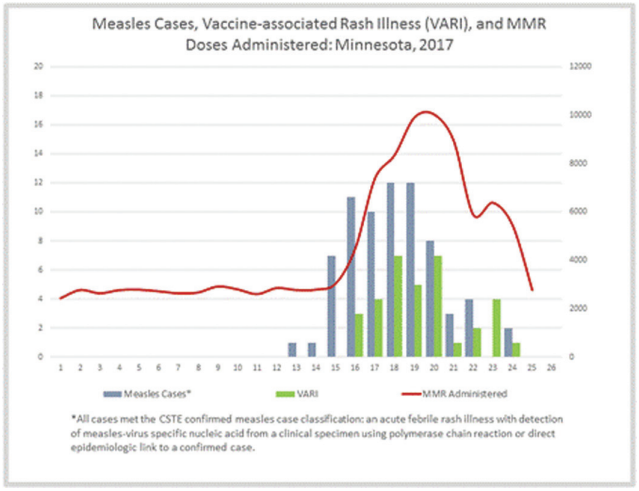
Conclusions. Surges in MMR administration and heightened community awareness during a measles outbreak can result in a large number of VARI, consuming considerable public health resources. When evaluating the need to suspect measles among patients with febrile rash, clinicians should consider time since MMR administration, clinical presentation, and history of measles exposure. Collecting appropriate specimens for timely virus genotyping could inform appropriate public health action.



Disclosures. All authors: No reported disclosures.

LB-9. Broad-spectrum Investigational Agent GS-5734 for the Treatment of Ebola, MERS Coronavirus and Other Pathogenic Viral Infections with High Outbreak Potential

Robert Jordan, PhD[1]; Alison Hogg, PhD[1]; Travis Warren, PhD[2]; Emmie De Wit, PhD[3]; Timothy Sheahan, PhD[4]; Michael Lo, PhD[5]; Veronica Soloveva, PhD[2]; Jessica Weidner, PhD[2]; Laura Gomba, MBA[2]; Friederike Feldmann, BS[3]; Jacqueline Cronin, BS[3]; Amy Sims, PhD[4]; Adam Cockrell, PhD[4]; Joy Feng, PhD[1]; Iva Trantcheva, FPD[1]; Darius Babusis, MS[1]; Danielle Porter-Poulin, PhD[1]; Roy Bannister, PhD[1]; Richard Mackman, PhD[1]; Dustin Siegel, PhD[1]; Adrian Ray, PhD[1]; Mark Denison, MD[6]; Christina Spiropoulou, PhD[5]; Stuart Nichol, PhD[5]; Tomas Cihlar, PhD[1]; Ralph Baric, PhD[4]; Heinrich Feldmann, MD, PhD[3]; Sina Bavari, PhD[2]; [1]Gilead Sciences, Inc., Foster City, California; [2]United States Army Medical Research Institute of Infectious Diseases, Frederick, Maryland; [3]Laboratory of Virology, Division of Intramural Research, National Institute for Allergy and Infectious Diseases, National Institutes of Health, Rocky Mountain Laboratories, Hamilton, Montana; [4]Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; [5]Centers for Disease Control and Prevention, Atlanta, Georgia; [6]Pediatrics, Vanderbilt University Medical Center, Nashville, Tennessee

Session: 228. Late Breaker Oral Abstracts
Saturday, October 7, 2017: 10:30 AM

Background. Recent viral outbreaks with significant mortality such as Ebola virus (EBOV), SARS-coronavirus (CoV), and MERS-CoV reinforced the need for effective antiviral therapeutics to control future epidemics. GS-5734 is a novel nucleotide analog prodrug in the development for treatment of EBOV.

Method. Antiviral activity of GS-5734 has been established in vitro against a wide range of pathogenic RNA virus families, including filoviruses, coronaviruses, and paramyxoviruses (EC_{50} = 37 to 200 nM) (*Warren et al., Nature 2016; Sheahan et al., Sci Transl Med 2017; Lo et al., Sci Rep 2017*). Herein, we describe the in vivo translation of the broad-spectrum activity of GS-5734 in relevant animal disease models for Ebola, Marburg, MERS-CoV, and Nipah.

