



Antibody responses to Hib polysaccharide conjugates when used with DTaP

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Human antibody responses to Hib polysaccharide (PS) conjugate vaccines have been evaluated separately and in combination with the North American Vaccine (NAVA) DTaP. In the first study, HbOC (HibTITER[®]) was concomitantly administered in an infant primary series (2, 4, 6 months) with NAVA DTaP (Certiva[™]), as well as with a DTwP (Tri-Immunol[®]) in a separate control arm. At 7 months of age, there was no significant difference between the 2 groups in the geometric mean concentration (GMC) of Hib PS-specific antibody or in the percentage of subjects that seroconverted with antibody levels ≥ 0.15 and ≥ 1.0 $\mu\text{g/ml}$. In a second study, a NAVA DTaP-IPV vaccine was tested at 3, 5, and 12 months of age with PRP-T (ActHIB[™]) given concomitantly or reconstituted with DTaP-IPV. At 13 months, while there was a significantly lower GMC of Hib PS-specific antibody for the reconstituted combination (6.1-6.9 versus 10.4-11.3 $\mu\text{g/ml}$), there was no significant difference in percentage of subjects with antibody levels ≥ 0.15 and ≥ 1.0 $\mu\text{g/ml}$ for both groups.

To address the issue of PS-specific antibody suppression for Hib combination vaccines, NAVA had formulated and preclinically evaluated a Hib conjugate vaccine using a recombinant meningococcal B porin (rPorB) as the carrier protein in order to enhance the immunogenicity of the Hib PS (Fusco et al., 1998, Vaccine 16[19]:1842-1849). This new Hib-rPorB conjugate vaccine was shown in rats to elicit 100-fold higher antibody levels when compared with licensed vaccines, HbOC (HibTITER[®]) and PRP-T (OmniHib[™]), that were used as reference standards. When Hib-rPorB and PRP-T were each tested in combination with DTaP-IPV in rats, there were lower PS-specific antibody titers that were not significantly different from the stand alone Hib vaccines; however, the 100-fold higher levels for Hib-rPorB were maintained in comparison with PRP-T. This Hib-rPorB vaccine is now in clinical trials, and a phase I study in adults has shown this vaccine to be well tolerated; immunogenicity results are pending. Future Hib-rPorB trials will allow for testing in combination with DTaP-IPV. It is anticipated that the greatly enhanced immune response observed with Hib-rPorB in animals will translate to higher levels in humans that would counteract any suppressive effects that might arise in combination vaccines.