Disclosures. **Maria Deloria Knoll, PhD**, **Merck** (Research Grant or Support)**Pfizer** (Research Grant or Support)

1183. Serum Bactericidal Activity Induced by Live Attenuated Pertussis Vaccine BPZE1 is Comparable to Boostrix™

Cheryl A. Keech, MD, PhD[1]; Andrew Gorringe, PhD[2]; Breeze Cavell, PhD[2]; Peter Goldstein, MS[1]; Keith Rubin, MD[1]; [1]ILiAD Biotechnologies, Weston, Florida; [2]Public Health England, Portland, England, United Kingdom

Session: P-69. Pediatric Vaccines

Background. In a Phase 2b, multi-center, placebo-controlled, randomized study, intranasal BPZE1 induced mucosal and serum antibodies to pertussis antigens and protected against subsequent colonization following attenuated challenge with BPZE1 3 months later. Boostrix™ also induced serum but not mucosal antibodies and did not protect against BPZE1 challenge. We have evaluated the induction of serum bactericidal activity (SBA) for *Bordetella pertussis* by BPZE1 or Boostrix vaccination. A previous study showed that Boostrix induction of SBA is dependent on Prn whereas *B. pertussis* infection induces SBA targeting Prn and other antigens.

Methods. A convenience set of subjects who had a broad range of Prn and PT IgG serum concentrations from treatment groups who received BPZE1+BPZE1 or Boostrix+Placebo (Day 1 and 85 vaccination) were randomly selected to assess SBA using *B. pertussis* strain B1917. Three timepoints (baseline, 28 days following first and second vaccination) were analyzed and interpolated 50% killing titers determined. The relationship to Prn IgG concentration was assessed.

Results. BPZE1 and Boostrix elicited similar and significant increases in SBA following vaccination. BPZE1 and Boostrix elicit anti-Prn IgG, with Boostrix eliciting higher concentrations. A greater SBA response relative to PRN IgG was observed for BPZE1 compared to Boostrix. SBA-Prn correlations were high post-Boostrix (0.74) as previously reported; correlation was lower (0.35) following BPZE1, suggesting the involvement of broader antigenic protection beyond Prn alone.

Table of GMT and GMFR in SBA and Prn IgG

Geometric Mean Titers (GMT) and Geometric Mean Fold Rise (GMFR) in SBA and Prn IgG						
Vaccination First (Day 1) + Second (Day 85)	Assay	Baseline (Day 1)	Day 28 following first vaccination (Day 29)		Day 28 following second vaccination (Day 113)	
		GMT (95%CI)	GMT (95%CI)	GMFR* (95% CI)	GMT (95%CI)	GMFR* (95% CI)
BPZE1 + BPZE1 (n=13)	SBA	91.0 (35.0, 238.0)	509.0 (340.0, 764.0)	5.6 (2.7, 11.9)	480.0 (305.0, 754.0)	5.3 (2.5, 11.0)
	Prn IgG IU/ml	47.0 (18.4, 121.0)	159.0 (80.7, 315.0)	3.4 (2.2, 5.3)	137.0 (78.1, 239.0)	2.9 (1.8, 4.7)
Boostrix + Placebo (n=17)	SBA	88.0 (39.0, 196.0)	599.0 (357.0, 1004.0)	6.8 (3.5, 13.2)	345.0 (156.0, 763.0)	3.9 (1.9, 8.2)
	Prn IgG (IU/ml)	31.0 (16.4, 58.7)	352.0 (204.0, 606.0)	11.4 (5.9, 21.8)	205.0 (96.6, 436.0)	6.6 (2.8, 15.8)
*Fold rise from baseline.						

Conclusion. In this exploratory investigation, the novel intranasal live-attenuated pertussis vaccine BPZE1 induced SBA titers that were similar to Boostrix using a *B. pertussis* strain representative of current disease isolates. SBA-Prn correlations were high post-Boostrix, consistent with prior reports showing Prn is the acellular vaccine antigen that mediates SBA. In contrast, BPZE1 bactericidal antibodies appear broader than Prn which may be important given the global rise of Prn-deficient *B. pertussis* strains.