Result. Therapeutic efficacy against multiple filoviruses with 80–100% survival was observed in rhesus monkeys infected with lethal doses of EBOV (Kikwit/1995 or Makona/2014) or Marburg virus and treated with once daily intravenous (IV) administration of 5 to 10 mg/kg GS-5734 beginning 3 to 5 days post-infection (p.i.). In all rhesus monkey filovirus infection models, GS-5734 significantly reduced systemic viremia and ameliorated severe clinical disease signs and anatomic pathology. In mice infected with MERS-CoV, twice daily subcutaneous administration of 25 mg/kg GS-5734 beginning 1 day p.i. significantly reduced lung viral load and improved respiratory function. In rhesus monkeys, once-daily IV administration of 5 mg/kg GS-5734 initiated 1 day prior to MERS-CoV infection reduced lung viral load, improved clinical disease signs, and ameliorated severe lung pathology. Finally, in African green monkeys infected with a lethal dose of Nipah virus therapeutic once-daily IV administration of 10 mg/kg GS-5734, starting 1 day p.i. resulted in 100% survival to at least day 35 without any major respiratory or CNS symptoms.

Conclusion. GS-5734 is currently being tested in a phase 2 study in male Ebola survivors with persistent viral RNA in semen. Lyophilized drug formulation has been developed that can be administered to humans via a 30-minutes IV infusion and does not require cold chain storage. Together, these results support further development of GS-5734 as a broad-spectrum antiviral to treat viral infections with high mortality and significant outbreak potential.

Disclosures. **R. Jordan**, Gilead: Employee, Salary. **J. Feng**, Gilead: Employee, Salary **I. Trantcheva**, Gilead: Employee, Salary. **D. Babusis**, Gilead: Employee, Salary. **D. Porter-Poulin**, Gilead: Employee, Salary. **R. Bannister**, Gilead: Employee, Salary **R. Mackman**, Gilead: Employee, Salary. **D. Siegel**, Gilead: Employee, Salary **A. Ray**, Gilead: Employee, Salary, **T. Cihlar**, Gilead: Employee, Salary.

1689b. Week 48 Results of EMERALD: A Phase 3, Randomized, Non-inferiority Study Evaluating the Efficacy and Safety of Switching from Boosted-protease Inhibitors (bPI) Plus Emtricitabine (FTC)/Tenofovir Disoproxil Fumarate (TDF) Regimens to the Once Daily (QD), Single-tablet Regimen (STR) of Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide (D/C/F/TAF) in Virologically Suppressed, HIV-1-infected Adults

Chloe Orkin, MD[1]; Jean-Michel Molina, MD, PhD[2]; Joel Gallant, MD, MPH, FIDSA[3]; Eugenia Negredo, MD PhD[4]; Joseph Gathe, MD[5]; Joseph Eron, MD[6]; Erika Van Landuyt, MD[7]; Erkki Lathouwers, PhD[7]; Veerle Hufkens, MSc[7]; Romana Petrovic, MSc[7]; Magda Opsomer, MD[7]; EMERALD Study Group [1]Barts Health NHS Trust, London, UK; [2]Department of Infectious Diseases, Saint-Louis Hospital,, Paris, France; [3]Southwest CARE Center, Santa Fe, New Mexico; [4]Germans Trias i Pujol University Hospital, Badalona, Spain; [5]Plaza Medical Center, Houston, Texas; [6]University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; [7]Janssen Pharmaceutica NV, Beerse, Belgium

Session: 188. HIV: Modern ART
Friday, October 6, 2017: 2:00 PM

Background. EMERALD is evaluating the efficacy and safety of switching from bPI + FTC/TDF regimens (control) to D/C/F/TAF 800/150/200/10 mg in virologically suppressed, HIV-1-infected adults. We present Week 48 primary results.

Method. EMERALD (NCT02269917) is a randomized, active-controlled, open-label, international, multicenter, parallel-group, non-inferiority trial. Virologically suppressed (viral load [VL] < 50 c/mL for ≥2 months), HIV-1-infected adults were randomized (2:1) to switch to D/C/F/TAF or continue control. The FDA-stipulated primary endpoint was non-inferiority of D/C/F/TAF vs. control regarding % virologic rebound (confirmed VL ≥ 50 c/mL or premature discontinuations with last VL ≥ 50 c/mL) cumulative through Week 48 (4% margin).

