H3N2 virus (median: 75.4 hours) was significantly shorter than in PLC (100.4 hours; P =0.0141) and was significantly shorter in patients with influenza B (74.6 hours) than in either PLC (100.6 hours; $P = 0.0138$) or Os (101.6 hours; $P = 0.0251$). Median time to cessation of viral shedding in BXM patients was 48 hours, significantly less than 96 hours in both PLC and Os patients. Systemic antibiotic use and influenza-related complications were significantly fewer in BXM (3.4% and 2.8%, resp.) than PLC (7.5% and 10.4%; $P = 0.0112$, and $P < 0.0001$). The incidence of any (25.1–29.7%) or serious adverse events (0.7–1.2%) did not differ significantly across the groups.

Conclusion. BXM was well-tolerated and associated with faster recovery and reduced risk of complications in HR influenza patients compared with PLC. It proved superior to Os in shortening the duration of virus replication and in resolving influenza B illness. Oral BXM is a promising treatment option for patients with risk factors for influenza complications.

Disclosures. **M. G. Ison**, Romark: Investigator, Research support. Shionogi: Scientific Advisor, Paid DSMB Member. Emergent BioScience: Investigator, Research support. Janssen: Investigator and Scientific Advisor, Consulting fee and Research support. GlaxoSmithKlein: Scientific Advisor, Paid DSMB Member. VirBio: Consultant, Consulting fee. Seqirus: Consultant, Consulting fee. **S. Portsmouth**, Shionogi Inc.: Employee, Salary. **Y. Yoshida**, Shionogi & Co., Ltd.: Employee, Salary. **T. Shishido**, Shionogi & Co., Ltd.: Employee, Salary. **F. Hayden**, Shionogi & Co., Ltd.: Scientific Advisor, Consulting fee (donated) and travel support for attending 6th ESWI meeting, 10–13 September 2017, Latvia, to present phase 3 OWH results. .**T. Uehara**, Shionogi & Co., Ltd.: Employee, Salary.

LB17. Age-Related Differences in Influenza Type/Subtype Among Patients Hospitalized with Influenza, FluSurv-NET—2017–2018

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Session: 213. Late Breaker Oral Abstracts: Influenza and Vaccines
Saturday, October 6, 2018: 10:30 AM

Background. The 2017–2018 influenza season had the highest rates of influenza hospitalizations since the 2009 H1N1 pandemic. We used data from the Influenza Hospitalization Surveillance Network (FluSurv-NET) to identify unique characteristics of the 2017–2018 season.

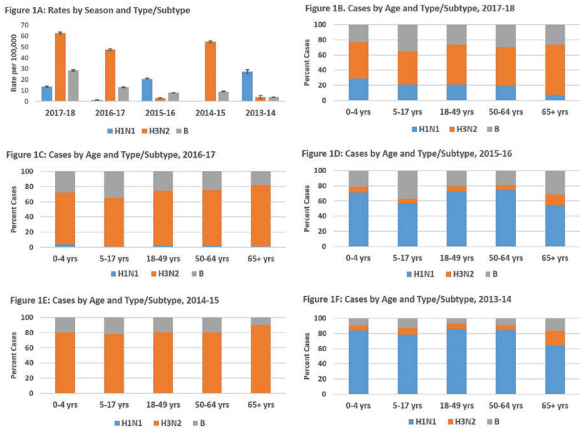
Methods. We included all patients residing within a FluSurv-NET catchment area, and hospitalized with laboratory-confirmed influenza during 2017–2018. We used multiple imputation, including age, surveillance site, and month of hospital admission as predictors, to impute influenza A subtype for 40–64% of cases across seasons with an unknown subtype. We calculated influenza hospitalization rates by type/subtype per 100,000 population. We compared 2017–2018 rates to rates during 4 prior seasons: 2016–2017, 2015–2016, 2014–2015, and 2013–2014.

Results. The overall unadjusted hospitalization rates per 100,000 population varied from 31.5 during 2015–2016 to 105.1 during 2017–2018. After imputing A subtype, the 2017–2018 season had the highest rates observed for H3N2 (62.8) and B (28.5) than in any previous season, and the third highest rate of H1N1 (13.5) (Figure 1A). During 2017–2018, rates in adult ≥65 years peaked 3 weeks before they peaked in children 0–4 years. In contrast, during the four prior seasons, rates in adults ≥65 years peaked during the same week or 1 week after they peaked in children 0–4 years. During 2017–2018, the distribution of influenza type/subtypes varied significantly by age group ($P < 0.0001$); for example, the proportion of cases with H1N1 ranged from 19 to 29% in those <65 years to only 7% in those ≥65 years. During 2017–2018, H1N1 (the nonpredominant A virus) contributed >25% of A cases across all age groups (except ≥65 years) vs. all prior seasons where the nonpredominant A virus contributed <10% of A cases across all age groups (except ≥65 years) (Figure 1B–F).

