University of Maryland Greenebaum Cancer Center

Cervical Cancer

- 11,000 cases and 4000 deaths in US
- 288,000 deaths worldwide each year
- Incidence in US
  - 2.7/100,000/year white
  - 5.9/100,000/year African American
- Incidence in Haiti
  - 94/100,000/year

Cervical Cancer Mortality

- 30% in US (pap smears)
- 60% worldwide
- Approaches 100% in developing countries – delay in diagnosis

Papillomavirus and Cervical Cancer

- More than 30 types of papillomavirus
- 95+% of cervical cancers contain detectable HPV DNA
- 80% of cancers associated with HPV 16,18,33 and 45
- 70% of cancers associated with HPV 16 and 18
- Associated with other cancers as well

Papillomavirus vaccine development

- HPV monovalent (HPV 16) vaccine shown to protect against persistent infection 2002
- Schlegel lab (Georgetown) develops bivalent vaccine against HPV 16/18 – licensed through Medimmune to GSK

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Efficacy of a bivalent L1 virus-like particle vaccine in prevention of infection with human papillomavirus types 16 and 18 in young women: a randomised controlled trial

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Summary

Background Vaccination against the most common oncogenic human papillomavirus (HPV) types, HPV-16 and HPV-18, could prevent development of up to 70% of cervical cancers worldwide. We did a randomised, double-blind, controlled trial to assess the efficacy, safety, and immunogenicity of a bivalent HPV-16/18 L1 virus-like particle vaccine for the prevention of incident and persistent infection with these two virus types, associated cervical cytological abnormalities, and precancerous lesions.

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Findings In the according-to-protocol analyses, vaccine efficacy was 91·6% (95% CI 64·5–98·0) against incident infection and 100% against persistent infection (47·0–100) with HPV-16/18. In the intention-to-treat analyses, vaccine efficacy was 95·1% (63·5–99·3) against persistent cervical infection with HPV-16/18 and 92·9% (70·0–98·3) against cytological abnormalities associated with HPV-16/18 infection. The vaccine was generally safe, well tolerated, and highly immunogenic.

Interpretation The bivalent HPV vaccine was efficacious in prevention of incident and persistent cervical infections with HPV-16 and HPV-18, and associated cytological abnormalities and lesions. Vaccination against such infections could substantially reduce incidence of cervical cancer.

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Vaccination against human papillomaviruses shows great promise

It took almost 10 years from the discovery of an association between human papillomavirus (HPV) and cervical cancer[1] to the finding of HPV type 16 in cervical cancer tissue.[2] It took another 10 years to show that past infection with HPV16 increases the risk for subsequent development of invasive cervical cancer,[3] and yet another decade to show that the seven most prevalent HPV types cause 87% of all cervical cancers.[4] By comparison, the creation of HPV virus-like-particle (VLP) vaccines has been a rapid breakthrough. VLPs mimic the true structure of the virion and induce a striking antibody response after vaccination.[5] 2 years ago, Koutsky et al[6] showed that vaccination with HPV16 VLPs protected 768 vaccinated women from persistent HPV16 infection.

In today's *Lancet*, Diane Harper and colleagues now expand this rapid development in a phase 2 trial in just over 1100 participants, a study that lasted 2·5 years. VLPs of the two most important oncogenic HPV types, HPV16 and HPV18, were combined in a preventive vaccine. According-to-protocol and intention-to-treat analyses showed high efficacy for this bivalent vaccine against both the incident and persistent HPV16 and HPV18 infections. This efficacy turned out to be excellent even though the most sensitive method, vaginal self-sampling, was used to define the endpoints.

Second Generation Vaccine

- Current vaccine expensive, requires refrigeration
- GST/HPV L1 fusion protein
- Produced in tobacco plants
- Simple extraction and purification process
- No refrigeration necessary

Papillomavirus Vaccine and Cervical Cancer

- May be justifiable in developed world because of high cost of current screening methodology
- Vaccination in developing world could save more than 200,000 lives annually.