Result. 1141 patients were randomized and treated (N = 763 D/C/F/TAF; N = 378 control); median age 46; 18% women; 76% white; 58% on >2 previous ARVs (prior to screening regimen); 15% with previous non-DRV virologic failure (VF). Virologic rebound through Week 48 was non-inferior for D/C/F/TAF (2.5%; n = 19) vs. control (2.1%; n = 8) (Δ0.4%, 95% CI: −1.5%; 2.2%; P < 0.001). Most rebounders (12/19 [63%] vs. 4/8 [50%]) resuppressed by Week 48 without change in therapy. Week 48 virologic suppression rates (VL < 50 c/mL; FDA Snapshot) were 94.9% vs. 93.7% (Δ1.2%, 95% CI: −1.7%;4.1%) and VF rates (VL ≥ 50 c/mL; Snapshot) were 0.8% vs. 0.5% (Δ0.3%, 95% CI: −0.7%;1.2%), with no discontinuations for VF. No resistance-associated mutations related to any study drug were observed.

Adverse events (AEs) were similar between arms: AE-related discontinuations (1.4% vs. 1.3%); grade 3–4 AEs (6.8% vs. 8.2%); serious AEs (4.6% vs. 4.8%); and no deaths. Renal and bone parameters favored D/C/F/TAF vs. control. TC and LDL-C slightly favored control vs. D/C/F/TAF, with no clinically significant difference in TC/HDL-C ratio between arms (Table 1).

Conclusion. Percentage of virologic rebound after switching to D/C/F/TAF was non-inferior to control cumulative through Week 48, with high suppression rates (94.9%), no resistance development, better bone and renal safety parameters and similar TC/HDL-C ratio. D/C/F/TAF maintains the high genetic barrier to resistance of darunavir with the safety advantages of TAF, even in patients with a history of non-DRV VF.

Table 1: Changes from baseline at Week 48 in renal, lipid, and bone parameters

	D/C/F/TAF N=763	Control N=378	P-value*
Median change in $eGFR_{cys}$ mL/min/1.73m²	0.0	-1.9	0.005
Median change in $eGFR_{Cr}$ mL/min/1.73m²	-0.7	-0.6	0.146
Median changes in renal biomarkers			
Urine protein: creatinine ratio (mg/g)	-22.25	-7.37	<0.001
Urine albumin: creatinine ratio (mg/g)	-0.76	+0.40	<0.001
Urine Retinol Binding Protein: creatinine ratio (µg/g)	-27.09	+19.66	<0.001
Urine Beta-2-Microglobulin: creatinine ratio (µg/g)	-67.02	+20.24	<0.001
Median change in fasting lipids			
Total cholesterol (mg/dL)	+19.7	+1.3	<0.001
HDL-C (mg/dL)	+2.7	0.0	<0.001
LDL-C (mg/dL)	+15.7	+1.9	<0.001
Triglycerides (mg/dL)	+5.3	+4.9	0.957
TC/HDL-C ratio	+0.20	+0.10	0.036
Changes in BMD	N=209	N=108	
Lumbar spine			
Median % change from baseline	+1.47	-0.38	<0.001
Increase by ≥3%	31.8%	8.9%	ND
Decrease by ≥3%	7.8%	19.8%	ND
Total hip			
Median % change from baseline	+1.41	-0.11	<0.001
Increase by ≥3%	20.2%	4.1%	ND
Decrease by ≥3%	2.1%	8.2%	ND

*Between treatment comparison assessed by van Elteren test, controlling for boosted PI used at screening; $eGFR_{cys}$ = eGFR based on serum cystatin C (CKD-EPI formula); $eGFR_{Cr}$ = eGFR based on serum creatinine (CKD-EPI formula); HDL-C = high-density lipoprotein-cholesterol; LDL-C = low-density lipoprotein-cholesterol; TC = total cholesterol; BMD = bone mineral density; ND = not determined.

Disclosures. C. Orkin, Janssen Pharmaceuticals: Grant Investigator, Scientific Advisor and Speaker's Bureau, Consulting fee, Research grant, Speaker honorarium and Travel bursary to attend conference. MSD: Grant Investigator, Scientific Advisor and Speaker's Bureau, Consulting fee, Research grant, Speaker honorarium and Travel bursary to attend conference. Viiv Healthcare: Grant Investigator, Scientific Advisor