Figure 1. Pseusoneutralization titers in children over time.

Figure 1.A. Pseudoneutralizing antibody titers over time in 27 children with documented SARS-CoV-2 infection followed prospectively over time shown as weeks, x axis.

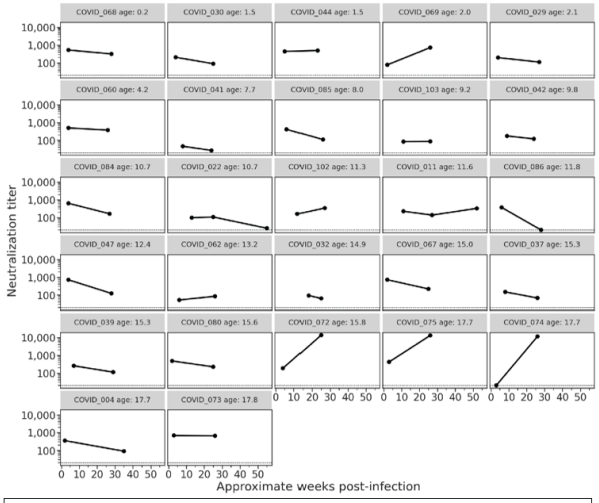


Fig. 1 B. Cases complicated by immunosuppression or multiple blood transfusions in 5 children with documented SARS-CoV-2 infection followed prospectively over time shown as weeks, x axis.

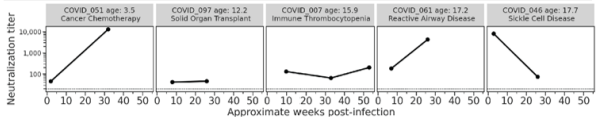


Figure 2. Nucleocapsid-binding antibody titers in children over time.

Figure 2. A. Nucleocapsid antibody over time in 27 children followed prospectively over time (in weeks, x axis) following approximate or documented SARS-CoV-2 infection, shown as the Abbott index as determined by the Abbott Architect assay. Dotted line indicates level of detection with this assay.

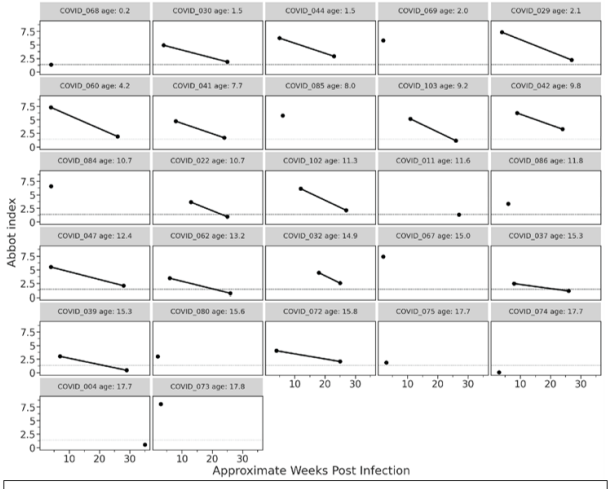
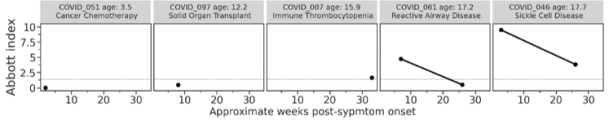


Figure 2 B. Nucleocapsid antibody in cases complicated by immunosuppression or multiple blood transfusions in 5 children followed prospectively over time (in weeks, x axis) following approximate or documented SARS-CoV-2 infection, shown as the Abbott index as determined by the Abbott Architect assay. Dotted line indicates level of detection with this assay.



Conclusion. We show neutralizing Abs wane to a small degree over 24wks post-SARS-CoV-2 infection and remain detectable in most children. In contrast, anti-N Abs decreased, becoming undetectable in some children by 24wks. These findings add to understanding of the natural history of SARS-CoV-2 immunity in children.

