Type: Poster Presentation

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Is a compact prefilled auto-disable injection system (cPAD) cost effective for pentavalent vaccine?

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Background: The pentavalent combination vaccine is the WHO-recommended form of the DTP-HepB-Hib vaccine. It is available in single dose vial (SDV), multi-dose vials (MDV) and soon in a compact prefilled auto-disable injection system (cPAD). A costing model was developed and used in three countries to perform a Cost-Effectiveness Analysis (CEA) of these three presentations.

Methods & Materials: The model included the costs of vaccine, safe injection equipment, storage, transport, distribution, vaccine administration by health staff, waste management, start-up activities, coverage and wastage rates. The outcome was the incremental cost/saving per fully immunized child (FIC) for a switch to cPAD. The model was used in Peru, Ghana and Cambodia. Field visits to health facilities, interviews with key informants from immunization services and regulatory affairs were conducted.

Results: Based on vaccine price trends estimated for the year 2016, cPAD would be more cost-effective in Ghana compared to the current presentation (MDV-10) and in Peru (SDV). In Cambodia, cPAD would be less cost effective (SDV).

The most significant driver of the cost per FIC is the cost of the vaccine (including compensation for vaccine wastage) in any presentation: accounting for 85% of total cost in Peru and over 97% in the two other countries. The dominance of the vaccine price per dose and to a lesser extent the wastage rates and cost of safe injection equipment as drivers of the incremental cost per FIC show the potential to simplify future analyses. Programmatic contexts and perceptions of stakeholders influence the decision to introduce new vaccine presentations. Other factors include the potential for improved safety with cPAD, planned introduction of other vaccines and environmental issues relating to reduced waste generation.

Conclusion: Based on vaccine price estimated for the year 2016, the cPAD could be the most cost-effective presentation in many countries. For decision making and policy dialogue other factors (injection safety, programmatic aspects, etc.) may be important when considering shifting to a new vaccine presentation such as cPAD.

Conflict of interest: Crucell funded the study.

Table 1.

Table 1
Incremental costs of cPAD as compared to the current pentavalent presentation

	Cambodia, 2013-2020	Ghana, 2013-2017	Peru, 2013-2017
Incremental cost per FIC USD (%)	0.32 (+3.76%)	−0.58 (-6.41%)	−0.90 (-7.20%)

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Clinical development of a recombinant live attenuated tetravalent dengue vaccine

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Background: Takeda is developing a tetravalent, live attenuated dengue vaccine (LADV) consisting of a molecularly characterized, attenuated DENV-2 strain and three chimeras in which the prM and E genes of the attenuated DENV-2 were substituted with those of DENV- 1, -3 or -4 viruses.

Methods & Materials: Takeda is conducting Phase 1 and 2 clinical trials for the LADV

Results: The results of our Phase 1 and 2 clinical trials in healthy subjects support the safety and immunogenicity of the tetravalent vaccine. Administration of LADV was generally well-tolerated with mostly mild and transient local or systemic reactions. There were no related serious or severe adverse events (AEs), and no discontinuations due to vaccine-related AEs. The LADV induced neutralizing antibody responses to all four dengue viruses after one or two administrations.

Conclusion: These studies highlight the safety and immunogenicity of the tetravalent LADV vaccine in children and adults in dengue endemic countries. Based on our results from Phase 1 and 2 studies, the LADV warrants further evaluation in Phase 3 efficacy studies in children and adults in dengue-endemic countries.

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A large single-center retrospective analysis of neutralizing antibodies after intradermal pre-exposure rabies vaccination

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Background: Soldiers in the Belgian Defence are intradermally vaccinated for rabies pre-deployment since 2008 by a four injection schedule (day 0,7, 28, 365). Neutralizing antibody titers against rabies were tested 7 days after booster vaccination. Serology results of subjects, vaccinated between the 1st of april 2008 and the 31st of june 2013, were evaluated. A titer of the Rapid Fluorescent Focus Inhibition Test (RFFIT) $\geq$ 0,5 IU/ml is considered to be boostable. A titer > 3,0 IU/ml is considered to give sufficient protection and > 10 IU/ml a long-lasting immunity.

Methods & Materials: Soldiers in the Belgian Defence are intradermally vaccinated for rabies pre-deployment since 2008 by a four injection schedule (day 0,7, 28, 365). Neutralizing antibody titers against rabies were tested 7 days after booster vaccination. Serology results of subjects, vaccinated between the 1st of april 2008 and the 31st of june 2013, were evaluated. A titer of the Rapid Fluorescent Focus Inhibition Test (RFFIT) ≥ 0,5 IU/ml is considered to be boostable. A titer > 3,0 IU/ml is considered to give sufficient protection and > 10 IU/ml a long-lasting immunity.