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1184. A Phase 3, Multicenter, Randomized, Double-blind Study to Evaluate the Interchangeability of V114 and Prevnar 13™ with Respect to Safety, Tolerability, and Immunogenicity in Healthy Infants (PNEU-DIRECTION)

Adroniki Bili, MD[1]; Scott Dobson, MD[2]; Jeffrey Quinones, MD[3]; Wanatpreeya Phongsamart, MD[4]; Peninnah Oberdorfer, MD, PhD[5]; Pope Kosalaraksa, MD[6]; Ron Dagan, MD[7]; Marissa B. Wilck, MD[1]; Waldimir Vallejos, MD[1]; Christine Nunn, MS[1]; Richard McFetridge, B.S.[1]; Rong Fu, PhD[8]; Robert Lupinacci, M.S[1]; Luwy Musey, MD[1]; Kara Bickham, MD[1]; [1]Merck & Co., Inc., Kenilworth, New Jersey; [2]Parkside Clinical Research and Tribe Clinical Research, Greenville, South Carolina; [3]Clinical Research of Puerto Rico, Guayama, Puerto Rico; [4]Mahidol University, Bangkok, Krung Thep, Thailand; [5]Chiang Mai University, Chiang Mai, Chiang Mai, Thailand; [6]Khon Kaen University, Khon Kaen, Khon Kaen, Thailand; [7]Ben-Gurion University of the Negev, Beer Sheva, HaDarom, Israel; [8]MSD China, Shangai, Shanghai, China

Session: P-69. Pediatric Vaccines

Background. Pneumococcal diseases (PD) caused by *Streptococcus pneumoniae* are a major health concern globally. In children, currently licensed pneumococcal conjugate vaccines (PCVs) provide protection against PD from vaccine serotypes, but other non-vaccine serotypes have emerged and contribute to most residual disease. V114 is a 15-valent investigational PCV containing serotypes 22F and 33F in addition to the 13 serotypes shared by Prevnar 13™ (PCV13). This phase 3 study evaluated safety and immunogenicity of mixed PCV13/V114 regimens when changing from PCV13 to V114 at doses 2, 3, or 4.

Methods. In this double-blind trial, 900 infants were randomized in equal ratios to five treatment groups using a 3 + 1 immunization schedule (3-dose infant primary series followed by one toddler dose). Groups 2, 3, and 4 started with PCV13 and switched to V114 at doses 4, 3, and 2, respectively. Groups 1 and 5 received four doses of PCV13 and V114, respectively. Immunoglobulin G (IgG) responses to the 15 pneumococcal serotypes in V114 were measured at 30 days post-dose 3, prior to dose 4, and 30 days post-dose 4 (PD4). Primary immunogenicity analysis was based on 13 shared serotype responses at PD4. Safety was evaluated as the proportion of participants with adverse events (AEs).

Results. At 30 days PD4, IgG geometric mean concentrations (GMCs) for the 13 shared serotypes were generally comparable between V114/PCV13 mixed regimens (Groups 2-4) and participants that received the 4-dose PCV13 regimen (Group 1). Additionally, IgG GMCs for the 13 shared serotypes were generally comparable for participants that received the 4-dose V114 regimen (Group 5) and participants that received the 4-dose PCV13 regimen (Group 1). Infants given at least one dose of V114 mounted immune responses to two unique serotypes in V114 (22F and 33F). Frequency of injection-site and systemic AEs among study participants were generally comparable across all study groups.

Conclusion. V114 was well tolerated with a generally comparable safety profile to PCV13. For the 13 shared serotypes, both mixed-dose and 4-dose regimens of V114 induced generally comparable antibody responses to a PCV13 4-dose regimen. Study results support interchangeability of V114 with PCV13 in infants.

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1185. Oseltamivir Prescribing Patterns for Infants with Influenza and Factors Associated with Guideline Adherence

Haniah A. Zaheer, Bachelors of Science[1]; Sarah Chamseddine, MD[2]; Hui Liu, MS[3]; John V. Williams, MD[3]; Judith M. Martin, MD[3]; Anne-Marie Rick, MD MPH PhD[3]; [1]University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; [2]UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania; [3]University of Pittsburgh, Pittsburgh, Pennsylvania

Session: P-70. Pediatric Viral Studies (natural history and therapeutic)

Background. The Centers for Disease Control and Prevention (CDC) recommends oseltamivir be given to children < 2 years old with confirmed or suspected influenza as they are at high risk for complications. We sought to analyze oseltamivir prescribing patterns and to describe factors associated with adherence and non-adherence to CDC guidelines.