* This study was supported by CDC BAA75D301-20-R-67897

Disclosures. **Jesse Bloom, PhD**, **Flagship Labs 77** (Consultant)**Moderna** (Consultant) **Janet A. Englund, MD**, **AstraZeneca** (Consultant, Grant/Research Support)**GlaxoSmithKline** (Research Grant or Support)**Meissa Vaccines** (Consultant)**Pfizer** (Research Grant or Support)**Sanofi Pasteur** (Consultant)**Teva Pharmaceuticals** (Consultant)

LB10. Impact of SARS-CoV-2 Delta Variant on the Spectrum of Pediatric COVID-19 Disease in Arkansas

Jose R. Romero, MD[1]; Donald E. Warden, MPH[2]; Michael Cima, PhD, MPH[2]; [1]University of Arkansas for Medical Sciences, Little Rock, Arkansas; [2]Arkansas Department of Health, Little Rock, Arkansas

Session: 0. Late Breaker Abstracts: COVID-19 Vaccines, Epidemiology, and Clinical
Friday, October 1, 2021: 11:00 AM

Background. Pediatric SARS-CoV-2 infection is generally thought to be asymptomatic or result in mild COVID-19 disease, with a paucity of severe outcomes. However, SARS-CoV-2 variants, notably B.1.617.2 (WHO Delta), have changed the clinical landscape of COVID-19 in the United States. Delta became the dominant variant in Arkansas (AR) the 1st week of July 2021. Schools contributed to pediatric infections during the January 2021 surge in COVID-19 infections even with physical mitigation measures (PMM) that were removed in March 2021. We present preliminary data suggesting a shift in the clinical presentation of children with Delta variant infection.

Table 1.

Peak Month	*July 2020*	*January 2021*	*July 2021*	*p-value*
Cases	**3268**	**11735**	**8031**	
Hospitalization	**55**	**74**	**105**	**<0.0001**
ICU Admission	**6**	**11**	**18**	**0.0016**
Mechanical Ventilation	**2**	**2**	**8**	**0.0034**
Death	**0**	**0**	**1**	**0.3487**

Methods. Pediatric (ages ≤ 18 years) case records for the 3 months representing key inflection points of the COVID-19 Pandemic in AR were reviewed. Outcomes (hospitalizations, ICU admission, mechanical ventilation, death) were recorded by the Arkansas Department of Health (ADH) in a statewide database. Fisher's Exact Test was used with p-values < 0.05 indicating statistical significance.

Results. During July 2020, 3,268 pediatric cases were reported to ADH with 55 hospitalizations, 6 ICU admissions, 2 mechanical ventilations, and no deaths. A second peak in January 2021 included 11,735 pediatric cases, a 259.1% increase. Increases were also seen in hospitalizations (n=74), ICU admissions (n= 11), and mechanical ventilations (n=2). No deaths reported. The beginning of an exponential growth in cases during July 2021, before the opening of schools, included 8,031 pediatric cases. Despite 31.6% fewer cases than the previous peak, hospitalizations increased 41.9% (n=105) (p < 0.0001) and included increases in ICU and ventilator use of 68.6% (n=18) (p 0.0016) and 300% (n=8) (p 0.0034), respectively. One pediatric death was reported. (Tbl 1)

Conclusion. In the absence of PMM and despite the summer closure of schools, pediatric COVID-19 cases and severe outcomes increased significantly. Initial analysis of the AR July 2021 Delta variant surge indicates a statistically significant increase in pediatric COVID-19 disease and severity as indicated by a proportional increase in hospitalizations, ICU, and ventilator use. Further studies are warranted to better define Delta related childhood disease. Our findings also have implications for school PMM efforts.

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

LB1. Remdesivir for the Treatment of High-Risk Non-Hospitalized Individuals With COVID-19: A Randomized, Double-Blind, Placebo-Controlled Trial

