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.

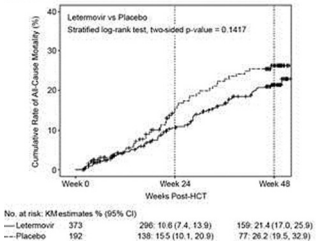
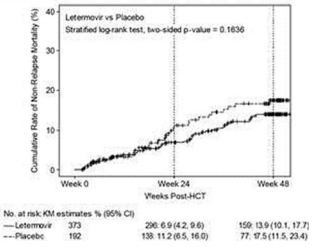


Figure 2.



Disclosures. **J. Maertens**, MSD: Consultant and Investigator, Consulting fee, Research grant and Speaker honorarium. **M. Schmitt**, MSD: Consultant and Investigator, Consulting fee. **F. M. Marty**, Merck & Co., Inc.: Consultant, Grant Investigator and Scientific Advisor, Consulting fee and Grant recipient. **P. Ljungman**, Merck & Co., Inc.: Consultant and Investigator, Consulting fee, Research grant and Speaker honorarium. **R. F. Chemaly**, Merck & Co., Inc.: Consultant and Investigator, Consulting fee, Research grant and Speaker honorarium. **N. A. Kartsonis**, Merck & Co., Inc.: Employee, Salary and stock/stock options. **J. Butterton**, Merck & Co., Inc.: Employee, Salary and stock, stock options. **H. Wan**, Merck & Co., Inc.: Employee, Salary and stock, stock options.**V. L. Teal**, Merck & Co., Inc.: Employee, Salary and Stock/stock options. **K. Sarratt**, Merck & Co., Inc.: Employee, Salary and stock & stock options. **Y. Murata**, Merck & Co., Inc.: Employee, Salary and stock and stock options. **R. Y. Leavitt**, Merck & Co., Inc.: Employee, Salary and stock, stock options. **C. Badshah**, Merck & Co., Inc.: Employee, Salary and stock, stock options

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

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Background. Human coronaviruses (HCoV) OC43, 229E, NL63 and HKU1 commonly cause upper respiratory tract infections, but can also cause severe lower respiratory tract disease. Increased use of diagnostic assays for respiratory viruses has facilitated detection and, since 2014, voluntary reporting of HCoV to the National Respiratory and Enteric Virus Surveillance System (NREVSS).

Methods. We reviewed weekly aggregate test results for HCoV OC43, 229E, NL63 and HKU1 voluntarily reported to NREVSS by U.S. hospital and clinical laboratories from July 1, 2014–April 30, 2017. Laboratories reporting any HCoV result using PCR were included, and the weekly percentage of positive HCoV tests by type was calculated. For a subset of HCoV detections reported to NREVSS via the Public Health laboratory Interoperability Project (PHLIP), which collects individual-level demographic data, we described age distribution and sex. Age distribution by HCoV type was compared using the Kruskal–Wallis test.

Results. 154 laboratories, across all 9 U.S. census divisions, reported 834,742 tests for HCoV; 18,514 (2.2%) were positive for HCoV-OC43, 8,363 (1.0%) for HCoV-NL63, 6,828 (0.8%) for HCoV-229E, and 5,170 (0.6%) for HCoV-HKU1. The percentage of tests positive for HCoV generally peaked between December and March (Figure 1). HCoV-OC43 showed distinct annual peaks with variation in magnitude by year. HCoV-HKU1 and NL63 had similar patterns, each with notable peaks during winter 2016 compared with 2015 or 2017. HCoV-229E showed a discernable peak in 2017 compared with the previous 2 years. Of 20,533 individuals with HCoV test results reported via PHLIP, 1,589 (7.7%) tested positive for any HCoV; 50% of HCoV-positive individuals were male, and the median age was 22 (range 0–96) years. Age distribution differed between HCoV types ($P < 0.01$, Figure 2).

