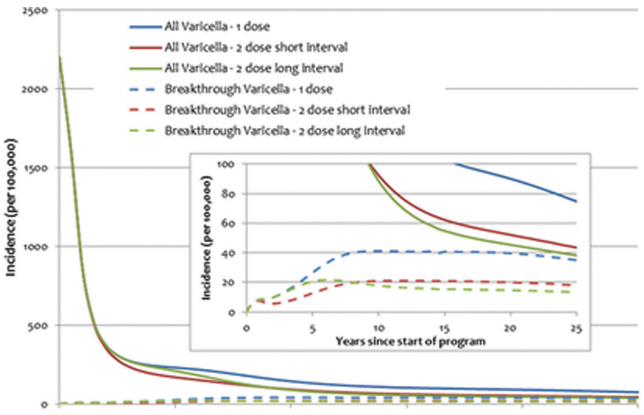

Figure 1: The projected health impact (incidence per 100,000 population) of universal varicella vaccination in Jordan considering three vaccination strategies: 1 dose administered at 12 months, 2 doses with a short interval (2nd dose 6 months after 1st, at 18 months) and 2 doses with a long interval (2nd dose 4 years after 1st, at 5 years). All varicella (across all age groups) is the sum of natural and breakthrough varicella. The inset graph is a more detailed view of the larger graph, with a y-axis going from 0-100, compared to the full y-axis ranging from 0 to 2500.

Disclosures. **W. Hayajneh**, Merck & Co., Inc.: Consultant, Consulting fee. **J. Maalouf**, Merck & Co., Inc.: Employee, Salary. **B. Kuter**, Merck & Co., Inc.: Employee, Salary.**T. Weiss**, Merck & Co., Inc.: Employee, Salary. **V. Daniels**, Merck & Co., Inc.: Employee, Salary. **L. Wolfson**, Merck & Co., Inc.: Employee, Salary.

1025. Serum and Lung Pharmacokinetics of ASN100, a Monoclonal Antibody Combination for the Prevention and Treatment of *Staphylococcus aureus* Pneumonia

Zoltan Magyarics, MD, PhD[1]; Fraser Leslie, BCPS[2]; Steven A. Luperchio, PhD[2]; Johann Bartko, MD[3]; Christian Schörgenhofer, MD[3]; Michael Schwameis, MD[3]; Ulla Derhaschnig, MD[3]; Heimo Lagler, MD[4]; Leopold Stiebellehner, MD[4]; Bernd Jilma, MD PhD[3]; Christopher Stevens, MD[2] and Eszter Nagy, MD, PhD[1]; [1]Arsanis Biosciences GmbH, Vienna, Austria, [2]Arsanis, Inc., Waltham, Massachusetts, [3]Department of Clinical Pharmacology, Medical University of Vienna, Vienna, Austria, [4]Department of Internal Medicine, Medical University of Vienna, Vienna, Austria

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Background. Monoclonal antibodies (mAbs) are well-suited for the prevention and treatment of acute bacterial infections. ASN100 is a combination of two fully human IgG1 mAbs, ASN-1 and ASN-2 that together neutralize six *Staphylococcus aureus* cytotoxins, alpha-hemolysin (Hla) and five leukocidins (HlgAB, HlgCB, LukED, LukSF [PVL] and LukGH) that are important in the pathogenesis of *S. Aureus* pneumonia. We aimed to characterize the pharmacokinetics (PK) of ASN100 in both serum and lung epithelial lining fluid (ELF) in male and female healthy volunteers.

Methods. The safety, tolerability, and serum and lung PK of single intravenous infusion of ASN100 was evaluated in a Phase 1 study. Eight subjects (3:1 randomization) in two double-blind cohorts received ASN100 (doses of 3600 mg or 8000 mg) or placebo. ASN-1 and ASN-2 were administered in a fixed dose 1:1 ratio. Twelve subjects received ASN100 open-label at doses of 3600 mg or 8000 mg and each underwent two bronchoalveolar lavage (BAL) fluid collections either on days 1 and 30 or on days 2 and 8 post-dosing. ASN-1 and ASN-2 concentrations were determined by ELISA. The ELF concentrations were normalized based on urea concentrations in serum and BAL fluid.

Results. No dose limiting toxicity was observed. Adverse events (AEs) showed no association of increased incidence with higher dose. All AEs were mild or moderate in severity, with 83.3% of subjects receiving ASN100 reporting at least one AE vs. 100% of placebo subjects. A dose proportional increase in serum peak and exposure (AUC) of ASN-1 and ASN-2 was observed and the serum PK of ASN-1 and ASN-2 were comparable (approximate half-life of each antibody was 3 weeks). Penetration of ASN-1 and ASN-2 into the ELF of the lung was observed at the first post-dose time point of 24 hours, peak concentrations were observed after day 2 and the mAbs remained detectable at day 30.

