


HPV VACCINE

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MAIN TYPES OF HIGH GRADE AND LOW GRADE HPV

□ High risks HPV :

- 16;18; 31;33;35;39;45;51;52;56;58;59;68;73;82

□ Low risks HPV :

- 6; 11; 40; 42; 43; 44; 54; 61; 70; 72; 81; CP6108

□ Potentially high risks HPV :

- 26; 53; 66



Human Papillomavirus

- Main precursor and principal causes of invasive cervical cancer (identification by PCR DNA in 99.7% of cases)
- Development of a vaccine early in 1980 after evident correlation between HPV and cervical cancer
- CC occurs 10 to 15 years after initial infection with HPV



Introduction

Two types of HPV vaccines actually available

□ Gardasil*

- Merck Quadrivalent vaccine protects against four types of HPV
 - Low risk HPV: 6, 11
 - High risk: 16, 18

□ Cervarix*

- GSK Bivalent vaccine protects against two types of HPV: 16, 18



MERCK QUADRIVALENT VACCINE GARDASIL*

- **non-infectious recombinant, quadrivalent vaccine**
- **prepared from the highly purified virus-like particles (VLPs) of the major capsid (L1) protein of HPV Types 6, 11, 16, and 18**



Gardasil®

- sterile liquid suspension prepared by combining
 - the adsorbed VLPs of each HPV type
 - and additional amounts of the aluminum-containing adjuvant
 - and the final purification buffer



Presentation

- GARDASIL is a sterile preparation for intramuscular administration.
- Each 0.5-mL dose contains approximately
 - 20 mcg of HPV 6 L1 protein,
 - 40 mcg of HPV 11 L1 protein,
 - 40 mcg of HPV 16 L1 protein,
 - and 20 mcg of HPV 18 L1 protein.



Gardasil composition

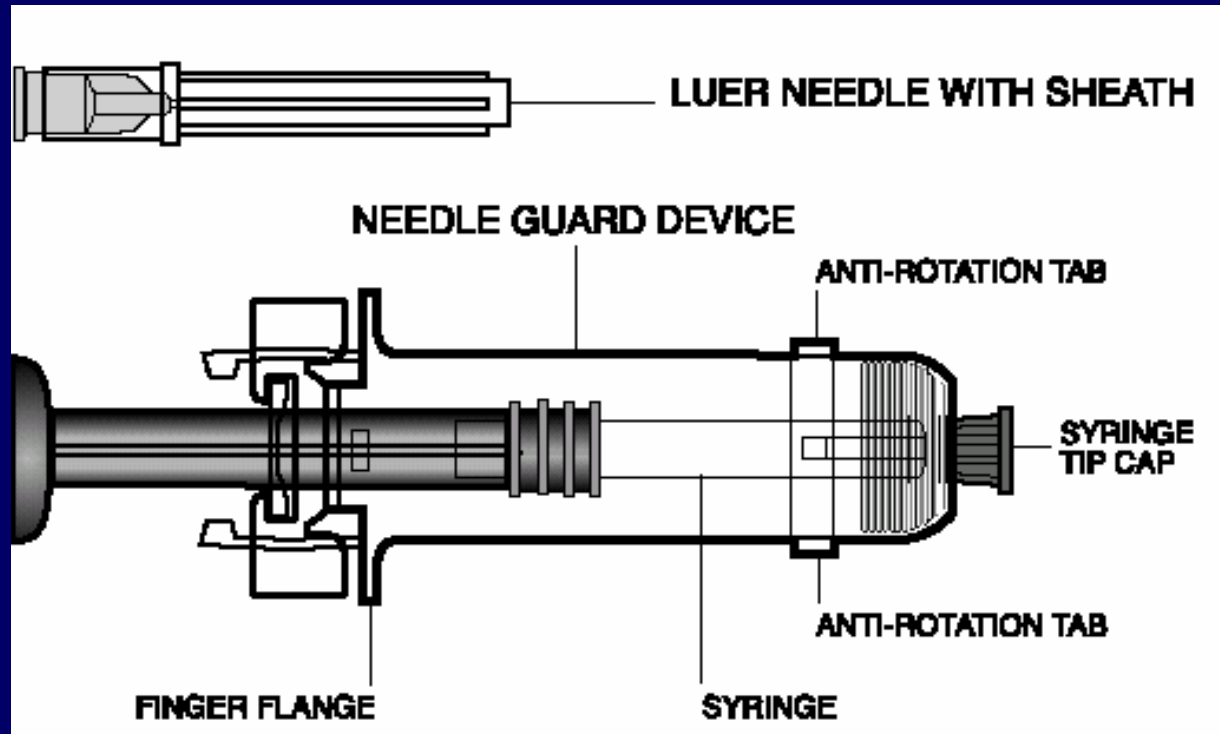
- Each 0.5-mL dose of the vaccine contains approximately
 - 225 mcg of aluminum (as amorphous aluminum hydroxyphosphate sulfate adjuvant),
 - 9.56 mg of sodium chloride,
 - 0.78 mg of L-histidine,
 - 50 mcg of polysorbate 80,
 - 35 mcg of sodium borate, and water for injection.
- The product does not contain a preservative or antibiotics.
- After thorough agitation, GARDASIL is a white, cloudy liquid.



