83.012

Long term immunogenicity following a booster dose of the inactivated Japanese encephalitis vaccine IXIARO®, IC51

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Background: IXIARO (JESPECT® in Australia, IC51), Intercell's recently approved Vero cellderived, inactivated Japanese Encephalitis vaccine, has been proven immunogenic and safe in a 0/ 28 Day primary immunization schedule in adults. Neutralizing antibody titers decline with time and booster doses are likely needed to obtain a longer lasting immune response. Objectives: To assess the effect of a booster dose on neutralizing antibody titers for up to 12 months after the booster.

Methods: In this open-label phase III trial, 198 subjects, who had received their primary immunization in a preceding randomized trial, were boosted with IXIARO 15 months after the primary immunization and followed up for 12 months. Neutralizing antibody titers were assessed by plaque-reduction neutralization test, PRNT on the day of boosting and 1, 6 and 12 months later. A PRNT50 $\geq$ 1:10 was the cut-off for seroconversion. Systemic and local tolerability were solicited with diaries for a 7 days period following the booster.

Results: Prior to the booster, 69.2% (137/198) of subjects had PRNT50 titers of $\geq$1:10. The seroconversion rate (SCR) was 100% (198/198) one month after the booster. Both at 6 months and 12 months after the booster, the SCR remained high at 98.5% (194/197 and 191/194 subjects, respectively). GMTs were 22.5 before the booster and 900, 487 and 361 at 1, 6 and 12 months after the booster. During 7 days after the booster, 30.8% of subjects reported solicited local reactions, and 23.2% reported solicited systemic adverse events.

Conclusion: An IXIARO booster 15 months after primary immunization induced higher neutralizing antibody titers than seen immediately after primary immunization (a mean 5.3- fold increase). The GMTs and SCRs remained at high levels for 12 months after the booster. A booster dose of IXIARO was generally well tolerated with a safety profile in line with the primary immunization.

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83.013

Cost effectiveness of Pneumovax® 23 stockpile to prevent secondary pneumococcal infections among a high-risk population in the United States during an influenza pandemic

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Background: Recent literature concludes that secondary bacterial infections (especially pneumococcal infections) were the leading cause of death during prior influenza pandemics. One strategy to prevent pneumococcal infections in adults during a future pandemic is to stockpile 23-valent pneumococcal polysaccharide vaccines.

Methods: We developed a model to estimate the health and economic impact of a stockpile of Pneumovax® 23 to prevent secondary bacterial infections among high-risk adults in the age group 18-64 during an influenza pandemic. We used the model to project the number of pneumococcal cases, hospitalizations, deaths, and days of work loss averted. To measure the incremental cost-effectiveness ratio (ICER), we used the cost per quality-adjusted life year (QALY) metric. We used remaining life expectancy of the population following the pandemic as the analytic horizon. Two pandemic scenarios were examined to assess differing pandemic severities: 1918 and 1958/68. We included the impact of other interventions also, such as prepandemic influenza vaccines, antivirals, non-pharmacologic interventions, and herd immunity to pneumococcal disease from use of 7-valent pediatric pneumococcal conjugate vaccine (PCV7). Finally, we examined the impact of Pneumovax® 23 shelf-life, likelihood of a pandemic, and stockpile management on the cost-effectiveness ratio.

Results: Under a 1918-type scenario, based on a population of 20 million high-risk adults, a Pneumovax® 23 vaccination program is projected to avoid 185,000 days of work loss, 12,100 pneumococcal cases, 1,690 hospitalizations, and 3,592 deaths. Under a 1958/68 scenario, the Pneumovax® 23 vaccination is projected to avert 40,000 days of work loss, 7,431 pneumococcal cases, 143 hospitalizations and 461 deaths. The cost-effectiveness ratios (ICERs) for the Pneumovax® 23 stockpile compared to no stockpile under the 1918 and 1958/68 scenarios are $4,661 and $83,039 per QALY respectively. The ICER for Stockpiling Pneumovax® 23 increases as the likelihood of a pandemic decreases. Given a fixed shelf life of Pneumovax® 23, the proportion of stockpile that can be put in the mainstream use every year also affects the ICERs.

Conclusion: Stockpiling Pneumovax® 23 can be a cost-effective strategy for reducing the health and economic burden of pandemic influenza in the high-risk U.S. population.

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83.014

Cost-effectiveness of the use 23-valent pneumococcal polysaccharide vaccine to prevent secondary bacterial infections related to pandemic influenza in Brazil

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Background: Secondary bacterial infections contributed to a significant number of deaths during prior influenza pandemics, and have also been shown to be associated with mortality during the 2009 H1N1 pandemic. The specific aim of this analysis was to assess the costeffectiveness of using 23-valent Pneumococcal Polysaccharide Vaccine (PPV23) at the beginning of or during an influenza pandemic to prevent

secondary bacterial infections among two cohorts of adults in Brazil.