Conclusion. Over approximately 3 seasons, peak positivity for HCoV occurred during winter months, and annual differences in circulation by HCoV type were observed. Continued testing and surveillance for HCoV will allow for further characterization of circulation trends over time and by geographic region, and improved understanding of the contribution of HCoV to the winter respiratory virus season.

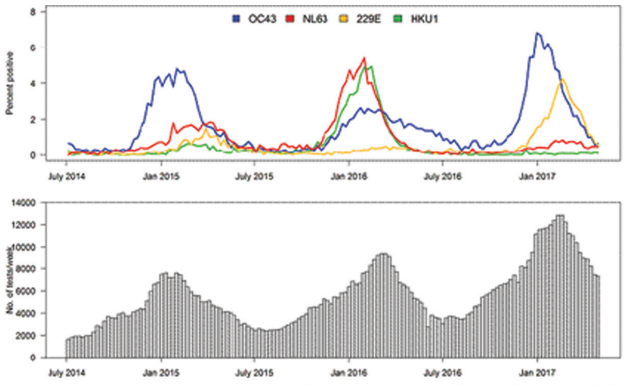

Figure 1. (A) Percentage of tests positive for human coronaviruses (HCoV) OC43, NL63, 229E, and HKU1 reported to the National Respiratory and Enteric Viruses Surveillance System (NREVSS) by week, July 1, 2014 – April 30, 2017. (B) Number of tests performed for HCoV reported to NREVSS by week, July 1, 2014 – April 30, 2017

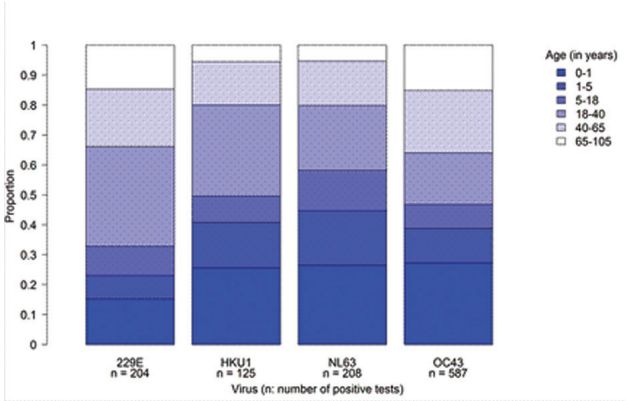

Figure 2. Age distribution of human coronaviruses 229E, HKU1, NL63 and OC43 positive tests reported to Public Health Laboratory Interoperability Project (PHLIP), October 2014 – April 2017.

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

1031. PCR Array Profiling of Antiviral Genes in Human Embryonic Kidney Cells Expressing Human Coronavirus OC43 Structural and Accessory Proteins

Meshal Beidas, MSc and Wassim Chehadeh, PhD; Microbiology, Kuwait University, Kuwait, Kuwait

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Background. Human coronavirus OC43 (HCoV-OC43) causes common cold, and is associated with severe respiratory symptoms in infants, elderly and immunocompromised patients. HCoV-OC43 is a member of *Betacoronavirus* genus that includes also the Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS) coronaviruses. Both SARS-CoV and MERS-CoV were shown to express proteins with the potential to evade early innate immune responses. However, the ability of HCoV-OC43 to antagonise the intracellular antiviral defences has not yet been investigated. The objective of this study was to investigate the role of HCoV-OC43 structural (membrane and nucleocapsid) and accessory (ns5a and ns2a) proteins in the modulation of antiviral gene expression profile in human embryonic kidney 293 (HEK-293) cells using PCR array analysis.

Methods. HCoV-OC43 membrane (M), nucleocapsid (N), ns5a and ns2a mRNA were amplified and cloned into the pAcGFP1-N expression vector (Clontech), followed by transfection in HEK-293 cells. Expression of M, N, ns5a and ns2a proteins were confirmed by indirect immunofluorescence test. Three days post-transfection, the cells were challenged by Sendai virus. The Human Antiviral Response PCR array system (Qiagen) was used to profile the antiviral gene expression in HEK-293 cells, using the fold regulation comparison and the manual normalisation methods.