Gardasil[®] presentation

- The prefilled syringe (0.5ml) is for single use only and should not be used for more than 1 individual.
- The vaccine should be used as supplied; no dilution or reconstitution is necessary. The full recommended dose of the vaccine should be used.
- Store refrigerated at 2 to 8°C.

Prefilled single-dose syringes





INDICATIONS AND USAGE

- **GARDASIL is a vaccine indicated in girls and women 9-26 years of age for the prevention of the following diseases caused by Human Papillomavirus (HPV) types 6, 11, 16, and 18:**
 - • **Cervical cancer**
 - • **Genital warts (condyloma acuminata)**

- **and the following precancerous or dysplastic lesions:**
 - • **Cervical adenocarcinoma *in situ* (AIS)**
 - • **Cervical intraepithelial neoplasia (CIN) grade 2 and grade 3**
 - • **Vulvar intraepithelial neoplasia (VIN) grade 2 and grade 3**
 - • **Vaginal intraepithelial neoplasia (VaIN) grade 2 and grade 3**
 - • **Cervical intraepithelial neoplasia (CIN) grade 1**



CONTRAINDICATIONS

- Hypersensitivity to the active substances or to any of the excipients of the vaccine.
- Individuals who develop symptoms indicative of hypersensitivity after receiving a dose of GARDASIL should not receive further doses of the same drug.



PRECAUTIONS

- This vaccine is not intended to be used for treatment of active genital warts; cervical cancer; CIN, VIN, or VaIN.
- This vaccine will not protect against diseases that are not caused by HPV.
- GARDASIL has not been shown to protect against diseases due to non-vaccine HPV types.
- As with all injectable vaccines, appropriate medical treatment should always be readily available in case of rare anaphylactic reactions following the administration of the vaccine.



Drug Interactions

- **Use with Other Vaccines**
- Results from clinical studies indicate that GARDASIL may be administered concomitantly (at a separate injection site) with hepatitis B vaccine (recombinant)
- Co-administration of GARDASIL with other vaccines has not been studied.



Use with Hormonal Contraceptives

- Use of hormonal contraceptives or lack of use of hormonal contraceptives did not alter vaccine efficacy.



Use with Systemic Immunosuppressive Medications

- Immunosuppressive therapies, including irradiation, antimetabolites, alkylating agents, cytotoxic drugs, and corticosteroids (used in greater than physiologic doses), may reduce the immune responses to vaccines.



