Abstracts of Submitted Presentations

S37 A PHASE 1C STUDY OF A DNA HEPATITIS B VACCINE IN HEALTHY PATIENTS NONRESPONSIVE TO LICENSED HEPATITIS B VACCINES: PRELIMINARY RESULTS

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Purpose: Depending upon age and co-morbidities, 5% - 50% of otherwise healthy subjects fail to produce antibody against hepatitis B surface antigen (anti-HBs), despite multiple doses/series of HBV vaccine. In this study we examined the immunogenicity and reactogenicity of a novel HBV DNA vaccine in healthy adult nonresponders to licensed HBV vaccines.

Methods: Ten subjects received the Powderject HBV vaccine consisting of the plasmid expression vector pWRG7128 encoding the entire HbsAg protein, coated onto microscopic gold beads and delivered to epidermal cells with a PowderJect XR1 device. Four deliveries of 500 mcg gold/1 Group 1 mcg HbsAg-pWRG7128 constitute one dose of vaccine, and each subject will receive 3 doses. Subjects were divided into Group 1 (nonresponsive after τ4 doses with licensed vaccine, n=6), and Group 2 (nonresponsive after 3 doses of licensed vaccine, n=4). All subjects were between 18-60 years old and healthy. Group 1 subjects had previously received a mean of 5.8 doses of licensed vaccine, and all Group 2 subjects exactly 3 doses.

Results: Twenty-eight days after receiving a single dose of the PowderJect vaccine, 2/6 (33%) of Group 1 subjects seroconverted (mean antiHBs = 354 mIU), and 4/4 (100%) of Group 2 subjects seroconverted (mean antiHBs =1,831 mIU). No serious adverse events were seen among any of the subjects. 5 subjects had transient, minor itching at the site of injection which resolved without treatment within 24 hours (n=4) and within 3 days (n=1).

Conclusions: This novel vaccine was safe and did not induce any moderate, severe or serious adverse events. Importantly, the vaccine was highly immunogenic, inducing protective levels of anti-HBs in 33% of subjects who were nonresponsive after receiving 6-9 doses of licensed vaccine, and 100% of subjects nonresponsive after 3 doses of vaccine.

S38 Antibody responses to bovine parainfluenza virus type 3 (PIV3) vaccination and human PIV3 infection in young infants.

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Data obtained from a phase 2 clinical trial in young infants was analyzed to evaluate the antibody responses to vaccination with bovine PIV3 (bPIV3) vaccine and infection with human PIV3 (hPIV3). Three treatment groups were included: placebo (n=66), 10^5 (n=64) or 10^6 (n=62) $TCID_{50}$ (50% tissue culture infectious doses) of bPIV3 vaccine. The treatment was administered by intranasal spray at 2, 4, 6 and 12-15 months of age. Five serum samples were collected at 2, 6, 7, 12-15 and 13-16 months of age. Four serological antibody markers were measured, including hemagglutination inhibition (HI) and IgA antibodies against bPIV3 and hPIV3. Overall, 1) homotypic and heterotypic HI antibody titers between bPIV3 and hPIV3 could be used to differentiate vaccination-induced response to bPIV3 from infection-induced response to hPIV3; 2) the cumulative incidence of hPIV3 primary infection (based on serologic response) by 13-16 months of age in the three groups were 49%, 16%, and 6%, respectively; and 3) compared with the placebo group, the cumulative incidence of developing a hPIV3 primary infection in the10^5 $TCID_{50}$ and 10^6 $TCID_{50}$ groups could be reduced 67% (95% CI: 31-85%) and 88% (95% CI: 51-97%), respectively.