Conclusion. ASN100 was safe and well tolerated at doses up to 8000 mg (4000 mg ASN-1 and 4000 mg ASN-2). The PK profiles of ASN-1 and ASN-2 were comparable following simultaneous administration. Significant lung concentrations of each mAb were demonstrated between day 1 and 30 post-dosing. These data support continued clinical development of ASN100 for the prevention and treatment of *S. Aureus* pneumonia.

Disclosures. **Z. Magyarics**, Arsanis Biosciences GmbH: Employee, Salary. Arsanis, Inc.: Shareholder, Share options. **F. Leslie**, Arsanis., Inc.: Employee and Shareholder, Salary. **S. A. Luperchio**, Arsanis Inc.: Employee and Shareholder, Salary. **B. Jilma**, Arsanis Biosciences GmbH: Investigator, Investigator fee. **C. Stevens**, Arsanis Inc.: Employee and Shareholder, Salary.**E. Nagy**, Arsanis: Employee and Shareholder, Salary.

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

Stockton Beveridge, MD[1]; Bhinnata Piya, MPH[2]; Laura Stewart, PhD[1]; Mary Louise Lindegren, MD, MPH[1]; Tiffanie Markus, PhD[1]; William Schaffner, MD, FIDSA, FSHEA[1] and Natasha B. Halasa, MD, MPH, FPIDS[1]; [1]Vanderbilt University School of Medicine, Nashville, TN, [2]Vanderbilt 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, 38.7% Black, 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.

	N	Ct-Median (IQR)	p-value	Days of Illness - Median (IQR)	p-value
Respiratory Syncytial Virus (RSV) Single	144	25.5 (22.86-29.03)	0.05	4 (3-5)	0.82
RSV-Co-detection	63	27.0 (23.47-33.82)		3 (3-7)	
Human Rhinovirus (HRV)-Single	289	27.5 (23.79-32.50)	0.000	3 (2-4)	0.002
HRV-Co-detection	117	32.8 (29.08-35.49)		3 (2-6)	
Adenovirus (AdV)-Single	79	28.7 (23.84-33.62)	0.001	3 (2-4)	0.06
Adv-Co-detection	7	32.8 (27.40–36.69)		3 (2-4)	
Human metapneumovirus (HMPV)-Single	75	28.8 (25.37-32.22)	0.75	4 (3-6)	0.45
HMPV-Co-detection	30	28.2 (24.86-33.11)		4 (3-7)	
Parainfluenza (PIV)-Single	36	25.2 (23.75-28.76)	0.005	3.5 (2-5.5)	0.34
PIV-Co-detection	15	28.8 (26.04-34.50)		3 (1–4)	
Flu-Single	127	26.6 (24.71-30.51)	0.34	3 (2-5)	0.83
Flu-Co-detection	26	28.0 (25.98-30.14)		3.5 (2-6)	

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.

Disclosures. **W. Schaffner**, Pfizer: Scientific Advisor, Consulting fee. Merck: Scientific Advisor, Consulting fee. Novavax: Consultant, Consulting fee. Dynavax: Consultant, Consulting fee. Sanofi-pasteur: Consultant, Consulting fee. GSK: Consultant, Consulting fee. Seqirus: Consultant, Consulting fee. **N. B. Halasa**, sanofi pasteur: Research Contractor, Research support. Astra Zeneca: Research Contractor, Grant recipient.

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

Christian Coles, PhD[1]; Wei-Ju Chen, PhD[1]; Jacqueline Owens Milzman, M.S.[1]; Elena Grigorenko, PhD[2]; Scott Robinson, MD[3]; Carol Jones, BS[1]; Nicole Moreno, BS[1]; Timothy Burgess, MD, MPH[4] and Leslie Malone, MS, MB(ASCP)CM[2]; [1]Infectious Disease Clinical Research Program, Uniformed Services University of the Health Sciences, Bethesda, Maryland, [2]Diatherix Laboratories, LLC, Huntsville, Alabama, [3]Martin Army Community Hospital, Fort Benning, Georgia, [4]Infectious 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 congregated 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

9). Nasal specimens were used to detect clinical and colonizing pathogens using the Diatherix TEM-PCR Respiratory Panel.