Joshua A. Hill, MD[1]; Roger Paredes, MD, PhD[2]; Carlos Vaca, MD[3]; Jorge Mera, MD[4]; Brandon J. Webb, MD[5]; Gilberto Perez, MD[6]; Godson Oguchi, MD[7]; Pablo Ryan, MD PhD[8]; Jan Gerstoft, MD[9]; Michael Brown, FRCP PhD[10]; Joshua Schiffer, MD, MSc[11]; Samuel Brown, MD, MS[12]; Morgan Katz, MD, MHS[13]; Adit A. Ginde, MD, MPH[14]; Gregory Camus, PhD[15]; Danielle P. Porter, PhD[16]; Robert H. Hyland, DPhil[17]; Shuguang Chen, PhD[15]; Kavita Juneja, MD[18]; Anu Osinusi, MD[18]; Frank Duff, MD[15]; Robert L. Gottlieb, MD[19]; [1]Fred Hutchinson Cancer Research Center; University of Washington, Seattle, WA; [2]Hospital Universitario Germans Trias i Pujol, Badalona, Catalonia, Spain; [3]Nuren Medical and Research Center, Miami, Florida; [4]Cherokee Nation Outpatient Health Center, Tahlequah, Oklahoma; [5]Intermountain Healthcare, Murray, UT; [6]Evolution Clinical Trials, Hialeah Gardens, Florida; [7]Midland Florida Clinical Research Center, DeLand, Florida; [8]Hospital Universitario Infanta Leonor, Universidad Complutense de Madrid, Madrid, Madrid, Spain; [9]University of Copenhagen, Copenhagen, Hovedstaden, Denmark; [10]University College London Hospitals NHS Foundation Trust, London, England, United Kingdom; [11]Fred Hutch, Seattle, Washington; [12]Intermountain Medical Center, Murray, Utah; [13]Johns Hopkins University, Baltimore, MD; [14]University of Colorado, Aurora, Colorado; [15]Gilead Sciences, Inc, Foster City, California; [16]Gilead Sciences, Inc., Foster City, California; [17]AlloVir, Chapel Hill, North Carolina; [18]Gilead, Foster City, California; [19]Baylor University Medical Center, Dallas, Texas

Session: 55. Late Breaker Abstracts: COVID-19 Treatment & Prophylaxis
Thursday, September 30, 2021: 5:15 PM

Background. Remdesivir (RDV) is a potent nucleotide prodrug inhibitor of the SARS-CoV-2 RNA-dependent RNA polymerase that has demonstrated efficacy in the

treatment of patients hospitalized with moderate to severe COVID-19. This Phase 3 (GS-US-540–9012) double-blind, placebo-controlled study compared the efficacy and safety of 3 days of RDV to standard of care in non-hospitalized, high-risk participants with confirmed COVID-19.

Table 1. COVID-19 related hospitalization or death, COVID-19 related medically attended visits or death, and Treatment Emergent Adverse Events

	Remdesivir	Placebo	Risk reduction	Hazard ratio (95%CI), p-value
COVID-19 related hospitalization or death by day 28	2/279 (0.7%)	15/283 (5.3%)	87%	0.13 (0.03-0.59), p =0.008
COVID-19 related medically attended visits or death by day 28	4/246 (1.6%)	21/252 (8.3%)	81%	0.19 (0.07-0.56) p= 0.002
	Remdesivir	Placebo		
Treatment-emergent adverse events (TEAE)	42.3%	46.3%		
Grade ≥ 3 TEAE	3.6%	7.1%		
Serious TEAE	1.8%	6.7%		

Methods. Participants were randomly assigned 1:1 to receive intravenous (IV) RDV (200 mg on day 1, 100 mg on days 2 to 3) or placebo. The primary efficacy endpoint was composite COVID-19 hospitalization or all-cause death by day 28 and compared using Cox proportional hazards model with baseline stratification factors as covariates. The primary safety endpoint was proportion of participants with treatment-emergent adverse events. Study enrollment was terminated early for administrative reasons in light of the evolving pandemic.

Results. 562 patients underwent randomization and started their assigned treatment (279, RDV; 283, placebo). Baseline demographics and characteristics were balanced across arms. Overall, 52% were male, 44% were Hispanic/Latino ethnicity and 30% were ≥ 60 years old. The most common comorbidities were diabetes mellitus (62%), obesity (56%; median BMI, 30.7), and hypertension (48%). Median baseline SARS-CoV-2 RNA nasopharyngeal viral load was 6.2 $\log_{10}$ copies/mL. Treatment with RDV significantly reduced COVID-19 hospitalization or all-cause death by day 28 (HR, 0.13; 95% CI, 0.03 – 0.59; p = 0.008; Table 1) compared to placebo. Participants receiving RDV also had significantly lower risk for COVID-19-related medically attended visits or all-cause death by day 28 compared to placebo (HR, 0.19; 95% CI, 0.07 – 0.56; p = 0.002; Table 1). No deaths occurred in either arm by day 28. There was no difference between arms in time-weighted average change in nasopharyngeal viral loads from baseline up to day 7. The proportion of patients with AEs was similar between arms (Table 1); the most common AEs in the RDV arm were nausea (11%), headache (6%), and diarrhea (4%).

