1818. Immunogenicity of Inactivated Varicella Zoster Vaccine (ZV<sub>IN</sub>) in Autologous Hematopoietic Stem Cell Transplant (auto-HSCT) Recipients <u>Michael Boeckh</u>, MD, FIDSA<sup>1</sup>; Ann Arvin, MD, FIDSA, FPIDS<sup>2</sup>; Kathleen Mullane, <u>D</u>O, FIDSA<sup>3</sup>; Drev J, Winston, MD<sup>4</sup>; Janice (Wes) Brown, MD<sup>5</sup>; Steven Pergam, MD, MPH, FIDSA<sup>6</sup>; Kimberly Hurtado, BS<sup>7</sup>; Lei Pang, PhD<sup>7</sup>; Ingi Lee, MD, MSCE<sup>8</sup>; Zoran Popmihajlov, MD, MS<sup>7</sup> and on behalf of the V212 Protocol 001 Study Team; <sup>1</sup>Pred Hutchinson Cancer Research Center, Seattle, Washington; <sup>2</sup>Division of ID/ Department of Ped, Stanford University School of Medicine, Stanford, California; <sup>3</sup>Medicine, University of Chicago Medicine, Chicago, Illinois; <sup>4</sup>University of California at Los Angeles Medical Center, Los Angeles, California; <sup>5</sup>Division of Blood and Marrow Transplant and Division of Infectious Diseases, Department of Medicine, Stanford University School of Medicine, Stanford, California; <sup>6</sup>Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, Washington; <sup>7</sup>Merck & Co., Inc., Kenilworth, New Jersey; <sup>8</sup>Merck & Co., Inc., North Wales, Pennsylvania

## Session: 229. Miscellaneous Advances in Vaccinology Saturday, October 7, 2017: 10:30 AM

**Background.** Recipients of auto-HSCT have an increased risk of herpes zoster (HZ) infection; however, live attenuated varicella-zoster virus (VZV) vaccine is contraindicated in these patients. In this pivotal Phase III study (V212-001; NCT01229267) inactivated VZV vaccine (ZV<sub>IN</sub>) reduced the rate of HZ infection compared with placebo (estimated vaccine efficacy, 63.8%) and was well tolerated. Immunogenicity of ZV<sub>IN</sub> recipients of auto-HSCT was assessed in the Phase III study as an exploratory objective.

**Methods.** Adults undergoing auto-HSCT were randomized to receive either  $ZV_{IN}(n = 560)$  or placebo (n = 564), administered in a 4-dose regimen. Doses 1 through 4 were administered ~30 days before and ~30, ~60, and ~90 days following auto-HSCT. VZV-specific immune responses were measured at Day 1, ~28 days post-vaccinations 3 and 4, and annually until the end of the study. VZV-specific antibody responses were measured by glycoprotein enzyme-linked immunosorbent assay (gpELISA) in all patients; cell-mediated immune responses were measured by VZV interferon-gamma enzyme-linked immunospot (IFN- $\gamma$  ELISPOT) assay in a randomized subset of patients (n = 403).

**Results.** Geometric mean titers (GMT) were significantly higher and the ratios of the gpELISA and IFN- $\gamma$  ELISPOT were significantly greater in the ZV<sub>IN</sub>group compared with the placebo group (Tables 1 and 2).

Table 1. GMT 28 days post-dose 4 (PD4)

|               | Vaccine                                       | Placebo                                       |  |
|---------------|---|---|--|
| gpELISA       | <b>n = 102</b><br>241.8 (95% CI: 186.2, 313.9 | <i>n</i> = 108<br>105.8 (95% CI: 84.6, 132.3) |  |
| IFN-γ ELISPOT | <b>n = 102</b><br>62.8 (95% CI: 45.8, 86.2)   | <i>n</i> = 116<br>10.4 (95% CI: 7.9, 13.7)    |  |

Table 2. Ratios of geometric mean fold rise between the vaccine and placebo groups ( $\mathrm{ZV}_{\mathrm{NV}}$  placebo)

|                                    | gpELISA(n = 764)          | IFN- $\gamma$ ELISPOT( $n = 339$ ) |  |
|------------------------------------|---------------------------|------------------------------------|--|
| Pre-vaccination and 28 days<br>PD4 | 1.79 (95% CI: 1.39, 2.32) | 5.41 (95% CI: 3.60, 8.12)          |  |
| Pre-vaccination and 1 year<br>PD4  | 1.30 (95% Cl: 0.99, 1.71) | 4.12 (95% CI: 2.62, 6.47)          |  |

**Conclusion.**  $ZV_{IN}$  elicited higher VZV-specific humoral and cell-mediated responses in adult auto-HSCT recipients when compared with placebo ~28 days and ~1 year post-dose 4. These results indicate that  $ZV_{IN}$  is immunogenic in these patients who are ineligible for live attenuated HZ vaccine, which is consistent with previously observed clinical efficacy.