Results. A total of 90 recruits were enrolled in the study. Twelve recruits were lost due to training attrition in the first week of the study. The participants were male and the mean age was 23 yo (SD 4.9). There were 10 (13%) cases of ILI reported among the 78 remaining participants, 6 in week 1, 3 in week 2 and 1 in week 9. The most frequently detected pathogens in the 10 symptomatic cases were coronavirus (5, 50%), rhinovirus (4, 40%), other enterovirus (3, 30%), and influenza A (2, 20%). Pathogen co-detections were common, 8 out 10 cases were associated with 2 pathogens, representing 7 unique combinations. While rhinovirus and coronavirus were most common among asymptomatic trainees, 10% had detectable influenza A. Detection of multiple pathogens was common in the first two weeks of training (50% among those who had viral detection). The study is still in progress.

Conclusion. Symptomatic ILI was associated with coronavirus, rhinovirus, and enterovirus, in addition to influenza in the early weeks of training. Coronavirus and rhinovirus also circulated widely among healthy recruits, along with influenza. The findings will inform ILI control strategies for congregated military trainees.

Disclosures. **E. Grigorenko**, Diatherix Laboratories: Employee, Salary.**L. Malone**, Diatherix Laboratories: Employee, Salary.

1028. Pharmacokinetics (PK) and Safety of Intravenous (IV) Brincidofovir (BCV) in Healthy Adult Subjects

Mary Beth Wire, PharmD; Marion Morrison, MD; Maggie Anderson, BS; Thangam Arumugham, PhD; John Dunn, PhD and Odin Naderer, PharmD; Chimerix, Durham, North Carolina

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Background. BCV is a lipid conjugate nucleotide that has shown rapid viral clearance in patients with adenovirus infection and improved survival in animal models of smallpox. In preclinical studies in rats, IV BCV dosed twice weekly for up to 29 days was not associated with gastrointestinal (GI), hematopoietic, hepatic, or renal toxicity. This study evaluated the safety and PK of IV BCV in healthy subjects.

Methods. In this double-blind study, subjects were randomized 3:1 to receive IV BCV or placebo in sequential single ascending dose cohorts (Table 1). Plasma PK samples were collected over 7 days and assayed by HPLC-MS. Plasma BCV PK parameters were determined by non-compartmental analysis and dose proportionality was assessed. Safety assessments were collected over 14 days.

Results. Forty healthy male subjects (18–46 years, 83% White) were enrolled and completed the study. Plasma BCV Cmax and AUC∞ increased in proportion to dose (Table 1). AEs and alanine aminotransferase (ALT) elevations were dose- and infusion duration-related (Table 1). GI AEs were mild. All AEs and ALT elevations were transient and no serious AEs occurred.

Table 1. IV BCV PK and Safety

	BCV 10 mg 2 h Infusion (*n* = 6)	BCV 25 mg 2 h Infusion (*n* = 6)	BCV 50 mg 2 h Infusion (*n* = 9)	BCV 50 mg 4 h Infusion (*n* = 9)	Pooled Placebo (*n* = 10)
Plasma BCV PK					
Cmax (ng/mL)	613 (25%)	1412 (27%)	2952 (19%)	1586 (14%)	NA
AUC∞ (ng h/mL)	1312 (26%)	2889 (37%)	5948 (19%)	6570 (15%)	NA
Drug-related AEs					
Diarrhea	0	0	1 (11%)	3 (33%)	0
Nausea	0	0	0	2 (22%)	0
Decreased appetite	0	0	0	1 (11%)	
Headache	0	0	2 (22%)	2 (22%)	0
Pain, phlebitis at infusion site	0	0	1 (11%)	0	0
Elevated liver transaminases[a]	0	0	0	1 (11%)	0

Cmax and AUC∞ presented as geometric mean (%CVb).
[a]ALT >2x ULN in 2 BCV 50 mg 4h infusion and 1 placebo subjects; 1 ALT elevation considered an AE.

Conclusion. Single doses of BCV 10–50 mg administered as a 2h IV infusion were well tolerated and not associated with significant clinical or laboratory abnormalities. BCV IV 10 mg and BCV IV 50 mg achieved geometric mean plasma BCV AUC∞ similar to and 4.5-fold, respectively, values achieved with BCV oral 100 mg tablets (Cmax = 251 ng/mL and AUC∞ = 1394 ng hours/mL). These data support evaluation of repeat dose administration in healthy subjects and virally-infected patients.

Disclosures. **M. B. Wire**, Chimerix: Employee and Shareholder, Salary. **M. Morrison**, Chimerix: Employee and Shareholder, Salary.**M. Anderson**, Chimerix: Employee and Shareholder, Salary. **T. Arumugham**, Chimerix: Employee and Shareholder, Salary. **J. Dunn**, Chimerix: Employee and Shareholder, Salary. **O. Naderer**, Chimerix: Employee and Shareholder, Salary.