Methods: We created an initial decision model to evaluate the cost-effectiveness of PPV23 used as part of a comprehensive pandemic plan in the United States. This model was adapted to reflect cost data from Brazil. Two cohorts of 6 million Brazilian adults, aged 20-64, were modeled: high-risk adults and critical workers. The model compares costs and disease outcomes associated with two vaccination scenarios: PPV23 vaccination and no PPV23 vaccination. Outcomes are based on attack rates from two prior pandemic types: severe (1918) and moderate (1957/1968). PPV23 effectiveness was assumed to be 59%. Vaccine costs consisted of dose and administration costs. Costs are reported in 2008 Brazilian reals. Cost effectiveness results are reported as incremental cost effectiveness ratios (ICER) using reals per Quality Adjusted Life Year (QALY).

Results: Under the assumption that no pandemic influenza vaccine is available, PPV23 could prevent approximately 15,000 pneumococcal disease cases in the high-risk population during a severe pandemic and 9,000 cases during a moderate pandemic. Among 6 million high-risk adults, the ICERs comparing the PPV23 vaccination scenario versus no PPV23 were estimated to be 1,700 reals per QALY for a severe pandemic and 18,000 reals per QALY for a moderate pandemic. Among 6 million critical workers aged 20-64, PPV23 could prevent 64,000 missed work days during a severe pandemic and 17,000 missed work days during a moderate pandemic.

Conclusion: The cost effectiveness ratios for mass vaccination of high risk individuals as well as critical workers using PPV23 in Brazil to prevent secondary bacterial infections related to pandemic influenza fall within the range generally considered to be cost-effective; however, the cost-effectiveness ratios depend on the severity of the pandemic.

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83.015

Impact study of hepatitis B vaccination in Sikkim - A north eastern state of India

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Background: Sikkim is a small state of India which introduced hepatitis B vaccination into its immunization schedule. Sikkim is the first state of India to introduce Hepatitis vaccination in the year 2004. Hepatitis B coverage for the state of Sikkim is approximately 10,000 children per year and immunization is done at 6, 10 and 14 weeks of age. Booster dose has not been incorporated in the immunization schedule. Since the time of introduction of immunization no impact study has been done in the vaccinated children. Whether the children being vaccinated mount an adequate antibody response against the vaccine needs to be investigated. An attempt was made to study the anti-HBs levels in a cross sectional study of children who received the vaccination against Hepatitis B.

Methods: 160 post vaccinated children and adolescents were included in the study. Only those who had completed three doses of the vaccination were included. Serum collected was tested using a commercially available sandwich ELISA kit. The quality control criteria were fulfilled and the data was analyzed. Anti-HBs Levels below 10 mIU/ml were considered as non responders and levels above 10 mIU/ml were considered as responders.

Results: 53.1% of the participants were males and 46.9% were females. Analysis of data revealed that 64.4% of the population under study were responders and 35.6% were non responders. Female participants who were non responders were greater than males (38.6%: 32.9%). No significant relation between age and response was seen.

Conclusion: The percentage of non-responders in the post vaccination children was significantly higher as compared to most studies conducted in other countries. No study has been done in India to see the impact of vaccination in children. Females seem to be non responders as compared to males contrary to some studies. Further studies need to be conducted to investigate the cause of this anomaly. Presuming that India is on the verge of introducing universal vaccination against HBV, preparedness to encounter the problem of non responders to vaccination needs to be addressed and a strategy developed to counter it.

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83.016

A vaccine derived poliovirus case in an immunocompromised argentinian child

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Background: Although poliomyelitis caused by wild-type poliovirus has been almost eradicated, especially in developed countries, vaccine associated paralytic poliomyelitis (VAPP) cases still continue to occur in Latin American countries. In Argentina, where OPV routine immunization policy is ongoing, the last wild poliovirus (WPV) case was registered in 1984. Since then, the several polio cases reported were VAPP and Vaccine Derived Poliovirus (VDPV) (first iVDPV case was detected in 1998).

Methods: To report a polio case caused by a VDPV in an immunodeficient patient diagnosed with polyclonal agammaglobulinemia.

Results: In May 2009 a 15 month-old patient was hospitalized in our institution for acute flaccid monoparesis in his left lower limb with areflexia, with residual paralysis 60 days after onset. The patient had a history of recurrent infections (sepsis meningitis and pneumonia).Vaccination calendar was completed for his age (DPt/Hib-HB & OPV: 3 doses). The child received OPV3, 8 months before. LCR 8 cells/prot 25 mg/100 mL/Glu 50 mg/ml with negative cultures (bacteria -mycobacterium, fungi). EMG showed pre-ganglionic injury. Spine MRI showed focal intramedullary cone and