Methods. We used a retrospective cohort of infants ≤ 12 months old born from January 1, 2011 to December 31, 2019 within the University of Pittsburgh Medical Center health system in Southwestern Pennsylvania and who had ≥ 2 well-child visits during their first year. Infants with laboratory-confirmed influenza from January 1, 2011 to April 30, 2020 were included. Electronic health records were reviewed to describe oseltamivir prescriptions and influenza-related characteristics. Factors associated with adherence and non-adherence to CDC influenza treatment guidelines were assessed with univariate logistic regression.

Results. Of 422 infants with laboratory-confirmed influenza, 86% were prescribed oseltamivir. The proportion of infants prescribed oseltamivir increased from an average of 63% during 2011-2016 to 90% during 2016-2020 (OR:5.2; 95%CI: 2.9-9.5). 96% of prescriptions instructed twice daily dosing, 2% had once daily, and 2% were unknown frequency. 91% of prescriptions were for 5 days, 7% had no duration, and 2% were for > 5 days. Infants ≥ 6 months of age compared to < 6 months were less likely to be prescribed oseltamivir (83.3% vs. 100%; p< 0.001); tested for influenza in the emergency room/urgent care (OR: 0.3; 95%CI: 0.2-0.6), or admitted to the hospital (OR:0.5; 95%CI:0.2-0.9). Infants were more likely to be treated with oseltamivir if they had a known influenza positive contact (OR:2.3; 95%CI:1.0-5.2) or had fever ≥ 38.0C (OR:2.0; 95%CI:1.2-3.5). There was no difference in prescribing practices based on history of prematurity or chronic medical conditions.

Conclusion. Adherence to CDC influenza treatment guidelines for infants is high and has improved over time. However, targeted education at high-risk contact points may further improve guideline adherence.

Disclosures. **John V. Williams, MD**, **GlaxoSmithKline** (Advisor or Review Panel member, Independent Data Monitoring Committee)**Quidel** (Advisor or Review Panel member, Scientific Advisory Board) **Judith M. Martin, MD**, **Merck Sharp and Dohme** (Consultant)

1186. Increased Respiratory Syncytial Virus (RSV) Viral Replication Leads to Increased Cytokine Production and Polarized Interferon Response in Infant Mucosal Epithelium

Rebecca M. Glowinski, BS[1]; Ki Wook Yun, MD;PHD[2]; Asuncion Mejias, MD, PhD, MsCS[1]; Octavio Ramilo, MD[1]; [1]Nationwide Children's Hospital, Columbus, Ohio;

[2]Seoul National University College of medicine, Seoul

Session: P-70. Pediatric Viral Studies (natural history and therapeutic)

Background. RSV is the most frequent etiology of pediatric lower respiratory tract infection. Most children hospitalized for RSV are previously healthy without known risk factors. Children with mild disease managed as outpatients (OP) have higher viral loads than those hospitalized with severe disease. OP children have higher concentrations of the mucosal interferon (IFN), IFNλ2/3, and IP-10, but no differences in IFNλ1. We examined how RSV replication impacts cytokine production kinetics in the nasal mucosa.

Methods. Primary infant human nasal epithelial (iHNE) cells were collected from nasopharyngeal swabs and cultured on an air-liquid interface. Cultures were infected with 0.1 or 0.001 multiplicity of infection (MOI) of RSV-A, or mock infected. Concentrations of IFN-related (IFNα2, β, γ, λ1, λ2/3, and IP-10) and inflammatory (IL-1β, -6, -12, and TNFα) cytokines secreted to the apical and basolateral surfaces were quantified via immunoassay. Kinetics according to viral inocula were compared by ANOVA with Dunn post-hoc testing of the area under the curve (AUC) for each cytokine. Peak concentrations were compared according to MOI and secretion surface by 2-way ANOVA.

Results. AUC of IFNs in both surfaces of RSV infected cells were significantly higher than those of mock infected. The 0.1 MOI RSV inoculum resulted in significantly higher AUCs for all IFN cytokines on both surfaces than the 0.001 MOI. Peak IFNλ1 concentrations were higher on the apical than basolateral side; peak IFNλ2/3 concentrations were higher on the basolateral side than apical. AUCs of inflammatory cytokines in RSV infection were significantly higher on the basolateral, but not apical, surfaces than mock; all basolateral inflammatory cytokines were higher in the 0.1 MOI than the 0.001 MOI.

