

S1 Seroprotective Levels against Lyme Disease achieved after immunization with LYMErix™, Lyme Disease Vaccine (Recombinant OspA)

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LYMErix™ was approved by the FDA for use in those (15 to 70 years) desiring protection against Lyme disease (LD) based on a field trial (N=10,936) demonstrating efficacy of 78% against definite (laboratory confirmed) LD and 100% against asymptomatic infection after 3 doses. In dogs and mice, the degree of protection has been shown to correlate with the level of anti-OspA antibody. A statistical relationship between antibody levels and protection in preclinical models, as calculated by a logistic regression analysis has been demonstrated to accurately predict the probability of protection. In the field trial, vaccine was administered on a 0, 1, 12 month schedule. In an immunogenicity subset (n=267), there was a 5-fold increase in geometric mean anti-OspA titers at month 13 (one month following the third dose) compared to month 2 (one month following the second dose). Anti-OspA titers at month 2 were available from cases of definite LD who were year one vaccine failures (N=20) and the immunogenicity control subset (N=236, vaccinees not evaluated for LD). The reverse cumulative curves from these 2 cohorts were different. The year one data were used to determine the relationship between antibody titers and the risk of developing LD utilizing 3 different statistical methodologies: discriminant analysis, linear logistic regression and non-parametric logistic regression models. The results of the statistical analyses demonstrated that a statistical relationship exists between antibody levels and protection. In the field trial, 54% of subjects had IgG anti-OspA titers above 1200 ELU/ml after 2 doses (50% efficacy observed) and 92% of subjects had titers above 1200 ELU/ml after 3 doses (78% efficacy observed). An IgG anti-OspA antibody titer of 1200 ELU/ml prior to the tick season can be proposed as a surrogate marker of protection.

S2 A SINGLE BLINDED RANDOMISED TRIAL COMPARING TWO ADULT ACCELLULAR PERTUSSIS VACCINES WITH A LICENSED ADULT DIPHTHERIA-TETANUS VACCINE (ADT).

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Aim: to compare the safety and immunogenicity of two adult acellular pertussis vaccines with a licensed ADT vaccine.

Methods: 548 healthy adults (19-71 years) were randomised to 3 groups to receive diphtheria-tetanus-acellular pertussis (dTpa, SB), ADT (CSL), or acellular-pertussis (pa, SB). The latter 2 groups received pa or ADT one month later respectively. Adverse experiences (AE) were measured using a structured 14-day diary card. Specific antibody levels against three pertussis antigens (PT, FHA, PRN) and diphtheria and tetanus toxoids were measured using enzyme immunoassays.

Results: 15% (67/438) of subjects experienced moderate to severe local pain following dTpa, compared to 19% (10/54) and 11% (6/55) following initial doses of ADT and pa respectively. There were no significant differences between ADT and dTpa vaccines for general or local AEs. Similar percentages of initially susceptible subjects in dTpa and ADT groups developed anti-T (98% [63/64] vs 100% [19/19] and anti-D (84% [161/191] vs 89% [42/47]). dTpa and pa vaccines were immunogenic for each of the pertussis components. There were no significant differences in the vaccine response rates or GMTs between the dTpa and pa groups.

Conclusion: These two adult acellular pertussis vaccines were well tolerated in comparison with the ADT vaccine currently used in Australia. dTpa was as effective as ADT in boosting tetanus and diphtheria antibodies.

S3 Nasopharyngeal carriage of *Streptococcus pneumoniae* in infants given primary and booster doses of 7-valent pneumococcal conjugate vaccine. S Yeh, K Zangwill, H Lee, S-J Chang, DP Greenberg, S Partridge, VK Wong, E Curry, J Ward. Kaiser-UCLA Center for Vaccine Research, CA.

Nasopharyngeal *Streptococcus pneumoniae* (Sp) carriage precedes invasive disease and is an important factor in transmission. We evaluated the impact of a 7-valent pneumococcal conjugate vaccine (PCV) on nasopharyngeal (NP) carriage of Sp in infants. Infants from two coincident studies are included: In the PCV group, 120 infants received PCV at 2, 4, 6 and 12 mths of age containing serotypes 6B, 14, 19F, 23F, 18C, 4 and 9V linked to meningococcal outer membrane protein (Merck & Co., Inc). For controls, we evaluated 60 infants in a concurrent Hib vaccine study (no PVC given). In each group, NP cultures were obtained 5 times during the first 13 mths of life. We used standard methods of Sp culture, identification, and serotype determination and used longitudinal logistic regression models fit by generalized estimating equations (SAS PROC GENMOD) to estimate effects of age, daycare, antibiotic use and household density on NP carriage. Overall, 231/820 (28%) NP cultures grew Sp. Unadjusted, the proportions of vaccine serotype carriers (VSC) were similar in the PCV and non-PCV groups: 7% vs 5% at pre-vaccination, 24% vs 13% after the primary series, and 20% vs 21% one month following the booster dose, respectively (NS). Univariate analyses identified increased carriage with increasing age and daycare attendance, and decreased carriage with prior antibiotic use for all and VSC. Multivariate analyses did not reveal significant differences between groups in the proportion of children with Sp VSC over time. In the first 7 mths of life, however, multivariate analysis showed a 4.6 fold decrease in carriage of serotypes 19F and 14 (the most potent immunogens) compared to other vaccine serotypes (odds ratio 3.2 vs. 0.7, p<0.05). Interestingly, this effect was not seen after the booster dose (13 mths of age). This 7-valent PCV appeared to diminish NP carriage slightly during infancy, but only for the immunogenic serotypes (19F and 14) and this effect was not seen in the second year.

S4 Recombinant polyvalent vaccine against Melioidosis and Glanders. Kislichkin N.N.*^{1,2}, Kislichkina O.I.^{1,2}, Tikhonov N.G.³, Denisov I.I.³, Ilyukhin V.I.³

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It has appeared to be difficult to create effective live vaccines against dangerous infectious diseases such as Melioidosis and Glanders. Chameleon Pharma AS has developed a system for transfer of heterologous fragments of DNA from the gram negative virulent bacteria *Burkholderia pseudomallei* C141 and *Burkholderia mallei* U5 to the avirulent R-strain of *Francisella tularensis* (LVS R-strain). The resulting recombinant microorganisms show stability with respect to the transferred foreign gene, and they express capsule antigens of Melioidosis and Glanders. These recombinant microorganisms based on LVS R-strain generate colonies with particular morphology, and they show specific immunogenic properties (not virulence).

Animals immunized with these recombinant strains were subsequently challenged with virulent bacterium. 100% protection was observed when immunized guinea pigs and mice were challenged with lethal doses (1000 x DLM) of *Francisella tularensis* 503, whereas immunized guinea pigs and white rats showed 30-50 % protection against lethal doses (100 x LD50) of *B. pseudomallei* 141 and *B. mallei* U5 (10230).

Recombinant microorganisms with foreign DNA from *B. pseudomallei* C141 did not protect against Glanders and microorganisms with foreign DNA from *B. mallei* U5 did not protect against Melioidosis. We conclude that the avirulent recombinant strains based of LVS R strain might be perspective bivalent live vaccine candidates for Melioidosis and Tularemia or Glanders and Tularemia.