Conclusion. A 3-day course of IV RDV was safe, well tolerated and highly effective at preventing COVID-19 related hospitalization or death in high-risk non-hospitalized COVID-19 patients.

Disclosures. **Joshua A. Hill, MD**, Allogene (Individual(s) Involved: Self): Consultant; Allovir (Individual(s) Involved: Self): Consultant, Grant/Research Support; Amplyx (Individual(s) Involved: Self): Consultant; Covance/CSL (Individual(s) Involved: Self): Consultant; CRISPR (Individual(s) Involved: Self): Consultant; Gilead (Individual(s) Involved: Self): Consultant, Grant/Research Support; Karius: Grant/Research Support, Scientific Research Study Investigator; Medscape (Individual(s) Involved: Self): Consultant; Octapharma (Individual(s) Involved: Self): Consultant; OptumHealth (Individual(s) Involved: Self): Consultant; Takeda (Individual(s) Involved: Self): Consultant, Grant/Research Support, Scientific Research Study Investigator **Roger Paredes, MD, PhD**, **Gilead Sciences, Inc** (Grant/Research Support, Scientific Research Study Investigator, Advisor or Review Panel member) **Carlos Vaca, MD**, **Gilead Sciences, Inc** (Scientific Research Study Investigator) **Jorge Mera, MD**, **Gilead Sciences, Inc** (Consultant, Study Investigator (payment to employer not self)) **Gilberto Perez, MD**, **Gilead Sciences, Inc** (Scientific Research Study Investigator) **Godson Oguchi, MD**, **Gilead Sciences, Inc** (Scientific Research Study Investigator) **Pablo Ryan, MD PhD**, **Gilead Sciences, Inc** (Grant/Research Support, Scientific Research Study Investigator, Advisor or Review Panel member) **Jan Gerstoft, MD**, **Gilead Sciences, Inc** (Other Financial or Material Support, Study Investigator (payment to employer)) **Michael Brown, FRCP PhD**, **Gilead Sciences, Inc** (Scientific Research Study Investigator, Investigator for numerous remdesivir trials (employer received compensation)) **Morgan Katz, MD, MHS**, Roche (Individual(s) Involved: Self): Advisor or Review Panel member; Skinclique (Individual(s) Involved: Self): Consultant **Gregory Camus, PhD**, **Gilead Sciences** (Employee, Shareholder) **Danielle P. Porter, PhD**, **Gilead Sciences** (Employee, Shareholder) **Robert H. Hyland, DPhil**, **Gilead Sciences, Inc** (Shareholder, Other Financial or Material Support, Employee during the conduct of this trial) **Shuguang Chen, PhD**, **Gilead Sciences, Inc** (Employee, Shareholder) **Kavita Juneja, MD**, **Gilead Sciences, Inc** (Employee) **Anu Osinusi, MD**, **Gilead Sciences, Inc** (Employee, Shareholder) **Frank Duff, MD**, **Gilead Sciences, Inc** (Employee, Shareholder) **Robert L. Gottlieb, MD**, **Eli Lilly** (Scientific Research Study Investigator, Advisor or Review Panel member)**Gilead Sciences** (Scientific Research Study Investigator, Advisor or Review Panel member, Other Financial or Material Support, Gift in kind to Baylor Scott and White Research Institute for NCT03383419)**GSK** (Advisor or Review Panel member)**Johnson and Johnson** (Scientific Research Study Investigator)**Kinevant** (Scientific Research Study Investigator)**Roche/Genentech** (Scientific Research Study Investigator)

LB2. Safety and Efficacy of Combination SARS-CoV-2 Monoclonal Neutralizing Antibodies (mAb) BRII-196 and BRII-198 in Non-Hospitalized COVID-19 Patients