S39 Safety and Immunogenicity of a 4-Dose Short Interval Oral, Inactivated Whole Cell *Campylobacter* Vaccine Co-administered with Modified *Escherichia coli* Heat-labile (LT_{R192G}) Adjuvant in Volunteers

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Campylobacter species are a cause of foodborne illness globally and a major cause of traveler's diarrhea. Prior clinical studies with a killed *C. jejuni* whole cell vaccine (CWC) delivered with an adjuvant LT(R192G), a genetically modified *E. coli* heat-labile toxin, using a 2-dose oral regimen (14-day interval) induced CWC-specific IgA antibody secreting cells (ASC) and *in vitro* IFN-γ production. This regimen did not induce fecal IgA (sIgA) responses deemed important in protection. In the present study, 4 oral doses (days 0, 2, 4, 6) of CWC (10^{10} vaccine particles) given in combination with 25μg of LT(R192G) (n=15) were assessed. The placebo group (n=10) received bicarbonate buffer only. Following immunization, 3/15 vaccinees (20%) had mild-moderate diarrhea that resolved within 12-24 h but recurred with lessening severity following additional doses. The rate of diarrhea was no different than observed following the 2-dose regimen. No serious adverse events occurred. Fecal IgA responses were achieved in 62% of vaccinees (13-fold median rise from baseline), significantly higher than observed following the 2-dose regimen. Peak sIgA levels occurred at day 9 with elevated titers maintained to day 21. ASC responses were observed in 85% of vaccinees exceeding the 2-dose 62% response. Similar high response rates (85%) for both dosing regimens were observed with IFN-γ production. However, the magnitude trended toward higher IFN-γ levels with the 4-dose regimen. These findings indicate the 4-dose vaccine regimen is safe, induces intestinal and cellular immune responses that correlate with protection, and should be further evaluated for efficacy.

S40 Antibody persistence, PRP-specific immune memory & booster responses to DTPa/Hib vaccine in children primed with a new combination vaccine DTPa-HBV-IPV/Hib at 2, 4 and 6 mo. of age.

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Rationale: A new single-injection combination vaccine combining 6 antigens has been developed to accommodate the growing number of recommended pediatric vaccines.

Aim: To evaluate (1) immunogenicity of DTPa-HBV-IPV/Hib (PRP-T) given as a primary course & (2) compatibility with a licensed DTPa/Hib booster (reactogenicity & immunogenicity), antibody persistence 1yr after vaccination & Hib-specific memory.

Method: 368 healthy infants received DTPa-HBV-IPV/Hib at 2, 4 & 6mo. of age. 219 subjects received a booster dose of DTPa/Hib (PRP-T) & 70 subjects received a dose of DTPa & unconjugated PRP (PRP) vaccine at 18mo. Antibodies measured 1 mo. post primary (PoPr), pre- (PrB) & post booster (PoB). PRP subjects had blood drawn 7 days later. Seroprotective titers (SP) HBs ≥ 10mIU/mL; polio ≥ 8; PRP ≥ 0.15^a & ≥1.0^bμg/mL. *Seropositive (S+) pertussis titers ≥ 5ELU/mL.

Results: Most subjects had SP/S+ titers post primary, which persisted at a high level for 11 months. All subjects were S+/SP post booster.

	time	Pertussis*			PRP	HBs	Polio		
		PT	FHA	PRN	a (*b*)		1	2	3
SP &	PoPr	100	100	100	97.5 (75.9)	100	99.6	98.1	100
S+	*PrB*	*75.5*	*100*	*91.9*	*83.9(30.3)*	*95.4*	*90.4*	*90.6*	*99.5*
rates	PoB	100	100	100	100 (99.1)	*Antigens not in booster*			
	PoPr	73.9	290.7	142.9	2.77	1331	280	325	1196
GMT	*PrB*	*7.6*	*42.4*	*18.9*	*0.52*	160	47.0	52.9	138
	PoB	84.9	604	552	53.7	*Antigens not in booster*			

Anti-PRP GMTs rose from 0.45 to 5.7 μg/mL 10 days after plain PRP boosting. After DTPa/Hib boosting, pain, swelling & redness >20mm, fever >39.5°C were seen in 1%, 37%, 27% & 1.4% of children.

Conclusions: DTPa-HBV-IPV/Hib was immunogenic with good antibody persistence over the following 11mo. Post primary Hib-specific memory was demonstrated.