Conclusions. Several unique characteristics may have contributed to the high hospitalization rates observed during 2017–2018. Rates in older adults, who were predominantly infected with H3N2, peaked several weeks prior to children in contrast to prior seasons. Higher overall rates of H3N2 and B were observed in 2017–2018 compared with these prior seasons and substantial H1N1 co-circulation also occurred with marked variability by age group.

Disclosures. **E. J. Anderson**, NovaVax: Grant Investigator, Research grant. Pfizer: Grant Investigator, Research grant. AbbVie: Consultant, Consulting fee. MedImmune: Investigator, Research support. PaxVax: Investigator, Research support. Micron: Investigator, Research support. **H. K. Talbot**, Sanofi Pasteur: Investigator, Research grant. Gilead: Investigator, Research grant. MedImmune: Investigator, Research grant. Vaxinnate: Safety Board, none. Seqirus: Safety Board, none.

Figure. Hospitalization Rates and Distribution of Influenza Type/Subtype by Season and Age Group, FluSurv-NET, 2013–14 to 2017–18



LB18. An Enveloped Virus-like Particle (eVLP) Cytomegalovirus (CMV) Vaccine Is Immunogenic and Safe: Results of a First-in-Humans Study

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Session: 213. Late Breaker Oral Abstracts: Influenza and Vaccines
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Background. CMV is the most common cause of congenital infection and may result in permanent neurodevelopmental injury including vision and hearing loss. A vaccine to prevent transmission of CMV during pregnancy or to immunocompromised persons is a public health priority. Neutralizing antibodies (nAb) to the CMV envelope glycoprotein B (gB) in natural infection are thought to confer protection, but some vaccine candidates based on this protein alone have been insufficiently immunogenic. In this FiH dose-ranging, controlled, observer-blinded study the safety and immunogenicity of an eVLP expressing the ectodomain of gB fused to transmembrane and cytoplasmic domains of the vesicular stomatitis virus G protein (gB-G) was evaluated.

Method. Healthy CMV-seronegative 18–40 year olds at three sites in Canada (Vancouver, Montreal, Halifax) were randomized to one of four dose formulations (0.5 µg, 1 µg, or 2 µg gB content with Alum) or 1 µg gB without Alum, or placebo given on days 0, 56, and 168. Outcome measures were solicited and unsolicited adverse events (AE), severe AE, gB binding antibody titers and avidity assessment, and nAb to CMV infection of fibroblast and epithelial cells. A Data Safety Monitoring Board was in place.

Result. Among 128 participants, the most common solicited local and general AEs were pain and headache, respectively. No SAEs or withdrawals occurred. A dose-dependent boosting of nAb titers was observed after doses 2 and 3, with the highest titers in the Alum-adjuvanted 2.0 µg dose recipients. Fibroblast cell nAb were seen in 100% of 2.0 µg dose recipients, and epithelial cell nAb in 31%. Epithelial cell nAb was correlated with higher geometric mean gB binding titers, and there was a correlation between fibroblast and epithelial cell nAb titers.

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Conclusion. An eVLP CMV vaccine was immunogenic at very low doses in healthy seronegative adults and no safety signals were seen. Alum adjuvantation increased immunogenicity as did higher antigen content and multiple doses. This phase 1 trial supports further development of this eVLP CMV vaccine candidate.

ClinicalTrials.gov NCT02826798

Disclosures. **S. Gantt**, VBI Vaccines: Investigator, No direct financial benefit—company provided institutional support for clinical trial. **C. Quach**, VBI Vaccines: Investigator, No direct financial benefit—company provided institutional support for clinical trial. **D. E. Anderson**, VBI Vaccines: Employee and Shareholder, Salary. **F. Diaz-Mitoma**, VBI Vaccines: Consultant and Shareholder, Salary. **J. Langley**, VBI Vaccines: Investigator, No direct financial benefit—company provided institutional support for clinical trial.