Conclusion. Higher RSV inoculum induces higher concentrations of IFN-related cytokines on both sides of epithelial cells, and higher concentrations of inflammatory cytokines on the basolateral side. Differential secretion of IFNλ1 and IFNλ2/3 to the apical and basolateral surfaces suggests they may play different roles in immune response during RSV infection. These data support viral replication as an important factor influencing RSV pathogenesis and severity through cytokine production.

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1187. Neurodevelopmental Outcomes of Children with Congenital Cytomegalovirus (cCMV) Infection: Does Antiviral Treatment Matter?

Margaret R. Jia, BA[1]; Alexandra K. Medoro, MD[2]; Traci Pifer, RN[3]; Manish Rijal, MS[3]; Teresa Borghese, CPNP-AC[3]; Ursula M. Findlen, PhD[3]; MD S. Malhotra, MD[2]; Oliver Adunka, MD[4]; Masako Shimamura, MD[3]; Asuncion Mejias, MD, PhD, MsCS[3]; Nathalie Maitre, MD, PhD[3]; Pablo J. Sanchez, MD[2]; [1]The Ohio State University College of Medicine, Columbus, Ohio; [2]Nationwide Children's Hospital - The Ohio State University, Columbus, Ohio; [3]Nationwide Children's Hospital, Columbus, Ohio; [4]The Ohio State University Wexner Medical Center, Columbus, Ohio

Session: P-70. Pediatric Viral Studies (natural history and therapeutic)

Background. cCMV infection is a major contributor to childhood neurologic and cognitive disabilities including sensorineural hearing loss (SNHL). Neonatal treatment with ganciclovir/valganciclovir improves hearing outcomes, but its impact on neurodevelopmental outcomes remains an important knowledge gap. We describe the neurodevelopmental outcomes of children with cCMV infection and evaluate the effect of neonatal antiviral therapy on outcomes.

Methods. Since 2013, infants with cCMV infection referred to Nationwide Children's Hospital's NEO-ID Clinic have had a complete evaluation at diagnosis as well as follow-up neurodevelopmental assessments. Pertinent demographic, clinical, laboratory, radiographic, and follow-up data were obtained and managed using REDCap. Neurodevelopmental assessments were performed using Bayley Scales of Infant and Toddler Development (BSID) III/IV (cognitive, language, motor domains) at ~ 24 months of age. The Gross Motor Function Classification System was used to classify functional motor impairment. Neurodevelopmental outcomes were compared by receipt of antiviral therapy in early infancy.

Results. 95 infants (mean ± SD; gestational age 35 ± 5 wk, birth weight 2121 ± 948 g; Table 1) with cCMV infection had follow-up neurodevelopmental assessments. 62% had central nervous system involvement, 37% had SNHL, 23% developed cerebral palsy (CP), and 6% were diagnosed with autism spectrum disorder. The majority had normal BSID scores (≥ 85) in cognitive and motor domains (65% and 54%, respectively) while 48% had normal scores in the language domain. 35% had severe impairment (< 70) in ≥ 1 domain (Table 2). 9 children had clinically inapparent cCMV infection; 2 (22%) had abnormalities on BSID testing (1, cognitive score: 80; 1, cognitive, language, and motor scores: 65, 68, 73, respectively). 11 (12%) children, including 6 who received antiviral therapy, had severe neurodevelopmental impairment, with CP and severe (< 70) BSID scores in both the cognitive and motor domains.

Table 1. Demographic and Clinical Characteristics of 95 Children with Congenital CMV Infection by Receipt of Antiviral Treatment

	Antiviral Therapy		Total	P-value
	Yes	No		
No. of infants	58	37	95	
Sex				
Male	36 (62%)	15 (40%)	51 (54%)	0.06
Female	22 (38%)	22 (60%)	44 (46%)	
Race				
White (non-Hispanic)	34 (59%)	22 (60%)	56 (59%)	0.38
Black	14 (24%)	12 (32%)	26 (27%)	
Other	10 (17%)	3 (8%)	13 (13%)	
Gestational age (weeks)[#]	36 ± 4	32 ± 6	35 ± 5	0.01
Birth weight (g)[#]	2250 ± 788	1918 ± 1137	2121 ± 948	0.22
CNS involvement*	39 (67%)	20 (54%)	59 (62%)	0.28
Sensorineural hearing loss	25 (43%)	10 (27%)	35 (37%)	0.13
Cerebral palsy	16 (28%)	6 (16%)	22 (23%)	0.22
Autism spectrum disorder	4 (7%)	2 (5%)	6 (6%)	1.0

