

Final Abstract Number: 3.002

Session: Synergy of Bacterial Flora in the Nasopharynx: Impact on Prevention Strategies

Date/time: Friday, 20 June, 2008, 10:15-12:15 hrs

Room: Plenary Theatre

Antibody Responses Following Administration of 10-Valent Pneumococcal Non-Typeable *Haemophilus influenzae* Protein D-Conjugate Vaccine (PHiD-CV) in Filipino Infants

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Background: This double-blind, controlled study (107007/NCT00344318) evaluated the immune responses of the candidate vaccine, PHiD-CV (GlaxoSmithKline Biologicals), designed to protect infants against pneumococcal and non-typeable *Haemophilus influenzae* diseases, following co-administration with DTPw-HBV/Hib + OPV at 6-10-14 weeks of age (EPI schedule) in the Philippines.

Methods: 400 healthy Filipino infants 6 to 12 weeks of age were randomized (3:1) to receive either PHiD-CV or licensed 7vCRM vaccine (*Prevenar*TM/*Prevnar*TM) co-administered with DTPw-HBV/Hib + OPV. Vaccine immune responses were assessed one month post-dose III (22F-inhibition ELISA, ELISA, micro-neutralization assays).

Results: For each of the pneumococcal serotypes common between both vaccines, observed percentages of infants with antibody concentration $\geq 0.2\mu\text{g/mL}$ were within the same range for both groups (PHiD-CV group: $\geq 91.2\%$; 7vCRM group: $\geq 86.3\%$). At least 99.6% of PHiD-CV vaccinees had antibody concentrations $\geq 0.2\mu\text{g/mL}$ against pneumococcal serotypes 1, 5 and 7F. Anti-pneumococcal geometric mean antibody concentrations were within the same range for both vaccines except for serotypes 18C and 19F for which higher immune responses were observed in the PHiD-CV group. Moreover, immune responses of all co-administered vaccines were in line with previous observations, with the exception of responses against polio virus types 1 and 3 which seemed lower in the 7vCRM group. Based on these immunogenicity results, PHiD-CV could potentially prevent 79% of IPD in Filipino infants compared to 62% for 7vCRM (abstract# 3.003), reflecting the importance of the additional serotypes (especially 1 and 5) for IPD in the Philippines.

Conclusion: PHiD-CV elicited high immune responses for each of the 10 pneumococcal vaccine serotypes in infants vaccinated according to the 6-10-14 week's schedule. No evidence of negative immunological interference between PHiD-CV and co-administered vaccines was observed.

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Impact Estimate of the 10-Valent Pneumococcal Non-Typeable *Haemophilus influenzae* Protein D-Conjugate Vaccine (PHiD-CV) on Invasive Pneumococcal Disease (IPD) in Middle East and Asian Countries

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Background: The candidate PHiD-CV vaccine (GlaxoSmithKline Biologicals), contains 3 additional serotypes (1,5,7F) in comparison to the licensed 7vCRM vaccine (*Prevenar*TM/*Prevnar*TM).

Methods: Public health impact of PHiD-CV was estimated based on serotype-specific vaccine effectiveness (SSVE) values for 7vCRM¹, country-specific IPD serotype distribution and serotype-specific immunological differences between PHiD-CV and 7vCRM when co-administered at 6-10-14 weeks of age with DTPw-HBV/Hib and OPV vaccines in the Philippines (abstract# 3.002). SSVE's for PHiD-CV (each serotype in common with 7vCRM and 6A) were obtained by multiplying 7vCRM SSVE's by the ratio of the percentages of PHiD-CV- versus 7vCRM-vaccinated children reaching a predefined immunogenicity threshold one month after 3 primary doses. SSVE's for 19A (both vaccines) and for 1,5,7F (PHiD-CV) were set essentially equivalent to the % children achieving the threshold for each serotype. The overall impact of each vaccine in country-j ($IPD-IE_{overallj}$) is shown in equation 1 below.

Results: Using the 0.2µg/mL threshold (22F-ELISA) as basis of comparison and applying the IPD-IE to IPD serotype data from several countries, PHiD-CV is estimated to prevent approximately 59-85% of IPD while 7vCRM would prevent 38-75% as shown in table below. Similar results were obtained using ELISA 0.35µg/mL or OPA 1:8 as immunological thresholds for comparison. Since countries might be using different immunization schedules or DTPa-based co-administered vaccines, IPD-IEs were also computed using immunogenicity data from a European study in which PHiD-CV or 7vCRM were co-administered with DTPa-HBV-IPV + Hib-MenC at 2-4-6 months of age. Calculated IPD-IEs (PHiD-CV: 57-80%; 7vCRM: 36-74%) were within the same range as those mentioned above.

Conclusion: PHiD-CV would be predicted to prevent 59-85% of IPD in children depending on the relative importance of serotypes 1, 5, 7F in the above noted Middle East and Asian countries.

¹WhitneyCG Lancet 2006 368:1495-502.