

Innovations in Human Papillomavirus Vaccine



Topics

- 1. Current HPV vaccines
- 2. New development
- 3. What's next?



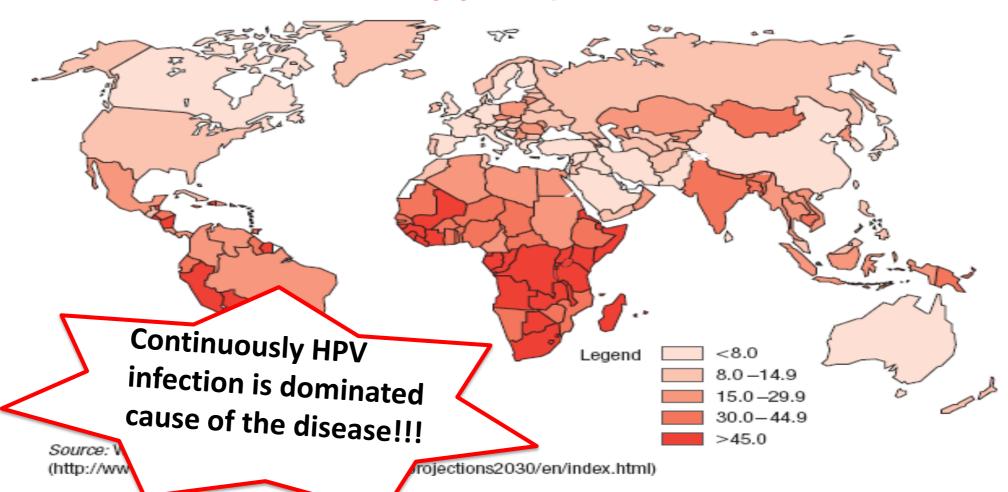
PART I CURRENT HPV VACCINES

Worldwide incidence of cervical cancer

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

Current HPV

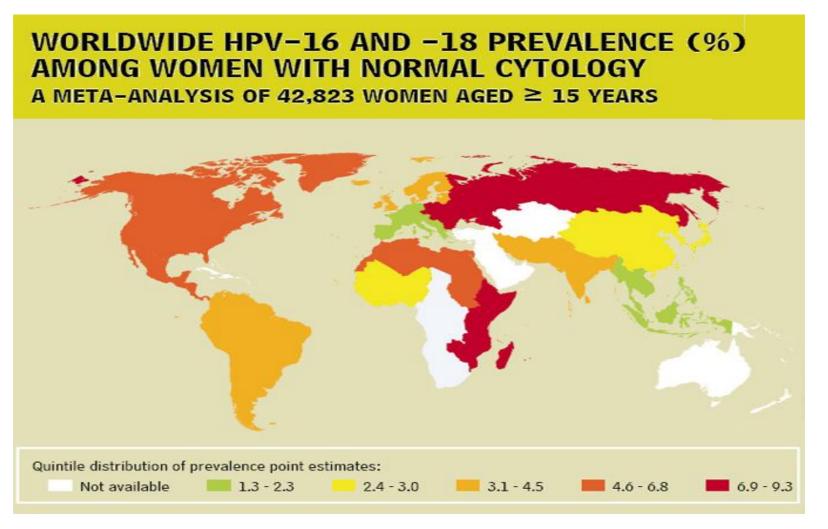
Vaccines



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

Current HPV

Vaccines

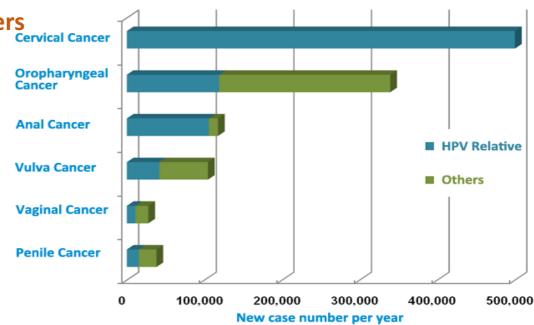


Human Papillomavirus Vaccine (HPV) —— World's first vaccine against cancer

- **Current HPV**
 - **Vaccines**

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- Persistent infection of certain high risk types of HPV can cause cervical cancer in women
 - More than <u>529,000 new cases</u> 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



HPV Vaccines

Current HPV

Vaccines

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.