Carcinogenesis, Mutagenesis, Impairment of Fertility

- GARDASIL has not been evaluated for the potential to cause carcinogenicity or genotoxicity.
- GARDASIL administered to female rats at a dose of 120 mcg total protein, which corresponds to approximately 300-fold excess relative to the projected human dose, had no effects on mating performance, fertility, or embryonic/fetal survival.



Pregnancy

- There were no vaccine-related fetal malformations or other evidence of teratogenesis.
- There were no treatment-related effects on developmental signs, behavior, reproductive performance, or fertility of the offspring.



Vaccine-related Injection-site

Adverse Experience (1 to 5 Days Postvaccination) (Injection site)	GARDASIL N= 5088)	PLACEBO N= 3470)
Pain	83.9	75.4
Swelling	25.4	15.8
Erythema	24.6	18.4
Pruritus	3.1	2.8



Dosage and administration

- GARDASIL should be administered intramuscularly as 3 separate 0.5-mL doses according to the following schedule:
 - First dose: at elected date
 - Second dose: 2 months after the first dose
 - Third dose: 6 months after the first dose



Method of Administration

- GARDASIL should be administered intramuscularly in the deltoid region of the upper arm or in the higher anterolateral area of the thigh.
- GARDASIL must not be injected intravascularly. Subcutaneous and intradermal administration have not been studied, and therefore are not recommended.



II - CERVARIX" GSK Biologicals HPV vaccine

- Bivalent vaccine
 - Composition: 20 µg of VLP's HPV 16 and 20 µg of VLP's HPV 18
 - Mode of administration: 3 injections
 - Mo, 1 month and 6 months
 - Already tested in some African countries, prevents around 73.4% of CC induced by HPV 16 and 18 (sample size 1113)
 - Induce very high immunologic response



CERVARIX[®] : Efficacy

- HPV 16 and 18: 99 to 100%
- HPV 45: 88%
- HPV 31: 54% only



Cervarix[®]

- Vaccination at early age induced very high immunologic response.
- Cervarix is a well tolerated vaccine.
- A multicentric study is actually implemented in some African countries, Cameroon will eventually be included in this study.
- Possibility to include later these vaccine in some African countries vaccination campaign program after studies on the field.



Conclusion

- Cervical cancer prevention in our countries must remain focused on routine screening (VIA, VILI, Paps smear when possible)
 - Training of personnel (MD, Gynecologists, Nurses)
 - Education of the population
 - Early intervention
- This strategy has reduced cervical cancer rates in developed countries by approximately 75% in compliant individuals by monitoring and removing premalignant dysplastic lesions.



PREVENTION OF CERVICAL CANCER IN DEVELOPING COUNTRIES

- **Primary prevention:**
 - **All methods that can reduce transmission of HPV**
 - **Abstinence**
 - **Fidelity**
 - **Vaccination against HPV (costly for poor countries)**



Secondary prevention

- **Identification and treatment of all precancerous lesions before their evolution to invasive CC**
 - **Screening campaigns using VIA, VILI, Paps smear, colposcopy and biopsy**
 - **Training of personnel for screening (gynaecologists, pathologists, nurses)**
 - **Vulgarisation of simple screening methods**
 - **Financial supports+++**



Future for developing countries

- **Training of personnel adapted to our context**
- **Development of screening campaign for precancerous lesions**
- **Vaccination against oncogenic HPV (costly!!!)**
- **Therapeutic vaccine**
- **Development of an adequate policy for cancer prevention**



Limitations for developing countries

- ❑ Gardasil®: High Cost ~ \$ 300 (CFA 180 000), more than one month salary of a young medical doctor
- ❑ ~30% of cancers are caused by types of HPV non concerned by actual vaccines.
- ❑ Absence of adequate cancer prevention policy
- ❑ Lack of Information and Education for the populations
- ❑ Viral HPV types not well known in various African countries



Thanks for your attention

- **The Reunification Monument in Yaounde**

