GSK Medicine: *Cervarix™* (HPV-1): GlaxoSmithKline (GSK) Biologicals' bivalent human papillomavirus (HPV) types 16 and 18 vaccine

Study No.: 114420 (EPI-HPV-025 BOD TW)

Title: Additional health and economic impact of the bivalent versus the quadrivalent HPV vaccine in Taiwan: results of a prevalence-based model

Rationale: This study was performed to compare the health and economic impact of HPV-1 vaccine and another licensed HPV vaccine (HPV-2).

Objectives:
To evaluate at the population level the potential differences in the annual impact with the HPV-1 versus the HPV-2 vaccine on cases prevented (pre-cancerous lesions, genital warts [GWs], cervical cancer [CC]) and costs in Taiwan. Costs were assessed from a healthcare payer's and a societal perspective

Indication: Immunization against HPV in women.

Study Investigators/Centers: GSK conducted study

Research Methods: Health economic modeling study

Data Source: Epidemiological and cost data were obtained from published sources. Efficacy figures were based on the latest results from each vaccine's respective clinical trial:

- In the base case analysis, costs were assessed from a healthcare payer's perspective, including National Health Insurance (NHI)-covered costs only.
- Five types of HPV-related lesions were included in the analysis: atypical squamous cells of undetermined significance (ASCUS), cervical intraepithelial neoplasia 1, 2 and 3 (CIN 1, CIN2/3), GW and CC. The annual numbers of new ASCUS, CIN1 and CIN2/3 cases (incidence) were retrieved from Taiwan Registry data and that of GW was sourced from the literature.
- The proportion of CIN2 and CIN 3 cases (CIN2/3) and their unit costs were retrieved from the literature.
- Unit costs for the treatment of ASCUS and GW were based on a survey from local clinics and retrieved from the literature.

Study Design: Static prevalence-based model to estimate vaccine effect over a one-year period at a steady state (when all women are fully vaccinated).

Study Population: HPV-vaccinated women in Taiwan.

Study Exposures, Outcomes:
The study groups were as follows:

- HPV-1 Group: Hypothetical group of women vaccinated with HPV-1 vaccine
- HPV-2 Group: Hypothetical group of women vaccinated with HPV-2 vaccine

Primary outcomes#:

- Annual number of lesions prevented by each vaccine*
- Lesion related total cost averted for the period of one year by each vaccine**
- Additional costs averted with the bivalent versus the quadrivalent vaccine***

*The annual number of lesions prevented by each vaccine were estimated by multiplying the number of cases observed in one-year (incidence data) by the corresponding lesion specific vaccine efficacy
**The lesion related total cost averted for the period of one year by each vaccine was estimated by multiplying the annual numbers of lesions prevented for each vaccine by treatment unit cost for each lesion type
***The additional costs averted with the bivalent versus the quadrivalent vaccine were estimated by comparing the total costs averted by each of the vaccines
#In this CTRS no distinction will be made between primary and secondary outcome, therefore all outcomes are considered as primary outcomes.

Data Analysis Methods:
A static prevalence-based model was developed, which estimates the differences in lesions, GW, CC, and costs from a healthcare payer's perspective prevented between the two vaccines over a one-year period at steady state (i.e. when all women are vaccinated). In addition, an analysis from a societal perspective was performed, including also indirect costs and out-of-pocket payments. Univariate sensitivity analyses were conducted, in which parameters were varied 20% up and down from the baseline value.

- In the model, incidence cases were multiplied by lifetime unit costs to estimate the overall treatment costs over a one year period.
- Vaccination coverage of 100% in 12-year-old girls was assumed. No discount was applied to costs since the model simulates the effect of vaccination over a one-year period.
- Vaccination costs were not included in the analysis as identical vaccination costs were assumed for both

vaccines resulting in a null incremental value while comparing both vaccines.

- For CIN2/3, lifetime unit costs were calculated using a weighted average of CIN2 and CIN3 costs.
- Lifetime unit costs of CC were calculated by multiplying the weighted average of the annual treatment costs of stage I-IV CC with the average CC case duration.
- For ASCUS, only an overall vaccine efficacy was available for both vaccines for inclusion in the analyses.
- The vaccine efficacy for each lesion was determined based on the proportion of vaccine type HPV 16/18/6/11 and the 10 most prevalent non-vaccine HPV types (-31,-45, -33, -52,-58,-35,-39,-51,-56,-59) in Taiwan for each lesion and respective vaccine efficacy on each type in a HPV-naïve population. No differences was assumed between the vaccines on the efficacy against vaccine HPV types 16/18; 98,0 % vaccine efficacy was applied to both vaccines.

Limitations: Not applicable

Study Results:
In accordance with the design of this particular mathematical modelling study, not all outcome measures ordinarily assessed in a routine clinical trial were analyzed. This summary presents only the results of those outcome measures that were analyzed in this mathematical modelling study.

Demographics/Baseline Characteristics	Not available

Primary Outcome Variable: Annual number of cases prevented with the bivalent and the quadrivalent vaccines (at steady state)

	HPV-1 Group	**HPV-2 Group**
ASCUS	6343	4571
CIN1	6668	4916
GW	0	7970
CIN2/3	4503	3273
CC	1445	1278

Primary Outcome Variable: Additional annual NHI-covered costs and societal costs (in NTS) averted with the bivalent vaccination versus the quadrivalent vaccination in Taiwan (at steady state)

	Additional NHI costs averted	**Additional societal costs averted**
ASCUS	885.701	1.594.262
CIN1	4.111.406	7.359.189
GW	-6.575.390	-11.835.702
CIN2/3	8.555.610	15.679.339
CC	33.716.078	46.666.270
Total costs	40.693.405	59.463.358

Primary Outcome Variable: Sensitivity of the additional annual NHI covered costs averted with the bivalent versus the quadrivalent vaccine to costs and cross protection (univariate analysis – difference in NTS)

Variable changed	**Min**	**Max**
Unit costs of ASCUS	40.516.265	40.870.545
Unit costs of CIN1	39.871.124	41.515.686
Unit costs of GW	39.378.327	42.008.483
Unit costs of CIN2/3	38.982.283	42.404.527
Unit costs of CC	33.950.189	47.436.621
Cross protection of the bivalent vaccine	22.207.951	59.178.859

Conclusion: This modeling exercise predicts that in the HPV-1 Group, ASCUS, CIN1; GW, CIN 2/3, and CC will be prevented in 6343, 6668, 0, 4503, and 1445 women , respectively, while these cases will be prevented in 4571, 4916, 7970, 3273, and 1278 women in the HPV-2 Group. Additional annual costs averted with the bivalent vaccination versus the quadrivalent vaccination will be of 40.693.405 NTS for the NIH covered costs and 59.463.358 NTS for the societal costs.

Publications:
Abstract: ADDITIONAL HEALTH AND ECONOMIC IMPACT OF THE BIVALENT VERSUS THE QUADRIVALENT HPV VACCINE IN TAIWAN: RESULTS OF A PREVALENCE-BASED MODEL, Ho. T.H., van Enckevort, P.J. & Demarteau, N. Poster presented at: ISPOR, 4th Asia-Pacific Conference, 5-7 September 2010, Phuket, Thailand.

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