Vaccine	Company	Market launch	2012 Sales (US\$)	2013 Sales (US\$)
Gardasil	Merck	Jan 2006	1.6 billion	1.8 billion
Cervarix	GSK	Sep 2007	362 million	230 million

PART II NEW DEVELOPMENT

Increased Valences



New

development

- > 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

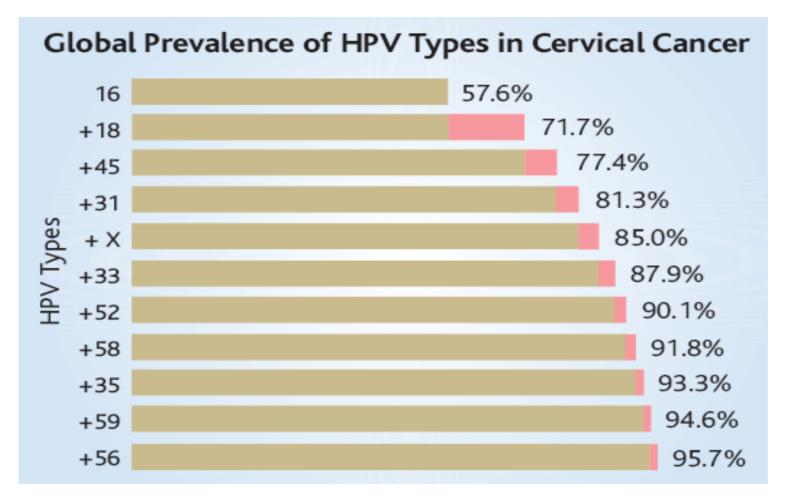
9-Valent HPV Vaccine

—— Stronger protect against Cervical Cancer

New

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development





New

development

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

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.



New

development

Immunogenicity of 2 vs. 3 doses of HPV vaccination in immunocompetent girls

Population: Immunocompetent females

Intervention: 2 doses of HPV vaccination in girls (9-14 years)
Comparison: 3 doses of HPV vaccination in girls or women

Outcome : Immunogenicity (GMT)

What is the scientific evidence of non-inferior immunogenicity of a 2 dose HPV vaccination schedule in girls (9-14 years) compared to a three dose schedule in girls or women?

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			Rating	Adjustment to rating		
	No. of studies/starting rating		4/ RCT 2/ observational	4		
Quality Assessment	Factors decreasing confidence	Limitation in study design ^{II}	Serious	-1		
		Inconsistency	None serious	0		
		Indirectness	None serious	0		
		Imprecision	None serious	0		
ality		Publication bias	None serious	0		
Ou	Factors increasing confidence	Large effect	Not applicable	0		
		Dose-response	Not applicable	0		
		Antagonistic bias and confounding	Not applicable	0		
	Final nume	erical rating of qual	ity of evidence	3		
Summary of Findings	State	ment on quality of	evidence	We are moderately confident in the estimate of effect on health outcome. The true effect is likely to be close to the estimate of the effect.		
		Conclusion		We are moderately confident that a 2-dose HPV schedule induces non-inferior immunogenicity compared to a 3-dose HPV schedule. Evidence from 3 RCTs as well as 2 non-randomized / non-controlled trials indicate that a two dose HPV schedule in girls induces non-inferior levels of GMT to HPV 16 and 18 than a three dose schedule in girls or women. Bridging studies allow assumption of efficacy of a 2-dose		

Efficacy of 2 vs. 3 doses of HPV vaccination in immunocompetent girls

Population: Immunocompetent females

Intervention: 2 doses of HPV vaccination in girls (9-14 years)
Comparison: 3 doses of HPV vaccination in girls or women

Outcome : Cervical Cancer

What is the scientific evidence of non-inferior immunogenicity of a 2 dose HPV vaccination schedule in girls (9-14 years) compared to a three dose schedule in girls or women?						
			Rating	Adjustment to rating		
	No. of studies/starting rating		4/ RCT 2/ observational	4		
Quality Assessment	Factors	Limitation in study design	Serious	-1		
LS:		Inconsistency	None serious	0		
8	decreasing	Indirectness	Serious	-2		
As	Communica	Imprecision	None serious	0		
₹		Publication bias	None serious	0		
- E		Large effect	Not applicable	0		
a	Factors increasing confidence	Dose-response	Not applicable	0		
		Antagonistic bias and confounding	Not applicable	0		
	Final numerical rating of quality of evidence			1		
	Statement on quality of evidence			We have very little confidence in the estimate of the effect on the health outcome.		
Summary of Findings	Summary of Findings Conclusion			No data vaccine efficacy against cervical cancer is available using a 2-dose HPV schedule despite non-inferior immunogenicity compared to a 3-dose HPV schedule. Evidence from 3 RCTs as well as 2 non-randomized / non-controlled trials indicate that a two dose HPV schedule in girls induces non-inferior levels of GMT to HPV 16 and 18 than a three dose schedule in girls or women. Bridging studies allow assumption of efficacy of a 2-dose vaccination schedule in girls (9-14 years).		

2-dose regiment VS. 3-dose regiment

2

New

development

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

What's next?

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.



