

# on Vaccine Research

## ABSTRACTS OF SUBMITTED PRESENTATIONS

**S29** Clinical Trials of Group B Streptococcal Conjugate Vaccines: Effects of Alum Adjuvant, and Booster Doses on Immunogenicity. L.C. Paoletti<sup>1\*</sup>, D.L. Kasper<sup>1</sup>, D. Molrine<sup>2</sup>, D. Ambrosino<sup>2</sup>, C.J. Baker<sup>3</sup>. <sup>1</sup>Channing Lab., Brigham and Women's Hosp., <sup>2</sup>Children's Hosp., Harvard Med. Sch., Boston, MA; <sup>3</sup>Baylor Coll. of Med., Houston, TX.

Phase 1 and 2 trials with vaccines against group B streptococcal (GBS) disease have demonstrated the safety and improved immunogenicity of conjugated compared with uncoupled capsular polysaccharide (CPS). Two recent trials sought to determine whether 1) adsorption of the conjugate vaccine to aluminum hydroxide would improve immunogenicity and 2) the CPS-specific IgG response could be boosted by administration of a second dose. Adsorption of type III CPS-tetanus toxoid (III-TT) conjugate vaccine to alum did not improve the immune response in healthy adult recipients of a 12.5 µg dose. Four weeks after vaccination, the geometric mean antibody concentrations (GMC) for the 15 recipients of III-TT with and without alum were 3.3 and 3.6 µg/ml, respectively. In the second trial, 36 healthy adults vaccinated with III-TT were given a second 12.5 µg dose 21 months later. Four weeks after the second dose, the type III CPS-specific IgG GMCs were similar to those measured 4 weeks after the primary vaccination, suggesting a lack of a booster response. However, 22% (8 of 36) of participants who had undetectable antibody concentrations (<0.05 µg/ml) before receiving the first III-TT dose exhibited a booster response to the second dose of III-TT with a the type III CPS-specific IgG GMC 3- to 4-fold higher than the GMC measured after the initial immunization. These results suggest that prior natural exposure to GBS may be responsible for the brisk IgG response to CPS noted in many adults after primary vaccination. Also, a second GBS conjugate vaccine dose would restore initial antibody levels in responders and may be required for those whose initial CPS-specific IgG concentrations are modest.

**S30** Epidermal Powder Immunization of Influenza Vaccine with Cholera Toxin Induces Mucosal Immune Responses and Protection. C. Erickson,<sup>1</sup> R. Endres,<sup>1</sup> L. Payne,<sup>1</sup> and D. Chen.<sup>1</sup> <sup>1</sup>PowderJect Vaccines Inc., Madison, WI

We have previously shown that epidermal powder immunization (EPI), by targeting antigens to the Langerhans cells in the epidermis, induces protective immunity in mice with an extremely small dose of influenza vaccine. In this study, we demonstrated that the effectiveness of EPI with influenza vaccine could be further augmented by co-delivering cholera toxin (CT), an adjuvant that is commonly used for mucosal immunization. In addition to a heightened serum antibody response, mucosal antibody responses to influenza vaccine was also detected when CT was used in the EPI. Fifty µg of CT (the highest dose tested) was well tolerated for EPI. In contrast, a dose of 10 µg of CT was found to be lethal when administered via the conventional intranasal route. Further, the purified native non-toxic B subunit of CT was as potent as CT in enhancing the immune responses to influenza vaccine and protection in the murine challenge model following EPI, suggesting that the adjuvanticity of CT and related molecules for EPI is independent of their toxicity. As mucosal adjuvants, CT and related molecules presumably work by promoting antigen uptake by M cells in the mucosa. Since EPI directly delivers antigens to the Langerhans cell rich epidermis, these adjuvants appear to work via a different mechanism for EPI.

**S31**

**WITHDRAWN**

**S32** Phase I Evaluation of an Intranasal Proteosome-Influenza Vaccine in Healthy Adults. J. Treanor,<sup>1</sup> D. Burt,<sup>2</sup> G. Lowell,<sup>2</sup> L. Fries.<sup>3</sup> <sup>1</sup>University of Rochester, Rochester NY, <sup>2</sup>Intellivax International Inc., Ville St-Laurent, Québec, and <sup>3</sup>Intellivax Inc., Baltimore, MD

We performed a randomized, dose-escalation phase I trial of intranasally (IN) administered proteosome-A/Beijing/262/95 (H1N1) influenza (OMP:HA) vaccine in healthy subjects with prevaccination serum hemagglutination-inhibiting (HAI) antibody to A/Beijing of ≤ 1:8. OMP:HA vaccine consisted of egg-grown, formalin inactivated A/Beijing antigen complexed non-covalently to proteosomes (meningococcal OMP) at a 4:1 weight ratio of OMP to hemagglutinin. Two doses were given by nasal spray at a 14-day interval, and dose escalation levels were 7.5 µg, 15 µg, and 30 µg of HA antigen. Controls received either 99-00 trivalent inactivated vaccine (containing A/Beijing) IM, or two doses of 15 µg of unformulated A/Beijing HA antigen IN. OMP:HA vaccine was well tolerated. No subject had fever, and the frequencies of systemic complaints were not different from controls. Mild rhinorrhea and/or nasal congestion were recorded on diary cards in 50% to 70% of OMP:HA recipients, but were transient and not associated with significant findings on physical exam. Four-fold or greater rises in serum HAI antibody occurred in 6/13 and 7/13 recipients of 15 or 30 µg OMP:HA respectively, and 11 subjects achieved a post-vaccination titer of ≥ 1:40. In contrast, only 1/8 recipients of unformulated HA antigen IN had a serum antibody response. Nasal secretion HA-specific IgA antibody levels in the 15 µg and 30 µg OMP:HA groups increased by 2.67 fold as assessed by kinetic ELISA, and were sustained at day 42. In the the 15 µg and 30 µg OMP:HA groups, 83% had a ≥ 4-fold rise in HAI, a ≥ 2-fold rise in nasal sIgA, or both. These results indicate that the proteosome-influenza vaccine for IN delivery merits further development and expanded clinical trials.