1022. Establishing Models of Herpes Simplex Virus Type 2 Superinfection of Herpes Simplex Virus Type 1 Seropositive Mice to Test The Efficacy of a Novel Vaccine
Natalie Ramsey, B.S.1, William Jacobs, PhD1 and Betsy C. Herold, MD, FIDSA, FPIDS2; Albert Einstein College of Medicine, Bronx, New York.1,2Department of Pediatrics and Microbiology-Immunology, Albert Einstein College of Medicine, Bronx, New York.

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Background. Multiple subunit vaccines that elicit neutralizing antibodies (nAbs) against the immunodominant HSV-2 glycoproteins D and/or B (gD and gB) were advanced into the clinic after demonstrating protection against disease in animal models. However, although the vaccines elicited nAbs in seronegative and boosted nAbs titers in seropositive (HSV-1−) participants were not prevented HSV-2 infection suggesting that nAbs alone are not sufficient. The results also indicate that current animal models are not predictive of clinical trial outcomes. We recently engineered a candidate single cycle virus strain deleted in gD (ΔgD-2) and showed that it elicits high titer non-neutralizing Abs that provide complete protection against HSV-1 or HSV-2. The Abs passively protect naïve mice and activate the Fc receptor to induce antibody-dependent cell mediated cytotoxicity (ADCC). We hypothesize that ΔgD-2 will protect HSV-1− individuals from HSV-2 because it elicits a different type of immune response.

To test this hypothesis, we established a model of HSV-2 superinfection in HSV-1− mice.

Methods. We infected mice by corneal scarification with serial dilutions of a clinical strain of HSV-1 (Bx1.1) to identify a sublethal dose associated with serumconversion. We then superinfected mice on the skin with HSV-2 and monitored for disease. The presence of virus in dorsal root ganglia (DRG), the site of HSV latency, was determined by quantitative PCR.

Results. Corneal infection with 10−4 PFU of HSV-1 resulted in disease in 18/29 (62%) mice and 13/18 survived. Serumconversion was documented in 9/13 survivors. Surviving mice were superinfected 2 weeks post-recovery with HSV-2. All of the mice developed signs of disease, but only 2/9 who were HSV-1− died compared with 4/4 seronegative mice (P = 0.02, Fisher exact test). HSV-2 DNA was detected in the DRG of 12/13 mice.

Conclusion. Sublethal HSV-1 corneal disease provides partial protection against HSV-2 superinfection and provides a model to test vaccine efficacy. We speculate that superinfection boosts preexisting nAb titers, a response consistent with immune repertoire freeze, but that ΔgD-2, because it elicits ADCC Abs, will observe repertoire freeze and provide greater protection against HSV-2 superinfection.

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1023. Sustained Lesion and Shedding Rate Reductions in Genital Herpes Patients 24 Months after Immunization with GEN-003, a Genital Herpes Immunotherapy

Thomas Heineman, MD, PhD1, Lisa K. Mcneil, PhD2; Thomas Oliphant, MS, PhD2; Tracey Weiss, MPH2; Vince Daniels, PhD2 and Laura Wolfsdon, PhD2; 1Department of Pediatrics, Jordan University of Science and Technology, Irbid, Jordan, 2Communicable Disease Department, Ministry of Health, Amman, Jordan. 3Department of Pediatrics, Princess Rahama Hospital, Irbid, Jordan. 4Medical Affairs, MSD Inc, Inc., Beirurat, Lebanon. 5Global Vaccine Medical Affairs, Merck & Co., Inc., Kenilworth, New Jersey.

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Background. Herpes simplex virus 2 (HSV-2) is the main cause of genital ulcers worldwide. GEN-003 is an investigational genital herpes immunotherapy composed of HSV-2 antigens gpD2TM and ICP4.2, and the saponin-based adjuvant Matrilix-M (MM2). In a Phase 2 dose-ranging study (GEN-003-001), 3 doses of GEN-003 reduced HSV-2 lesion rate (percent of days with genital lesions) and anogenital HSV-2 shed rate (percent of days with detectable virus). The antiviral effect of GEN-003 persisted to 12 months after the 3-dose vaccination regiment. We report here the results of an extension study to evaluate efficacy and immunogenicity of GEN-003 post-24 months post-vaccination.

Methods. GEN-003-002 subjects who received at least 1 dose of GEN-003 (dose groups: 30 or 60 µg of antigens combined with 25, 50 or 75 µg of MM2) were eligible to enroll in the extension study. At 24 months post-vaccination, anogenital swabs were collected twice daily for 28 days for HSV-2 DNA detection by quantitative PCR. During this period, subjects also reported genital herpes lesion data via a daily reporting tool. Blood samples were collected at the end of the swab collection period to evaluate humoral and cellular immune responses. HSV-2 immunoglobulin G (IgG) was measured by ELISA, and HSV-2 neutralizing antibodies were measured by a col- ometric assay. Cellular responses were evaluated in peripheral blood mononuclear cells using an interferon-g/gramyze B Fluorospot assay.

Results. 140 subjects were enrolled. At 24 months, those in the two best-performing dose groups (GEN-003-002b) demonstrated sustained reductions in HSV-2 virus shed (MM2). In a Phase 2 dose-ranging study (GEN-003-002), 3 doses of GEN-003 reduced HSV-2 antigens gD2DTMR and ICP4.2, and the saponin-based adjuvant Matrix-M2 was sustained from 12 to 24 months. Similarly, mean neutralizing antibody titers did not change significantly from month 12 to 24.

Conclusion. GEN-003 induces reductions in HSV-2 shedding and genital herpes lesion rates that persist to 24 months following treatment. Humoral immune responses to GEN-003 are maintained at 24 months after immunization.

