccine dose is administered earlier than 6 months after the first dose, a third dose should be administered.

Cervarix (Bivalent HPV vaccine): For girls aged 9–14 years a 2-dose schedule (0.5 mL at 0 and 6 months) is recommended. The second dose can be given between 5 and 7 months after the first dose.
PART III

WHAT’S NEXT?
What’s Next?

- More valences?
- Combos?

- Global efforts to expand routine immunizations: efforts from GAVI, Gates Foundation, etc.
- Immunizing males – is single-sex immunization going to work?
Revised WHO position on human papillomavirus vaccines

Updated position paper published on 24 Oct. 2014. WHO revised the number of doses recommended for human papillomavirus (HPV) vaccines for different age groups. Furthermore, WHO reiterates its recommendation that HPV vaccines should be included in national immunization programmes.
WHO Informal consultation on Recommendations to assure the quality, safety and efficacy of recombinant human papillomavirus virus-like particle (HPV-VLP) vaccines
11-12 November 2014, Geneva, Switzerland
The Supply Issue – Who’s Providing the Vaccine?

- Two companies supplying so far
- Two more companies in Phase 3 trials
- Several more in earlier stage

- Can these 4 companies supply the world?
- Needs for innovative ways to supply?
Established at

2005 03

Focus on --
Developing, manufacturing and marketing innovative vaccines, bioactive materials, and medical devices.

Committed to--
Increase the availability of high quality innovative Vaccines and Diagnostic reagents to combat infectious diseases globally.
Innovax – Products and Pipeline

Launched Product:
- Hepatitis E vaccine (E. coli)

Pipeline:
- Varicella, Registration
- HPV 2-valent (E. coli), Phase 3
- HPV multi-valent, pre-clinical
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