Teresa H. Evering, MD[1]; Mark Giganti, Ph.D.[2]; Kara W. Chew, MD, MS[3]; Michael Hughes, Ph.D.[2]; Carlee Moser, Ph.D.[2]; David Alain Wohl, MD[4]; Judith Currier, M.D., M.Sc.[5]; Joseph J. Eron, MD[6]; Arzhang Javan, M.D., M.P.H., D.T.M&H[7]; David A. Margolis, MD MPH[8]; Qing Zhu, PhD[8]; Ulises D'Andrea, MD[9]; Keila Hoover, M.D.[10]; Bharat R. Mocherla, M.D.[11]; Courtney Fletcher, Pharm.D.[12]; Jonathan Li, M.D., M.M.Sc.[13]; Davey Smith, M.D.[14]; Eric Daar; [1]Weill Cornell Medicine, New York, NY; [2]Harvard T.H. Chan School of Public Health, Boston, Massachusetts; [3]David Geffen School of Medicine at UCLA; [4]UNC School of Medicine, Chapel Hill, NC; [5]David Geffen School of Medicine at University of California, Los Angeles, Los Angeles, California; [6]University of North Carolina at Chapel Hill, Chapel Hill, North Carolina; [7]National Institute of Health, Bethesda, Maryland; [8]Brii Biosciences, Chapel Hill, North Carolina; [9]Instituto Medico Rio Cuarto, Rio Cuarto, Cordoba, Argentina; [10]Miami Clinical Research, Miami, Florida; [11]Las Vegas Medical Research, Las Vegas, Nevada; [12]University of Nebraska, Omaha, Nebraska; [13]Brigham & Womens Hospital, Boston, Massachusetts; [14]University of California, San Diego, San Diego, California

ACTIV-2 and AIDS Clinical Trials Group

Session: 55. Late Breaker Abstracts: COVID-19 Treatment & Prophylaxis
Thursday, September 30, 2021: 5:30 PM

Background. SARS-CoV-2 continues to spread and the development of safe and effective therapeutics for the prevention of severe disease remains a priority. BRII-196 and BRII-198 are non-competing anti-SARS-CoV-2 mAbs with YTE triple amino acid substitution in Fc to extend half-life and reduce receptor binding, that are being studied for treatment of COVID-19 in the ACTIV-2 Trial, sponsored by NIAID and led by ACTG.

Methods. ACTIV-2 evaluates safety/efficacy of investigational agents for treatment of non-hospitalized adults with mild-moderate COVID-19 under a randomized, blinded, controlled adaptive platform. BRII-196/BRII-198 (1000 mg each) as a single dose given as sequential infusions, or placebo to those at high risk of clinical progression (i.e., age ≥ 60 years or presence of other medical conditions) within 10 days of symptom onset and positive test for SARS-CoV-2. The primary endpoint was hospitalization and/or death through day 28. We report Phase 3 BRII-196/BRII-198 trial results per DSMB recommendation following an interim analysis.

Results. Between January and July 2021, 837 participants (418 active, 419 placebo) from sites in the US (66%), Brazil, South Africa, Mexico, Argentina and the Philippines were randomized and received study product at time of emerging variants. Median age 49 years (Q1, Q3: 39, 58), 51% female, 17% Black/African-American and 49% Hispanic/Latino, with median 6 days from symptom onset. At interim analysis 71% and 97% had a day 28 and 7 visit, respectively. For all available data at interim review, BRII-196/BRII-198 compared to placebo had fewer hospitalizations (12 vs. 45) and deaths (1 vs. 9). At day 28 of follow-up, there was an estimated 78% reduction in hospitalization and/or death (2.4 vs. 11.1%), relative risk 0.22 (95% CI: 0.05, 0.86), P=0.00001 (nominal one-sided). Grade 3 or higher adverse events (AEs) were observed less frequently among BRII-196/BRII-198 participants than placebo (3.8% vs. 13.4%) with no severe infusion reactions or drug related serious AEs.

Conclusion. BRII-196/BRII-198 was safe, well-tolerated, and demonstrated significant reduction compared to placebo in the risk of hospitalization and/or death among adults with mild-moderate COVID-19 at high risk for progression to severe disease.

Disclosures. **Kara W. Chew, MD, MS**, Amgen (Individual(s) Involved: Self): Grant/Research Support; Merck Sharp & Dohme (Individual(s) Involved: Self): Grant/Research Support **David Alain Wohl, MD**, Gilead Sciences (Individual(s) Involved: Self): Advisor or Review Panel member, Consultant, Research Grant or Support, Scientific Research Study Investigator; Janssen (Individual(s) Involved: Self): Advisor or Review Panel member; Merck (Individual(s) Involved: Self): Advisor or Review Panel member, Research Grant or Support; ViiV (Individual(s) Involved: Self): Advisor or Review Panel member, Research Grant or Support **Joseph J. Eron, MD**, **Gilead Sciences** (Consultant, Research Grant or Support)**Janssen** (Consultant, Research Grant or Support)**Merck** (Consultant)**ViiV** (Consultant, Research Grant