treated × 6 months) were included. Whole blood VL was determined by real-time PCR at a central laboratory before therapy (baseline, BL) and periodically for 6 months.

Results. In subjects treated for 6 months, increases in BL VL correlated with decreased probability of better hearing outcomes at 12 months (Figure 1), but clinically meaningful VL thresholds that predict SNHL were not identified (Table 1). Subjects treated for 6 weeks had no correlation between BL VL and SNHL. No correlation was found between BL VL and Bayley ND testing at 12 and 24 months for subjects receiving either treatment duration. Subjects treated for 6 months who achieved and sustained VL suppression (<2.5 log) between treatment day 14 and month 4 had better hearing outcomes at 6, 12, and 24 months (89% vs. 56%, $P = 0.01$; 100% vs. 63%, $P = 0.0007$; 94% vs. 68%, $P = 0.04$), but 56%–68% of subjects not achieving suppression still had improved hearing. Higher BL VL correlated with BL CNS involvement, thrombocytopenia, and transaminase elevation for subjects receiving either treatment duration, but with substantial overlap in quantity of virus detected (Figure 2). Subjects with >3 symptoms of congenital CMV at presentation had higher BL VL than subjects with ≤3 symptoms (3.75 log, range 1.00–5.65, vs. 3.38 log, range 1.00–5.36; $P = 0.005$).

Conclusion. Blood VL at BL and during therapy has little clinically meaningful predictive value for long-term outcomes in symptomatic congenital CMV.

Table 1

BL VL (log genome equivalent/ml)	Hearing outcome: Improved/ protected (no.)	Hearing outcome: Others (no.)	*P*-value	Negative predictive value (CI)	Positive predictive value (CI)
	12 months				
>3	43	20	0.10	93 (79–100)	32 (20–43)
≤3	13	1			
>4.5	8	9	0.01	80 (70–90)	53 (29–77)
≤4.5	48	12			
	24 months				
>3	42	14	0.72	83 (62–100)	25 (14–36)
≤3	10	2			
>4.5	10	5	0.32	79 (68–90)	33 (9–57)
≤4.5	42	11			

Figure 1

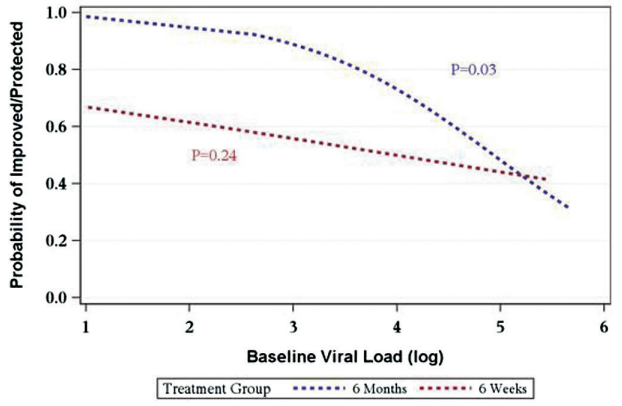
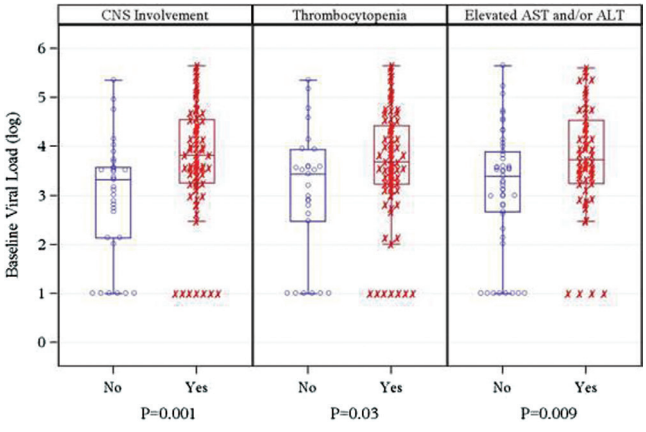


Figure 2



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948. Incidence of *UL97* Resistance Mutations in Infants with Congenital Cytomegalovirus Disease Receiving 6 Months of Oral Valganciclovir Therapy

Scott H. James, MD[1]; Ra'Shun L. Conner, MS, MBA[2]; David W. Kimberlin, MD, FIDSA, FPIDS[3]; Richard Whitley, MD, FIDSA[1]; Mark N. Prichard, PhD[2]; [1]Pediatrics, Division of Infectious Diseases, University of Alabama at Birmingham, Birmingham, Alabama; [2]University of Alabama at Birmingham, Birmingham, Alabama; [3]Pediatrics, University of Alabama at Birmingham, Birmingham, Alabama

Session: 121. Emerging Paradigms: Pediatric Viral Infections
Friday, October 6, 2017: 8:30 AM

Background. A recently completed Phase 3 randomized, controlled, double-blind, multicenter study of infants with symptomatic congenital cytomegalovirus (CMV) disease receiving 6 months of oral valganciclovir (VGCV) therapy represents the largest such population in which to evaluate treatment-emergent antiviral resistance. The most common mechanism of CMV antiviral resistance occurs through mutations in the CMV *UL97* gene that confer resistance to ganciclovir (GCV). Genotypic resistance analyses were performed on infants receiving 6 months of VGCV to assess the incidence of antiviral resistance due to *UL97* sequence variants.