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1026. Comparison of Viral Loads in Patients with Co-infections vs. Single-virus Infections

Stockton Beveridge, MD1; Bhimna Piyu, MPH2; Laura Stewart, PhD2; Mary Louise Lindgren, MD, MPH1; Tiffanie Markus, PhD1; William Schaffner, MD, FIDSA, FIDSA1 and Natasha B. Halasa, MD, MPH, FFIDS1; Vanderbilt University School of Medicine, Nashville, TN, 2Vanderbilt University Medical Center, Nashville, TN

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Background. Molecular testing for respiratory viruses in clinical practice is common, often with multiple viruses detected. Viral load has been correlated with illness severity, but correlation of co-detection of viruses and viral load is less clear. We sought to compare cycle threshold (Ct) values, a marker inversely related to viral load, between single vs. co-detection of common respiratory viruses.

Methods. Children <18 years with respiratory symptoms and/or fever who presented to the ED or were admitted were enrolled. Nasal/throat specimens were obtained and combined. Singleplex qRT-PCR was used to test for 11 respiratory viruses. Clinical and demographic information were collected.

Results. From 11/15/15-7/15/16, 1255 children were enrolled, with median age of 26.5 months, 53.4% male, 54.3% White, 6.4% other, and 23.5% Hispanic. The median days of illness were 3 days. Of the total cohort, 904 (72%) tested positive for at least one viral pathogen. Table 1 compares Ct values of single vs. co-detection for each individual virus.

Table 1

| Virus (RSV) | Median Ct | IQR | p-value | Days of Illness | Median Ct | IQR | p-value |
|-------------|-----------|-----|---------|----------------|-----------|-----|---------|
| Respiratory Syncytial Virus (RSV) | 27.9 | 26.3-29.5 | 0.002 | 3 (2-5) | 28.0 | 26.5-29.6 | 0.002 |
| Single | | | | | | | |
| RSV-Co-detection | 63 | 27.9 | 26.3-29.5 | 0.002 | 3 (2-5) | 28.0 | 26.5-29.6 | 0.002 |
| Human Rhinovirus (HRV)-Single | 278 | 255-301 | 0.002 | 3 (2-5) | 278 | 255-301 | 0.002 |
| HRV-Co-detection | 117 | 32.8 | 29.0-35.4 | 0.002 | 3 (2-5) | 28.0 | 26.5-29.6 | 0.002 |
| Adenovirus (AdV)-Single | 7 | 32.8 | 27.3-30.8 | 0.002 | 3 (2-5) | 28.0 | 26.5-29.6 | 0.002 |
| Adenovirus (AdV)-Co-detection | 7 | 32.8 | 27.3-30.8 | 0.002 | 3 (2-5) | 28.0 | 26.5-29.6 | 0.002 |
| Human metapneumovirus (HMPV)-Single | 278 | 255-301 | 0.002 | 3 (2-5) | 278 | 255-301 | 0.002 |
| HMPV-Co-detection | 30 | 28.0 | 24.1-32.3 | 0.002 | 3 (2-5) | 28.0 | 26.5-29.6 | 0.002 |
| Parainfluenza (PIV)-Single | 36 | 25.2 | 23.6-28.1 | 0.002 | 3 (2-5) | 28.0 | 26.5-29.6 | 0.002 |
| PIV-Co-detection | 15 | 28.0 | 26.0-34.5 | 0.002 | 3 (2-5) | 28.0 | 26.5-29.6 | 0.002 |
| Flu-Single | 127 | 26.6 | 24.1-30.5 | 0.002 | 3 (2-5) | 28.0 | 26.5-29.6 | 0.002 |
| Flu-Co-detection | 26 | 28.0 | 25.9-31.4 | 0.002 | 3 (2-5) | 28.0 | 26.5-29.6 | 0.002 |

Conclusion. Single detection with RSV, HRV, Adv, and PIV had lower Ct values, indicating higher viral loads, compared with co-detection with other viruses. Additional research is needed to understand the reason for lower viral loads for co-detection vs. single detection in select respiratory viruses.

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1027. Study to Address Threats of Acute Respiratory Infections among Congregate Military Populations (ATARI)

Christian Coles, PhD1; Wei-Ju Chen, PhD1; Jacqueline Owens Miltzman, M.S.1; Elena Grigorenko, PhD2; Scott Robinson, MD2; Carol Jones, BS3; Nicole Moreno, BS3; Timothy Burgess, MD, MPH1 and Leslie Malone, MS, MB/ASC/CPM2; Infectious Disease Clinical Research Program, Uniformed Services University of the Health Sciences, Bethesda, Maryland, 2Diatherix Laboratories, LLC, Huntsville, Alabama, Martin Army Community Hospital, Fort Benning, Georgia, 3Infectious Disease Clinical Research Program, Uniformed Services University, Bethesda, Maryland

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Background. More than 90% of active duty personnel receive influenza vaccinations yearly. Despite high coverage, influenza-like illnesses (ILI) remain a frequent cause of missed duty and hospitalizations, particularly in U.S. military recruits. More research is needed on the epidemiology and etiology of ILI to reduce the burden of respiratory infections in congregate military settings.

Methods. We conducted a prospective cohort study to assess ILI patterns among US Army recruits in a 9-week basic combat training course at Ft. Benning, GA. Demographic data, vaccination history, and information on recent illness were collected at enrollment in January 2017. Participants were divided into two platoons with staggered biweekly visit schedules. Visits occurred from reception through training, with nasal swabs and symptom surveys (all visits) and blood draws (weeks 8 and