1029. A Mortality Analysis of the Cytomegalovirus (CMV) Infection Letermovir Prophylaxis Trial in CMV-Seropositive Recipients of Allogeneic Hematopoietic Cell Transplantation (HCT)

Johan Maertens, M.D, PhD[1]; Michael Schmitt, MD[2]; Francisco M. Marty, MD, FIDSA[3]; Per Ljungman, MD, PhD[4]; Roy F. Chemaly, MD, MPH, FIDSA, FACP[5]; Nicholas A. Kartsonis, MD[6]; Joan Butterton, MD[6]; Hong Wan, PhD[6]; Valerie L. Teal, M.S.[6]; Kendra Sarratt, PhD[6]; Yoshihiko Murata, MD, PhD[6]; Randi Y. Leavitt, MD, PhD[6] and Cyrus Badshah, MD, PhD[6]; [1]Universitaire Ziekenhuizen Leuven, Leuven, Belgium, [2]University of Heidelberg, Heidelberg, Germany, [3]Dana-Farber Cancer Institute and Brigham and Women's Hospital, Boston, Massachusetts, [4]Karolinska University Hospital and Karolinska Institutet, Stockholm, Sweden, [5]Department of Infectious Diseases, Infection Control, and Employee Health, The University of Texas MD Anderson Cancer Center, Houston, TX, [6]Merck & Co., Inc., Kenilworth, New Jersey

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Background. In a Phase III randomized, double-blind, placebo-controlled study of CMV-seropositive HCT recipients, letermovir prophylaxis significantly reduced the incidence of clinically significant CMV infections (CS-CMVi) through 24 weeks post-HCT. We investigated the impact of letermovir prophylaxis on mortality through Week 48 post-HCT.

Methods. Adult CMV-seropositive allogeneic HCT recipients with undetectable plasma CMV DNA at screening who could initiate treatment by Week 4 post-HCT were eligible. Subjects stratified by high or low CMV disease risk were randomized 2:1 to letermovir dosed at 480 mg/d (240 mg/d if on cyclosporine) or placebo PO or IV through Week 14 post-HCT. Time to all-cause mortality and non-relapse mortality (defined as death due to any reason other than the indication for HCT) through Week 48 post-HCT are presented using Kaplan–Meier (KM) plots censored at study discontinuation for reasons other than death/non-relapse death or upon study completion. Distribution of time to mortality endpoints was tested by stratified log-rank tests using two-sided *P*-values.

Results. This analysis included all 565 patients randomized and treated with ≥1 dose of study drug. Subjects began study drug a median of 9 days post-HCT; 36.5% started post-engraftment. The observed KM event rate for all-cause mortality was lower in the letermovir group (10.6%) than the placebo group (15.5%) at Week 24 post-HCT, and remained lower through Week 48 post-HCT (21.4% vs. 26.2%) (Figure 1). The observed K–M event rate for all-cause mortality in subjects who developed CS-CMVi was also lower in the letermovir group (4.6%) than the placebo group (17.1%) at Week 48 post-HCT. The observed KM event rate for non-relapse mortality was lower in the letermovir group (6.9%) vs. the placebo group (11.2%) at Week 24 post-HCT, and remained lower in the letermovir group (13.9%) than the placebo group (17.5%) through Week 48 post-HCT (Figure 2).

Conclusion. All-cause and non-relapse mortality were reduced in the letermovir group compared with the placebo group through Week 48 post-HCT (relative risk reduction ~18% and ~21%, respectively). These results are consistent with a clinically meaningful survival benefit for letermovir prophylaxis.

Figure 1.

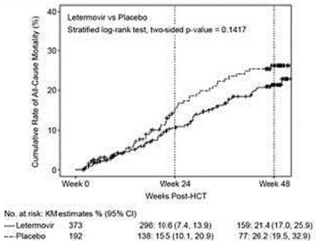
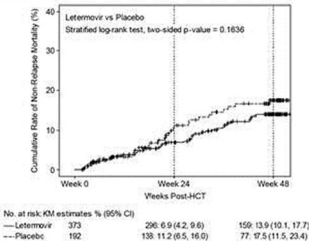


Figure 2.



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1030. Human Coronavirus Circulation in the USA, 2014–2017

Holly M. Biggs, MD, MPH[1]; Marie E. Killerby, VetMB, MPH[1]; Amber K. Haynes, MPH[2]; Rebecca M. Dahl, MPH[3]; Susan I. Gerber, MD[1] and John T. Watson, MD, MSc[1]; [1]Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, [2]IHRC Inc., contracting agency to Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, [3]Maximus Federal, contracting agency to Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia