Abstracts of Submitted Presentations

13 Assessing Safety of Simultaneous/Concurrent Vaccinations (SCV)
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Objective: Given the large number of permutations of SCV possible, especially with new vaccine-preventable diseases, pre-licensure evaluation of the safety of each permutation of SCV is limited. We explored the use of VSD for more complete safety data on SCV.

Methods: The VSD links automated immunization and medical records of ~2% of the U.S. population from four Managed Care Organizations (MCO). Using 1992-1995 data from one MCO, we compared the relative incidence of medical visits within one week after each vaccine combination with that of prior OPV alone.

Results: The incidence of nine permutations of SCV among 17,783 children 0-11 months of age and 17 permutations of SCV among 13,396 children 12-23 months of age was compared. For all permutations, the relative incidence of medical visits post-SCV did not differ significantly from that post-OPV. The sample size, relative risk and confidence interval for the most common permutations in 0-11 month olds were: DTaP- Hib (903, 0.86, 0.81-0.92), DTP- Hib-OPV (210, 0.72, 0.51-1.01), DTP- Hib- HepB-OPV (927.0, 0.84, 0.76-0.93) and DTP- Hib- MMR-OPV (279.0, 0.75, 0.57-0.99). These results were similar when adjusted for frequency of medical visits within a week before vaccination, a possible cause of confounding by contraindication.

Discussion: Our data suggest that: 1) VSD is a useful means to expand data on safety of SCV post-licensure, 2) SCV is a safe way to complete the increasingly complex childhood immunization schedule, and 3) expansion of similar analyses to the entire VSD data set is warranted.

14 A Pilot, Ascending Dose Study of the Safety and Adjuvant Activity of Subcutaneous (SC) Recombinant Human IL-12 (rhl-12) with Hepatitis B Vaccine in Healthy, Older Adults
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Objective: Assess the safety and adjuvant effect of rhl-12 in healthy adults ages 50-70 years.

Study Design: Doses of 0.1, 1, 2, or 4 mcg of rhl-12 were evaluated. Subjects were enrolled in sequential cohorts to receive the standard 3 dose regimen of intramuscular (IM) Recombivax-HB® 10 mcg at days 0, 1, and 6. All subjects received 3 SC injections of rhl-12 or placebo concurrent with the vaccine administration within 3 cm of the IM injection site. Within a dosing cohort, subjects were randomly assigned to receive 0, 1, 2, or 4 injections of rhl-12 or placebo. Escalation to a higher-dose cohort occurred after a demonstration of a satisfactory safety experience within the prior dosing cohort.

Results: Preliminary safety and serologic data are available. A total of 34 subjects were enrolled (17 to rhl-12, 17 to placebo). The overall pattern and severity of observed adverse events were similar between vaccine/placebo and vaccine/placebo rhl-12 recipients. The 4 mcg dose of rhl-12 had more adverse events than the lower dose levels or placebo. Local injection site reactions, headache, asthenia, myalgia, nausea and upper respiratory symptoms were most commonly reported, and were mild to moderate in severity. Two injections of rhl-12 were associated with an increased geometric mean titer (GMT/MI) of anti-HBsAb 30 days after the final vaccine injection compared with vaccine only (placebo only: 706, 1 mcg: 1413; p=0.01; 2 mcg: 890, p=0.05; 4 mcg: 1728, p=0.01).

Summary: Subcutaneous administration of low doses of rhl-12 was well-tolerated, with evidence of adjuvant effect, when administered concurrently with intramuscular hepatitis B vaccine.

15 Safety of a Combined Diphtheria-Tetanus-Acellular Pertussis (DT%4
Tricomponent Po)-Hepatitis B (HB)-Inactivated Poliovirus (IPV) Admixed with Haemophilus influenzae type b (Hib) Vaccine in Infants
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The combination of injection site reactions in combination vaccine studies is problematic. When local reactions at a single injection site for the combination vaccine are compared to local reactions at more than one site for simultaneously administered separate component vaccines, a seemingly lower incidence of reactions can be masked. One method commonly used is to compare the single combination vaccine injection site to the most frequent of the multiple injection sites; but the dose not account for reactors that invariably occur at other separate injection sites. We recently completed an open, randomized, multicenter trial that evaluated the safety of a combined tricomponent (DTP-Hib-OPV) given as a single injection compared to separate, concurrent administrations of DTP-Hib (2 doses) given in arm 1, Hib (ImmuPlex®) and OPV (OPV255) in 268 healthy infants at 2, 4, and 6 months of age. Rates of local reactions at the DTP-Hib-OPV injection site were compared to those reported at the recent meningococcal (MCV-4) separate injection site (paediatricians' report: 23.0% vs. 23.3% redness; 17.4% vs. 26.0% swelling; 10.9% vs. 11.2%; respectively) and at the local vaccination site (parent's report: 23.0% vs. 11.0% redness; 17.4% vs. 11.2% swelling; 10.9% vs. 11.2%; respectively). The incidence of systemic reactions was also similar. In order to account for the fact that children who received the combination vaccine had ten injection reactions at one site (one limit) versus those in the control group could experience local reactions at three sites (two limits), a further analysis was undertaken.

% of Doses in Which One or Both Limbs Involved

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<th>DTP-Hib-IPV/Hib&quot;</th>
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<td>DTP-Hib</td>
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Legend: Data from DTP-Hib: All Doses: * One injection; ** Two injections

Dr. Blatter: The percentage of doses followed by a report of a specific local reaction in at least one limb was slightly higher overall in the separate injection (DTP-Hib, Hib, and Hib) group than in the single injection (DTP-Hib/Hib/OPV/Hib) group. Additionally, 1/2 to 2/3 of all reports in the triple injection group involved both limbs.

16 Response to Japanese Encephalitis Vaccine in HIV-infected Children, Bangkok, Thailand
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JE vaccine is a component of the EPIs in northern Thailand, where JE and HIV infection both are prevalent. To evaluate JE vaccine immune response and safety in HIV-infected children, we retrospectively studied HIV-infected and uninfected children born in HIV-negative mothers, who had received 2 JE vaccine doses at 12 months as part of routine pediatric care. Excluding 5 children with pre-existing antibodies, 6 of 14 (43%) HIV-infected and 8 of 27 (67%) HIV-uninfected children developed JE neutralizing antibodies (GMT > 10 (OR 0.3, P = 0.04)); the absolute difference in response was 31% (95% CI: 6.7-56.7%). Among these with positive tests, the GMT of HIV-infected children was lower than that of control children (15.1 vs. 73.8, P = 0.17). Among HIV-infected children, JE vaccine responders had slightly higher CD4+ counts than nonresponders (1750 vs. 1400, P = 0.6). No significant vaccine-associated adverse events were noted.