Methods. Resistance analyses were performed by conventional DNA sequencing of the *UL97* gene at multiple time points. Following CMV DNA extraction from frozen whole blood specimens, the *UL97* gene was amplified with a double nested polymerase chain reaction method and sequenced to identify polymorphisms and mutations that might confer GCV resistance.

Results. Forty-six infants with symptomatic CMV disease who received a 6-month course of VGCV underwent resistance analysis to identify *UL97* sequence variants. In addition to a range of natural polymorphisms known to have no effect on antiviral susceptibility, 2 subjects developed *UL97* mutations known to confer resistance to GCV (A594V and G598S detected in one subject; E596G detected in another), yielding an incidence of 4%. Each of these resistance mutations occurred in specimens collected after at least 4 months of antiviral therapy. As evaluated in the original Phase 3 trial, neither of these infants showed an improvement in hearing outcome.

Conclusion. The development of treatment-emergent *UL97* resistance mutations was determined in a controlled study population of infants with congenital CMV disease receiving 6 months of VGCV. This targeted resistance analysis demonstrated an incidence approaching the total incidence of antiviral resistance for CMV disease in some immunocompromised populations, such as solid-organ transplant recipients. Further studies within this study population are warranted to elucidate the risk of emerging antiviral resistance and to assess clinical impact as well as the potential need for combination antiviral therapy.

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949. Programmatic Congenital CMV Universal Screening Program

Maria Carrillo-Marquez, MD[1,2]; Benjamin Rohde, BS[3]; Ryan Tomlinson, BS[4]; Jacqueline Blanch, CNA[4]; Lana Bradford, RN[5]; Young-In Kim-Hoehamer, PhD[4]; Lisa Harrison, MLT[6]; Stephen Pace, BS[7]; Joe Davis, BS[2]; Chirag Patel, Montana[8]; Anami Patel, PhD[8]; Sandra R. Arnold, MD, MSc[9]; John P. Devincenzo, MD[10]; [1]Pediatrics, University of Tennesse Health Science Center, Memphis, Tennessee; [2]Le Bonheur Children's Hospital, Memphis, Tennessee; [3]Children's Foundation Research Institute, Le Bonheur Children's Hospital, Memphis, Tennessee; [4]Department of Pediatrics, University of Tennessee School of Medicine, Memphis, Tennessee; [5]Pediatrics, Le Bonheurs Children Hospital, Memphis, Tennessee; [6]Pediatrics, University of Tennessee Health Science Center, Memphis, Tennessee; [7]University oF Tennessee Health Science Center, Memphis, Tennessee; [8]Molecular Diagnostics Laboratory, Le Bonheur Children's Hospital, Memphis, Tennessee; [9]Pediatrics, University of Tennessee Health Sciences Center, Memphis, Tennessee; [10]Department of Microbiology, Immunology, and Molecular Biology, University of Tennessee School of Medicine, Memphis, Tennessee

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Background. CMV is the most common congenital infection (cCMV). Traditional identification strategies including hearing screen and physical exam are insensitive and miss affected infants. To improve identification of infected newborns, we established a universal, institutional cCMV newborn screening program.

Methods. All newborns born or transferred to nurseries in a hospital system in Memphis, Tennessee between March 2016 and April 2017 were screened for cCMV. Infant saliva was collected on a Copan swab prior to discharge and within 2 weeks of birth. Specimens were centrally processed using a real-time CMV PCR assay (Simplexa™ CMV) (DiaSorin, Cypress CA) amplifying the UL83 gene, and the 3M Integrated Cycler. Parents received educational materials on cCMV testing and natural history prior to specimen collection. All patients with a positive screen had a full evaluation including physical exam, eye exam, hearing testing, CBC, chemistries and head ultrasound (HUS).

Results. There were 35/6,114 (0.6%) positive screens. Of 35, 16 (45.7%) were male and 5 (14%) were less than 37 weeks gestation. Thirty-one of 35 saliva specimens were collected on day 0 or 1 of life. All patients were evaluated by an infectious disease specialist at a median of 15 days of age. Confirmatory urine PCR was positive in 25/33 (76%) tested. Overall, 11/25 (44%) with confirmed congenital CMV were symptomatic. This included 28% with microcephaly and 20% with low birth weight. Six (24%) failed newborn hearing screening of one or both ears. Other abnormalities included thrombocytopenia (5%), elevated ALT (10%), elevated direct bilirubin (5%), and abnormal HUS (11/25, 44%), of which 7/11 had lenticulostriate vasculopathy and 2/11 had intracranial calcifications. Twelve infected infants had an eye examination and none had retinitis. Eleven infants were offered therapy and five were treated. Ten of 25 congenitally infected infants had audiology follow-up by 6 months with four abnormal. All infants were referred for early intervention.