Relevé épidémiologique hebdomadaire 24 OCTOBER 2014, 89th YEAR / 24 OCTOBRE 2014, 89* ANNEE No. 43, 2014, 89, 465-492

Organisation mondiale de la Santé

465 Vaccins contre le papilloma de l'OMS, actabre 2014

Human papillomavirus vaccines: WHO position paper, October 2014

Introduction

In accordance with its mandate to provide guidance to Member States on health policy matters, WHO issues a series of regularly updated position papers on vaccines and vaccine combinations against diseases that have an international public health impact. These papers are concerned primarily with the use of vaccines in largescale immunization programmes. They summarize essential background information on their respective diseases and vaccines, and conclude with the current WHO position concerning their use in the global

The papers are reviewed by external experts and WHO staff, and reviewed and endorsed by the WHO Strategic Advisory Group of Experts (SAGE) on immunization (http://www.who.int/immunization/ sage/en/). The GRADE methodology is used to systematically assess the quality of available evidence. A description of the process followed for the development of vaccine position papers is available at: http://www.who.int/immunization/position_papers/position_paper_process.pdf.

The position papers are intended for use mainly by national public health officials and managers of immunization programmes. They may also be of interest to nternational funding agencies, vaccine advisory groups, vaccine manufacturers, the medical community, scientific media and the public.

This document replaces the first WHO position paper on vaccines against diseases caused by human papillomaviruses (HPV), published in 2009. It focuses primarily on the prevention of cervical cancer, but also considers the broader spectrum of cancers and other diseases preventable by HPV vaccination. In April

Vaccins contre le papillomavirus humain: note de synthèse de l'OMS, octobre 2014

No. 43

Introduction

Conformément à son mandat qui est de fournir des conseils aux Etats Membres sur les questions relatives aux politiques sanitaires, l'OMS publie une série de notes de synthèse régulièrement actualisées sur les vaccins et les associations vaccinales contre les maladies qui ont des répercussions sur la santé publique internationale. Ces notes de synthèse, qui portent essentiellement sur l'utilisation des vaccins dans le cadre de programmes de vaccination à grande échelle, résument les considérations générales essentielles sur les maladies et vaccins concernés et présentent en conclusion la position actuelle de l'OMS concernant leur utilisation dans le contexte mondial.

Ces notes sont soumises à des experts à l'extérieur et à l'intérieur de l'OMS et sont examinées et approuvées par le Groupe stratégique consultatif d'experts sur la vaccination (SAGE) de POMS (http://www.who.int/immunization/sage/ en/). La méthodologie GRADE est utilisée pour évaluer de manière systématique la qualité des éléments disponibles. Une description du processus suivi pour l'élaboration des notes de synthèse sur les vaccins est disponible à l'adresse suivante: http://www.who.int/immunization/position_ papers/position_paper_process.pdf.

Ces notes sont principalement destinées aux responsables nationaux de la santé publique et aux administrateurs des programmes de vaccination. Toutefois, elles peuvent également présenter un intérêt pour les organismes internationaux de financement, les groupes consultatifs sur les vaccins, les fabricants de vaccins, la communauté médicale, les médias scientifiques et le grand public.

Ce document remplace la première note d'information de l'OMS sur les vaccins contre les maladies dues à des papillomavirus humains (PVH), publiée en 2009. Elle porte principalement sur la prévention des cancers du col de l'utérus, mais passe également en revue le large spectre des cancers et autres maladies évitables par la vaccination anti-PVH. En avril 2014, le SAGE a

WORLD HEALTI ORGANIZATION

GANISATION MONDIAL DE LA SANTÉ

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What's next?

Upcoming events

Health topics

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



- 3
- What's next?

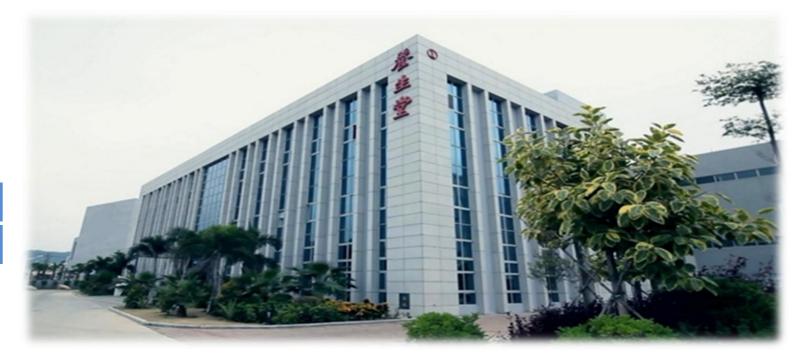
- Two companies supplying so far
- > Two more companies in Phase 3 trials
- Several more in earlier stage
- Can these 4 companies supply the world?
- Needs for innovative ways to supply?



Innovax

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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