HPV vaccines

Updated results in 2018

F X Bosch
IDIBELL / ICO
Rumania 2018
Potential conflict of interest

- Research and educational institutional grants:
  GSK, SPMSD, Merck, Qiagen
- Personal / speaking / travel grants:
  GSK, SPMSD, Merck, Qiagen, RMS

This presentation is the sole responsibility of the author
HPV vaccines in 2017

bi-valent HPV vaccine (Cervarix)

- 16 (20μg)  
- 18 (20μg)

ASO4-AL

quadri-valent HPV vaccine (Gardasil)

- 6 (20μg)  
- 11 (40μg)  
- 16 (40μg)  
- 18 (20μg)

AAHS 250

nine-valent HPV vaccine (Gardasil 9)

- 6 (30μg)  
- 11 (40μg)  
- 16 (60μg)  
- 18 (40μg)  
- 31 (20μg)  
- 33 (20μg)  
- 45 (20μg)  
- 52 (20μg)  
- 58 (20μg)  

AAHS 500
**HPV vaccines in 2017+**

### bi-valent HPV vaccine (Cervarix)

<table>
<thead>
<tr>
<th>HPV Type</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>20µg</td>
</tr>
<tr>
<td>18</td>
<td>20µg</td>
</tr>
<tr>
<td>31</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td></td>
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</tbody>
</table>

### nine-valent HPV vaccine (Gardasil 9)

<table>
<thead>
<tr>
<th>HPV Type</th>
<th>Dose</th>
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<tbody>
<tr>
<td>6</td>
<td>30µg</td>
</tr>
<tr>
<td>11</td>
<td>40µg</td>
</tr>
<tr>
<td>16</td>
<td>60µg</td>
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<td>18</td>
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<tr>
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<td>20µg</td>
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</tr>
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<td>52</td>
<td>20µg</td>
</tr>
<tr>
<td>58</td>
<td>20µg</td>
</tr>
</tbody>
</table>

**ASO4-AL**

- 80+% of GW
- 90+% of JRRP
- 70+% of CX
- 80% other HPV related cancers
- VE irrespective of type: > 90%
- VE 5 types > 95%
- 5% of cervical cancer

**AAHS 500**

- 60+% of GW
- 90+% of JRRP
- 70+% of CX
- 80% other HPV related cancers
- VE irrespective of type: > 90%
- VE 5 types > 95%
- 5% of cervical cancer

**VE irrespective of type: > 90%**

**VE 5 types > 95%**

**5% of cervical cancer**
HPV type-specific contribution to cervical cancer and potential for prevention of existing vaccines

VIRAL TYPES

<table>
<thead>
<tr>
<th>Type</th>
<th>RC %</th>
<th>Gardasil</th>
<th>Cervarix</th>
<th>Gardasil9</th>
</tr>
</thead>
<tbody>
<tr>
<td>16+18</td>
<td>71</td>
<td>95+%</td>
<td>95+%</td>
<td>95+%</td>
</tr>
<tr>
<td>+31</td>
<td>75</td>
<td>Parcial</td>
<td>Parcial</td>
<td>95+%</td>
</tr>
<tr>
<td>+33+45</td>
<td>84</td>
<td>-</td>
<td>Parcial</td>
<td>95+%</td>
</tr>
<tr>
<td>+52+58</td>
<td>89</td>
<td>-</td>
<td>?</td>
<td>95+%</td>
</tr>
<tr>
<td>6 + 11</td>
<td>90</td>
<td>90 %</td>
<td>-</td>
<td>90 %</td>
</tr>
</tbody>
</table>

![Graph showing relative contribution and 95% confidence interval](image)

Type specific Vaccine efficacy

- de Sanjosé S et al. Lancet Oncol, 2010
- Serrano B et al. Infect Ag Cancer, 2012
- Schiller J et al Vaccine 30 S 5 2012
- Lehtinen M et al. Nat Rev Clin Oncol. 10 2013
POPULATION STUDIES: OUTCOME HPV INFECTIONS

Prevalence surveys in Australia
Vaccination in 2007 + up to age 26 with 70% coverage for the three dose regime
DIFFERENCES IN HPV PREVALENCE BETWEEN PRE (WHINURS) AND POST VACCINATION (VIP) PERIODS

Tabrizi S., HPV TODAY 28/29 2013
Changes in the prevalence of human papillomavirus following a national bivalent human papillomavirus vaccination programme in Scotland: a 7-year cross-sectional study

Kimberley Kavanagh, Kevin G Pollock, Kate Cuschieri, Tim Palmer, Ross L Cameron, Cameron Watt, Ramya Bhatia, Catherine Moore, Heather Cubie, Margaret Cruickshank, Chris Robertson

16/18

31/33/45

Other HR

Any

K. Kavanagh et al. Lancet Inf Dis 2017
Outcome: Genital warts
HPV 6/11
Declines in under 21 years of age: women from 18.6% to 1.9% heterosexual men from 22.9% to 2.9%
Around 93% reduction of GW – consistent with results in other countries