Disclosures. M. Boeckh, Merck: Investigator, Research Contractor and Scientific Advisor, Consulting fee and Research support; GlaxoSmithKline: Research Contractor, Research support; A. Arvin, Merck: Scientific Advisor, Consulting fee; K. Mullane, Merck: Scientific Advisor, Grant recipient; D. J. Winston, Merck: Grant Investigator and Scientific Advisor, Consulting fee and Grant recipient; J. Brown, Merck: Clinical adjudication and site investigator and Investigator, Consulting fee; Cellerant Therapeutics: Consultant, Cellerant developing and executing clinical trials of myeloid progenitor cells in neutropenia for which I hold the patent; S. Pergam, Merck: Consultant and Investigator, Consulting fee; K. Hurtado, Merck: Employee and Shareholder, Salary; L. Pang, Merck: Employee and Shareholder, Salary; I. Lee, Merck: Employee, Salary; Z. Popmihajlov, Merck & Co., Inc.: Employee and Shareholder, Salary

# 1819. Vaccine effectiveness against influenza-associated hospitalization among children aged < 13 years using a hospital-based surveillance system in Minnesota, 2013 – 2016

Ashley Fowlkes, MPH<sup>1</sup>; Hannah Friedlander, MPH<sup>2</sup>; Andrea Steffens, MPH<sup>1</sup>; Kathryn Como-Sabetti, MPH<sup>2</sup>; Dave Boxrud, MSc<sup>3</sup>; Sarah Bistodeau, BS<sup>4</sup>; Anna Strain, PhD<sup>2</sup>; Jill M. Ferdinands, PhD, MSc<sup>1</sup>; Sandra S. Chaves, MD, MSc<sup>1</sup>; Carrie Reed, DSc, MPH<sup>1</sup> and Ruth Lynfield, MD, FIDSA<sup>2</sup>; <sup>1</sup>Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia; <sup>2</sup>Minnesota Department of Health, St. Paul, Minnesota; <sup>3</sup>Minnesota Department of Health, Minneapolis, Minnesota; <sup>4</sup>Public Health Laboratory, Minnesota Department of Health, St. Paul, Minnesota

Session: 229. Miscellaneous Advances in Vaccinology Saturday, October 7, 2017: 10:30 AM **Background.** Due to marked variability in circulating influenza viruses each year, annual evaluation of the vaccine's effectiveness against severe outcomes is essential. We used the Minnesota Department of Health's (MDH) Severe Acute Respiratory Illness (SARI) surveillance to evaluate vaccine effectiveness (VE) against influenza-associated hospitalization over three influenza seasons.

**Methods.** Residual respiratory specimens from patients admitted with SARI were sent to the MDH laboratory for influenza RT-PCR testing. Medical records were reviewed to collect patient data. Vaccination history was verified using the state immunization registry. We included patients aged  $\geq 6$  months to < 13 years, after which immunization reporting is not required, hospitalized from the earliest influenza detection after July through April each year. We defined vaccinated patients as those  $\geq 1$  dose of influenza vaccine in the current season. Children aged < 9 years with no history of vaccinated children were excluded. We estimated VE as 1 minus the adjusted odds ratio (x100%) of influenza vaccination among influenza cases vs. negative controlls, controlling for age, race, days from onset to admission, comorbidities, and admission month.

**Results.** Among 2198 SARI patients, 763 (35%) were vaccinated for influenza, 180 (8.2%) were partially vaccinated, and 1255 (57%) were unvaccinated. Influenza was detected among 202 (9.2%) children, and significantly more frequently among children aged  $\geq$ 5 years (17%) compared with younger children (7.4%). The adjusted VE in 2013–14 was 68% (95% Confidence Interval: 34, 85), but was non-significant during the 2014–15 and 2015–16 seasons (Figure). Estimates of VE by influenza A subtypes varied substantially by year; VE against influenza B viruses was significant, but could not be stratified by year. VE was impacted when live attenuated influenza vaccine recipients were excluded.

**Conclusion.** We report moderately high influenza VE in 2013–14 and a point estimate higher than other published estimates from outpatient data in 2014–15. These results, underscore the importance of influenza vaccination to prevent severe outcomes such as hospitalization.