LB19. Progress Toward a Vaccine for Maternal Immunization to Prevent Respiratory Syncytial Virus (RSV) Lower Respiratory Tract Illness (LRTI) in Infants

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Session: 213. Late Breaker Oral Abstracts: Influenza and Vaccines
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Background. RSV is the leading cause of infant LRTI and hospitalization worldwide. The greatest burden of severe disease is in term infants <5 months old. Novavax

is developing an aluminum-adjuvanted RSV F nanoparticle vaccine for use in the third trimester of pregnancy, with the goal of preventing medically significant infant RSV LRTI in the first 3–6 months of life via transplacental transfer of maternal antibodies.

Method. After dose-finding studies in 1,050 women, we studied vaccine safety and immunogenicity in a Phase 2 trial in 50 healthy third trimester pregnant women. Safety was assessed in mothers and infants, focusing on pregnancy and peri-partum outcomes. We measured binding and functional RSV antibodies in mothers at baseline, day 14, delivery, and days 35 and 180 post-partum, in cord blood, and in infant sera on days 14, 35, 60, and 180 of life. Anti-F antibody specificities were probed with biolayer interferometry and monoclonal antibodies (mabs) to known epitopes.

Result. In Phase 2, RSV F nanoparticle vaccine was immunogenic, safe, and well-tolerated in pregnant women. Anti-F IgG and neutralizing antibodies were elicited. Increases in antibodies competitive with mabs to neutralizing epitope sites Ø, VIII, II, and IV, and also the p27 domain displayed by the pre-fusogenic F protein, were present in maternal and infant sera of vaccinated subject pairs. Transplacental transfer of RSV antibodies was more efficient (110 to 120%) in women immunized >30 days before delivery compared with those vaccinated later; RSV antibody $t_{1/2}$ ranged from 30 to 41 days in infants. We have subsequently enrolled 4,636 pregnant women and their infants in a global observer-blind, randomized, placebo-controlled Phase 3 trial assessing efficacy against medically significant RSV LRTI. In November 2017, an informational analysis performed by an independent statistician, the sponsor remaining blinded, yielded a posterior probability of ≥90% that efficacy was >0%.

Conclusion. RSV F nanoparticle vaccine is immunogenic in pregnancy, and neutralizing antibodies, including those competing for pre-and post-fusion F epitopes, are transferred efficiently transplacentally. An analysis of Phase 3 efficacy against medically signifcant infant RSV LRTI is projected for Q1, 2019.

Disclosures. **L. Fries**, Novavax: Employee and Shareholder, Salary. **D. N. Thomas**, Novavax: Employee, Salary. **G. Smith**, Novavax: Employee and Shareholder, Salary. **J. Plested**, Novavax: Employee, Salary. **P. Piedra**, Novavax: Collaborator, Consultant, Research Contractor and Scientific Advisor, Consulting fee, contract fees for immunologic assays and Research support. **N. Patel**, Novavax: Employee and Shareholder, Salary. **I. Cho**, Novavax: Employee and Shareholder, Salary. **G. Glenn**, Novavax: Employee and Shareholder, Salary.

LB20. Impact of School-Located Influenza Vaccination on Vaccination Coverage, School Absenteeism, and Influenza Hospitalization

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Session: 213. Late Breaker Oral Abstracts: Influenza and Vaccines
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Background. School-located influenza vaccination programs aim to increase influenza vaccination coverage and produce indirect effects by interrupting influenza transmission. We evaluated the impact of a program that delivered the inactivated influenza vaccine in 2016–2017 to elementary schools in a large, diverse urban school district in Oakland, California on vaccination coverage, school absenteeism, and influenza hospitalization.

Methods. We conducted a prospective cohort study and used pre-program data from the California Department of Education on school characteristics to identify a control school district with similar characteristics to the program district. We measured parent recall of student influenza vaccination in surveys in 2017 in 44 schools per district (N = 6,070). We obtained absence data from school districts and influenza hospitalization data for district catchment areas prior to and during the program. We used generalized linear models to estimate difference-in-differences (DIDs) in absence rates during influenza season adjusting for month, race, and grade to account for differences in pre-program rates. Standard errors accounted for school clusters. For influenza hospitalization, we estimated cumulative incidence rates using census data to obtain the population size and risk ratios (RR) using modified Poisson regression.

Results. Vaccination coverage was 56.7% in control schools and 63.9% in program schools (difference = 7.2%; 95% CI 3.6%, 10.8%). 24% of students in program schools were vaccinated at school. Absences per 100 days were 5.40 vs. 6.68 in program vs. control sites for all absences and 3.01 vs. 3.60 for illness-related absences; DIDs were statistically significant for illness absences. Among all ages, the risk ratio for influenza hospitalization in program vs. control districts was 0.65 (95% CI 0.55, 0.78) among all ages and 0.71 for adults 65 or older (95% CI 0.57, 0.89). Hospitalization was too rare among elementary aged students to estimate RRs in that group.