* Central nervous system (CNS) involvement defined as abnormal brain imaging (cranial ultrasound, computed tomography, or magnetic resonance imaging) consistent with CMV infection; chorioretinitis; or microcephaly
# Mean ± S.D.

Table 2. Neurodevelopmental Outcomes Based on Testing with the Bayley Scales of Infant and Toddler Development (BSID) III/IV

	Antiviral Therapy		Total	P-value
	Yes	No		
No. of infants	58	37	95	
Age at evaluation (months)	22 ± 11	22 ± 10	22 ± 10	0.61
Cognitive score	88 [70-95]	90 [80-95]	90 [75-95]	1.0
≥ 85	35 (61%)	26 (70%)	61 (65%)	
70-84	11 (19%)	5 (14%)	16 (17%)	0.66
< 70	11 (19%)	6 (16%)	17 (18%)	
Language score	85 [68-98]	83 [71-91]	83 [71-96]	0.61
≥ 85	29 (50%)	17 (46%)	46 (48%)	
70-84	13 (22%)	13 (35%)	26 (27%)	0.34
< 70	16 (28%)	7 (19%)	23 (24%)	
Motor score	85 [67-91]	87 [79-94]	85 [70-96]	0.86
≥ 85	30 (53%)	20 (56%)	50 (54%)	
70-84	11 (19%)	10 (28%)	21 (23%)	0.38
< 70	16 (28%)	6 (17%)	22 (24%)	
Worst score in any domain	76 [59-91]	79 [70-85]	79 [62-89]	0.77
≥ 85	21 (36%)	12 (32%)	33 (35%)	
70-84	13 (22%)	16 (43%)	29 (30%)	0.08
< 70	24 (41%)	9 (24%)	33 (35%)	

* Values reported as mean ± s.d. or median [IQR]

Conclusion. A substantial proportion of children with cCMV infection had moderate (29%) or severe (33%) neurodevelopmental impairment, CP, or autism spectrum disorder, irrespective of antiviral treatment. Urgency exists for antenatal preventive strategies and vaccine development.

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1188. The Effect Of The COVID-19 Pandemic On Influenza-Related Hospitalization, Intensive Care Admission And Mortality In Canadian Children

Helen E. Groves, PhD, MBBCh BAO[1]; Jesse Papenburg, MD[2]; Kayur Mehta, MD[3]; Julie A. Bettinger, PhD[4]; Manish Sadarangani, BM BCh, DPhil[4]; Scott Halperin, MD[5]; Shaun Morris, MD, MPH, DTM&H, FRCPC, FAAP[6]; [1]The Hospital for Sick Children, Toronto, Toronto, Ontario, Canada; [2]Departments of Pediatrics and Medical Microbiology, McGill University Health Centre, Montreal, QC, Canada, Montreal, Quebec, Canada; [3]McGill University, Montreal, Quebec, Canada; [4]University of British Columbia, Vancouver, British Columbia, Canada; [5]IWK Hlth Ctr, Halifax, NS, Canada; [6]Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada

IMPACT investigators

Session: P-70. Pediatric Viral Studies (natural history and therapeutic)

Background. The COVID-19 pandemic resulted in unprecedented implementation of wide-ranging public health measures globally. During the pandemic, dramatic decreases in seasonal influenza virus detection have been reported worldwide. Information on pediatric influenza-related hospitalizations is limited. We describe influenza-related hospitalization in Canadian children during the 2020/2021 influenza season compared to ten previous seasons.

Methods. Data on influenza-related hospitalizations, intensive care unit (ICU) admissions and in-hospital deaths in children across Canada were obtained from the Canadian Immunization Monitoring Program, ACTive (IMPACT). This national surveillance initiative comprises 90% of all tertiary care pediatric beds in Canada. The total study period included eleven influenza seasons from September 2010 to April