Results: 6598 subjects started pre-exposure rabies vaccination in the Belgian Army in these period. 1658 subjects were excluded due to lack of certainty of intradermal injection method 4940 subjects started intradermal rabies vaccination 4285 finished initial vaccination (d0, 7, 28) 1363 had a fourth vaccination (booster) 881 had a serology test (RFFIT) done after booster vaccination Median age was 36.4 year (with a standard deviation of 9,2), Gender was in 96.1% male. Neutralizing Antibodies were as follows: - 100% (881) of subjects had RFFIT above 0,5 IU/ml; - 83,3% (734) of subjects had a long-lasting immunity whit RFFIT above 10 IU/ml; - 96.6% (851) of subjects had a RFFIT above 3.0 IU/ml. We observed a delay in days of serology testing (mean = 145 (SD 6,3/range 7–1603).

Conclusion: The Classical (day 0, 7, 28, 365) Intradermal Pre-exposure Vaccination is Immunogenic and Very Promising to tackle the problem of Volume Shortage in Biologicals worldwide. Neutralizing Antibodies after four intradermal rabies injections are considered to be boostable in 100% of cases and protective in 96,6% of subjects in this largest cohort of intradermal vaccination worldwide.

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Progress towards elimination of rubella and congenital rubella syndrome in Singapore: Are we there yet?

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Background: Singapore has a comprehensive national childhood immunization programme which includes rubella. The objectives of this study were to describe the epidemiology of rubella in Singapore from 2003 to 2012, and assess its progress in implementing key control strategies against the disease, measured against the targets set by the World Health Organization (WHO) Western Pacific Regional Office (WPRO) of reducing rubella and congenital rubella syndrome (CRS) incidence to below 10 indigenous cases per million population and 10 cases per million live-births, respectively, by 2015.

Methods & Materials: Epidemiological data on all suspected and laboratory-confirmed rubella cases notified to the Ministry of Health for the period 2003-2012 were used. Data on vaccination coverage was obtained from the National Immunization Registry. To assess population immunity against rubella, two National Seroprevalence Surveys (NSS) were conducted based on residual blood samples of adult residents from the National Health Surveys in 2004 and 2010.

Results: The incidence of rubella ranged from 12–37 per million population during the 10-year period. The age-specific incidence rate of rubella was the highest in children below 5 years of age. The incidence of indigenous cases decreased from 36.2 in 2008 to 10.7 per million population in 2012. The susceptibility to rubella in women aged18-44 years decreased significantly from 15.8% in 2004 to 11.0% in 2010 (p = 0.001). Non-residents constituted 51% of the cases notified among women in this reproductive age group. There were nine cases of CRS reported during this period, and over 66% were imported cases. In the past decade, the annual vaccination coverage against measles, mumps and rubella (MMR) among Singapore residents at 2 years of age and students aged 11-12 years had been maintained between 93% and 96%. For school entrants aged 6-7 years and those aged 11 years, the annual coverage rate was between 92% and 95% from 2008 to 2012.

Conclusion: Singapore has made progress and is on track towards elimination of rubella and CRS. The NCIP has been successful in increasing the population immunity against rubella and preventing CRS through concerted efforts. The current high vaccination coverage and vigilant case surveillance should be sustained.

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Synthetic hexasaccharide of the capsular polysaccharide of *S. pneumoniae* type 14 induces cytokines

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Background: Cytokines play a crucial role in immune response. The influence of synthetic oligosaccharides on the cytokine production is not completely investigated. Aim. The study of the cytokine production in mice in response to a conjugate of a synthetic hexasaccharide fragment of the capsular polysaccharide of *S.pneumoniae* type 14 and BSA as a model protein carrier.

Methods & Materials: The hexasaccharide-BSA conjugate (HC) was prepared by the squarate method and contained, according to the MALDI-TOF data, 18 hexasaccharide residues on average. Sera from mice after immunization with HC were tested in flow cytometry using test system FlowCytomixMouse Thl/Th2 10plex (BenderMedSystems). The subisotypes of IgG were determined in ELISA using HC as a well-coating antigen. The protective activity of HC was evaluated by challenge of the immunized mice with *S. pneumoniae* type 14.

Results: Intraperitoneal injection of HC adsorbed on alum hydroxide in CBA mice led to appearance of IL-1β, IL-5, IL-6, IL-10, IL-17, TNFα, GM-CSF that increased in 2 hours and remained at the same level within 24 hours as compared with control mice. Bichromatic increase in concentration of IFNγ began to rise later - 4 h after