Conclusion. Elementary school-located influenza vaccination increased influenza vaccination and decreased school absence and influenza hospitalization. There was an indirect effect on hospitalization in the elderly and nonelementary aged groups.

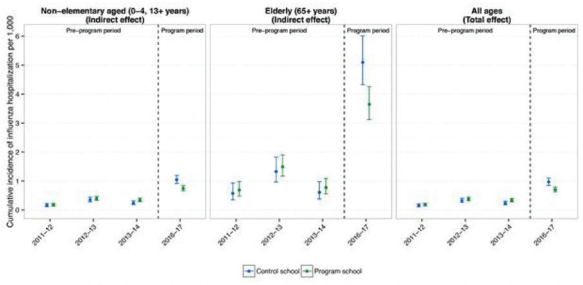

Figure caption: Influenza hospitalization rates per 1,000 in school-located influenza vaccine program and control schools prior to and during the program. Note: 2014-15 and 2015-16 are excluded from the figure because the program delivered the live attenuated influenza vaccine those years, which was later shown not to be effective. Thus, no effects on influenza hospitalization are expected in those years.

Disclosures. **All authors:** No reported disclosures.

LB21. Preemptive Therapy (PET) vs. Prophylaxis for Prevention of Cytomegalovirus (CMV) Disease in High-Risk Donor Seropositive/Recipient Seronegative (D+R−) Liver Transplant Recipients (LTR): A NIH-Sponsored, Randomized, Controlled, Multicenter Trial

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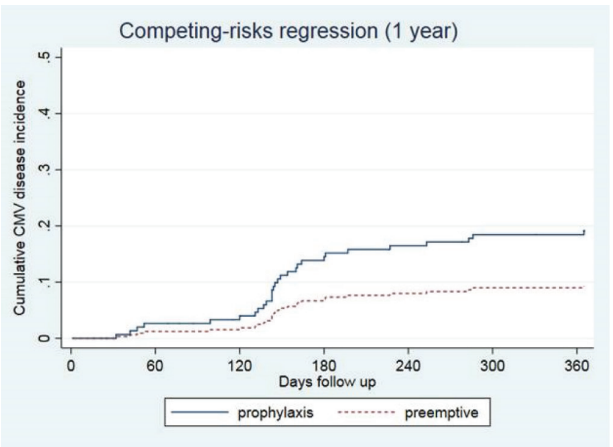
Session: 275. Featured Oral Abstract
Saturday, October 6, 2018: 4:05 PM

Background. Current guidelines preferentially recommend valganciclovir (VGCV) prophylaxis over PET in most D+R− organ transplant populations, but adequately powered direct comparative clinical trials are lacking.

Methods. D+R− LTR were randomly assigned (1:1, stratified by site and T-cell depleting induction) to receive either PET (weekly plasma CMV DNAemia at central laboratory for 100 days, with VGCV 900 mg bid for DNAemia at any level, until two consecutive negative weekly tests) or prophy (VGCV 900 mg qd for 100 days). The primary outcome was CMV disease by 12 months as adjudicated by an independent, blinded, endpoint committee in ITT population. Secondary outcomes were opportunistic infections (OIs) (invasive fungal and bacterial), neutropenia (ANC < 1000/μL), acute rejection, graft loss, and mortality assessed at12 months.

Results. From October 2012 to June 2017, 205 patients were randomized at six centers; 100 to PET, 105 to prophy. The incidence of CMV disease was 9% (9/100) in PET and 19% (20/105) in prophy (P = 0.039) with majority of difference due to post-prophylaxis disease: 6% in PET vs. 17% in prophy (P = 0.027). CMV disease included syndrome in 55% (16/29) and end-organ in 45% (13/29), with similar proportions in two groups. Secondary outcomes were not different for PET and prophy groups: OIs (19% vs. 21%), neutropenia (34% vs.. 28%), acute rejection (27% vs. 27%), graft loss (2% vs. 2%), and mortality (10% vs. 6%), respectively, P > 0.05 for all comparisons. Mortality at last follow-up (median 3.2 years) was not different for PET vs. prophy (14% vs. 18%, P = 0.43).

Conclusions. PET significantly reduced the incidence of CMV disease compared with prophy in D+R- LTR, and was associated with similar other clinical outcomes. Current guidelines should be revised to recommend PET over prophylaxis in this setting, and similar trials conducted in other D+R− transplant populations. (Funded by NIAID; ClinicalTrials.gov# NCT01552369.)



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