OUTCOME: CIN 2/3 - CARCINOMA IN SITU

Largely consistent for both vaccines
Decline in CIN 2+ in Australia by age (2002-2014) now impacting up to 30 years

Figure 1: Trends in prevalence rates of high grade histologically confirmed cervical abnormalities (CIN2+) diagnosed in Victorian women, Australia, by age group, 2000-2014

Population impact on cervical cancer incidence: the nordic countries registration control

Cohorts recruited into Phase III trials (both vaccines) passively followed up by the network of cancer registration
Finland: Incidence of cancer in girls aged 14-17 by HPV vaccination status
Vaccinated 9,500 & Non-vaccinated 18,000

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Vaccinated women. Number and Rates(10x5) 66,000 person years</th>
<th>Non vaccinated women Number and Rates (10x5) 124,000 person years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervix</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Vulva</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Anal / Vaginal</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>All HPV related</td>
<td>0</td>
<td>10</td>
</tr>
</tbody>
</table>

Vaccine efficacy estimates: 100% (95% CI 16-100)

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Vaccinated women. Number and Rates(10x5)</th>
<th>Non vaccinated women Number and Rates (10x5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Thyroid</td>
<td>1</td>
<td>9</td>
</tr>
<tr>
<td>Melanoma</td>
<td>3</td>
<td>13</td>
</tr>
<tr>
<td>Other skin</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

Luostarinen T. et al IJC 2018
Vaccine balance over safety
Weight of the evidence

Sore arm
Fainting from vaccination

All suspected claims have been declared inconsistent after careful examination
Recognizing that the risk “0” does not exist in biology

Over 100,000 subjects in RCT
Over 240 M doses distributed
Estimated 60M vaccinated
8 WHO reviews on safety
62 countries (30 in Europe) introduced routine HPV vaccination
13+ countries introduced male vaccination…

OVERWHELMING and UNANIME SUPPORT OF THE VACCINATION PROGRAM
Reports of the Global Advisory Committee on Vaccination Safety (GACVS) & Strategic Advisory Group of Experts in immunization (SAGE) in relation to the HPV vaccine

- Doses: 60M
- Countries: 109
- 2006: Syncope, Anaphylaxis
- 2007: Pregnancies
- 2008: Massive psychogenic reaction
- 2009: Autoimmunity
- 2010: Venous thromboembolism
- 2011: Premature ovarian failure
- 2012: Chronic regional pain syndrome
- 2013: Aluminum, multiple sclerosis
- 2014: Vasculitis CNS
- 2015: Guillen Barre
- 2016/7: Orthostatic postural tachycardia POTS

Institut Català d’Oncologia
ESTIMATED INCIDENT CERVICAL CANCER AVERTED BEFORE AGE 75 YEARS IN 118 MILLION WOMEN EVER TARGETED BY HPV VACCINATION PROGRAMMES BY THE END OF 2014

960,000 cases predicted
445,000 cases averted

3-doses
At least one dose
unvaccinated
Non 16/18 in vaccinated

Bruni 2016 Lancet Glob Health
MALE HPV VACCINATION:

Further increase protection of women by interrupting transmission
Protect vaccinated males against HPV-induced cancers

Herd protection is lost when individuals leave the herd...
### Quadrivalent HPV Vaccine Efficacy Studies in Men

<table>
<thead>
<tr>
<th>Vaccine efficacy against EGL, (mostly GW) in men</th>
<th>Vaccine efficacy against anal intraepithelial lesions in MSM</th>
</tr>
</thead>
<tbody>
<tr>
<td>90.6% (70-98)</td>
<td>77.5% (40-93)</td>
</tr>
<tr>
<td>Giuliano et al. NEJM 2011 Per protocol cohorts</td>
<td>Palefsky et al. NEJM 2011 Per protocol cohorts</td>
</tr>
</tbody>
</table>
COST BENEFIT BALANCE: GENERAL CONSIDERATIONS

**Women only**

- Highest burden of severe disease is in women
- High cost of the vaccine
- Herd protection may be sufficient for both genders if high female vaccination rates are achieved (*requires stable heterosexual populations*)

**Include males**

- Recognition of the HPV etiology of significant number of cancers in males
- Impact of GW’s & global burden of disease / health services requirements
- Trends in sexual practices in many countries. MSM, high risk groups
- Interrupting the transmission chain to other partners
- *Powerful herd effects and program resilience if both genders are included*

Australia, US, Canada, Austria, Italy, Argentina... 13+ countries
prospects

• Vaccination of girls will *continue and expand* under the two dose regimes (i.e. GAVI countries)
  – *One-dose* regime
  – Vaccination of *boys*
  – Vaccination of *middle aged women*
  – Vaccination of *high risk groups*

• *Elimination of cervical cancer* is being proposed as part of the new edition of the WHO’s millennium goals