#### Adjusted vaccine effectiveness against influenza-associated hospitalization 2013 - 2015

| Subgroup                         | Influenza Positive<br>Vaccinated<br>/Total (%) | Influenza Negative<br>Vaccinated<br>/Total (%) |                         | Adjusted Vaccine<br>Effectiveness %<br>(95% CI) |
|----------------------------------|--|--|-------------------------|---|
| Any vaccination type             |  |  |                         |   |
| Season (all influenza)           |  |  |                         |   |
| 2013 - 2014                      | 12/47 (25.5)                                   | 254/497 (51.1)                                 | <b></b>                 | 63.4 (26.9, 81.7)                               |
| 2014 - 2015                      | 20/88 (22.7)                                   | 227/724 (31.4)                                 | • ·                     | 42.4 (-0.4, 67.0)                               |
| 2015 - 2016                      | 18/55 (32.7)                                   | 232/607 (38.2)                                 | ·                       | 43.2 (-9.9, 70.6)                               |
| Influenza type and season        |  |  |                         |   |
| 2013-14: A/H1N1pdm09             | 9/35 (25.7)                                    | 285/573 (49.9)                                 | beauties and the second | 67.7 (31.2, 84.8)                               |
| 2015-16: A/H1N1pdm09             | 16/46 (34.8)                                   | 233/611(38.1)                                  | ·                       | 42.5 (-14.3, 71.1)                              |
| 2014-15: A/H3N2                  | 10/49 (20.4)                                   | 232/744 (31.2)                                 | ,                       | 39.8 (-14.4, 68.4)                              |
| All seasons: Influenza B         | 7/25 (28.0)                                    | 751/1928 (39.0)                                | ++                      | 57.7 (21.2, 77.2)                               |
| Excluding live attenuated vaccin | e recipients                                   |  |                         |   |
| Season (all influenza)           |  |  |                         |   |
| 2013 - 2014                      | 11/48(22.9)                                    | 259/538(48.1)                                  | h                       | 65.2 (25.9, 83.7)                               |
| 2014 - 2015                      | 19/85 (22.4)                                   | 195/693 (28.1)                                 | ·                       | 32.7 (-19.4, 62.1)                              |
| 2015 - 2016                      | 13/50 (26.0)                                   | 215/590 (36.6)                                 |                         | 56.4 (9.1, 79.1)                                |
| Influenza type and season        |  |  |                         |   |
| 2013-14: A/H1N1pdm09             | 6/32 (18.8)                                    | 261/548 (47.6)                                 |                         | 71.4 (33.1, 87.8)                               |
| 2015-16: A/H1N1pdm09             | 11/41 (26.8)                                   | 217/594 (36.5)                                 | ·                       | 58.1 (9.4, 80.6)                                |
| 2014-15: A/H3N2                  | 10/47 (21.3)                                   | 200/711(28.1) -                                |                         | 24.6 (-44.6, 60.7)                              |
| All seasons: Influenza B         | 6/24 (25.0)                                    | 678/1853 (36.6)                                | ·                       | 55.7 (15.9, 76.7)                               |
|                                  |  |  | <b>i</b>                | -   |
|                                  |  | -50  |                         | 100   |
|                                  |  |  | Vaccine Effectiveness % |   |
|                                  |  | Less effective                                 |                         | More effective                                  |

Disclosures. All authors: No reported disclosures.

## 1820. Impact of Prior Vaccination History on Risk of Vaccine Failure with Live Attenuated and Inactivated Influenza Vaccines in Children, 2013–14 through 2015–16

Huong Q. McLean, PhD, MPH<sup>1</sup>; Herve Caspard, MD, ScD<sup>2</sup>; Marie R. Griffin, MD, MPH<sup>7</sup>; Manjusha Gaglani, MBBS<sup>4</sup>; Timothy R. Peters, MD<sup>5</sup>; Katherine A. Poehling, MD, MPH<sup>5</sup>; Christopher S. Ambrose, MD, MBA<sup>6</sup> and Edward Belongia, MD<sup>1</sup>; <sup>1</sup>Marshfield Clinic Research Institute, Marshfield, Wisconsin; <sup>2</sup>MedImmune, Gaithersburg, Maryland; <sup>3</sup>Vanderbilt University Medical Center, Nashville, Tennessee; <sup>4</sup>Pediatrics; Pediatric Infectious Diseases, Baylor Scott & White Health, Texas A&M University Health Science Center College of Medicine, Temple, Texas; <sup>5</sup>Wake Forest School of Medicine, Winston-Salem, North Carolina; <sup>6</sup>AstraZeneca, Gaithersburg, Maryland

# Session: 229. Miscellaneous Advances in Vaccinology Saturday, October 7, 2017: 10:30 AM

**Background.** Prior season vaccination may influence influenza vaccine effectiveness; however, little is known about the impact of prior vaccination or vaccine type received. We assessed prior vaccination history and risk of influenza in children over 3 seasons.

Methods. Children aged 2–17 years seeking outpatient care for febrile acute respiratory illness were recruited during the 2013–14 through 2015–16 seasons (1 vaccine-mismatched H3N2 season and 2 H1N1pdm09 seasons) at 4 US sites. Influenza was confirmed by RT-PCR. Vaccination data for the season of enrollment (current) and 3 prior seasons were obtained from medical records and immunization registries. Among children who received 1 dose of influenza vaccine during the current season, risk of vaccine failure (ie, PCR-confirmed influenza) was estimated using test-negative design with logistic regression models adjusted for age, season, enrollment site, enrollment week (relative to peak), and outpatient visits. Risk of failure with live attenuated influenza vaccine (IIV) were modeled