Results. Around 50–60 genes were downregulated by HCoV-OC43 proteins, the most prominent genes being those critical for the activation of transcription factors involved in the antiviral response like interferon regulatory factors (IRFs) and activator protein 1 (AP-1). Among the most important downregulated genes were those coding for Interferons (IFNs) mitogen-activated protein kinases (MAPKs), pro-apoptotic and pyroptotic proteins (Caspases, cathepsins, tumour necrosis factor), pro-inflammatory cytokines (Interleukins), pattern recognition receptors (PRRs; toll-like receptors and NOD-like receptors) and their signaling transduction proteins (TICAM1, MAVS).

Conclusion. This study shows for the first time that similarly to SARS-CoV and MERS-CoV, HCoV-OC43 has the ability to downregulate the transcription of genes critical for the activation of different antiviral signaling pathways.

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

1032. Human Coronavirus (HCoV) Infection Among Adults in Cleveland, Ohio: An Increasingly Recognized Respiratory Pathogen

Anubhav Kanwar, MD[1]; Suresh Selvaraju, PhD[2] and Frank Esper, MD[3]; [1]Medicine, Division of Infectious Diseases and HIV Medicine, Case Western Reserve University School of Medicine/UH Cleveland Medical Center, Cleveland, Ohio, [2]Microbiology, Metrohealth Medical Center, Cleveland, Ohio, [3]Rainbow Babies and Children's Hospital, Cleveland, Ohio

Session: 139. Adult Viral Infection
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Background. Human Coronaviruses (CoV) have been long recognized as a common cause of respiratory tract disease including severe respiratory tract illness, yet there are few recent studies characterizing disease among adults in the United States. Here, we describe CoV infections and clinical characteristics among adults (>18 years) presenting with respiratory illness in Cleveland, Ohio.

Methods. Between February 1, 2016 and April 30, 2017, 2949 nasopharyngeal swab specimens were analyzed by NxTAG Respiratory Pathogen Panel in adults presenting with respiratory illness at MetroHealth Medical Center. Clinical data were collected on adults whose samples screened positive for CoV-HKU1, CoV-OC43, CoV-229E or CoV-NL63.

Results. Coronaviruses were detected in 192 (6.5%) adults including 105 (3.5%) OC43, 67 (2.3%) 229E, 13 (0.4%) HKU1 and 7 (0.2%) NL63. The majority of adults with coronavirus infection were females (66.2%) with a median age of 53 years. Common comorbidities included smoking (40.0%), asthma (38.0%), COPD (35.4%), and inhaled corticosteroid use (28.6%). Eighty-five (46.4%) required admission to the hospital. Common presenting symptoms included shortness of breath (42.7%) and cough (31.0%) whereas fever was uncommon (12.5%). Gastrointestinal symptoms were more common in HKU1 and NL63 infected adults. Seventy-three percent of coronavirus disease occurred between the months of January and March. Despite the recognition of coronavirus infection, 70 (36.5%) received antibiotics for their disease.

Conclusion. This study provides needed insight into clinical characteristics and severity associated with coronavirus infection in adults. Coronavirus infection should be considered in differential diagnosis of respiratory tract illness in adults including those that require hospitalization, have a history of smoking and have pulmonary comorbidities.

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

1033. Evaluation of Serum TNF-alpha, IL-6, IL-10, and IFN-gamma Levels in Patients with Crimean–Congo Hemorrhagic Fever

Hülya Yilmaz, MD[1]; Gürdal Yilmaz, Professor[2]; Ugur Kostakoglu, Assistant professor[3]; Mustafa Arslan, MD[4]; Süleyman Caner Karahan, Professor[5] and Iftihar Koksal, Professor[2]; [1]Department of Medical Biochemistry, Health Sciences University, Kanuni Training and Research Hospital, Trabzon, Turkey, [2]Department of Infectious Diseases and Clinical Microbiology, Karadeniz Technical University, Medical Faculty, Trabzon,