Early Outcomes from the Utah’s Hearing Targeted Early CMV Screening

Stephanie Browning McVicar, AuD; Albert Park, MD
Nondisclosure:

• None of my grants relevant to this presentation

• Data on valganciclovir is for off label use and is not FDA approved
Case History (Before 2013):

- DD 19 mo with progressively hearing
- Failed newborn hearing screen
- Hearing testing @ 5 weeks of age indicated mild hearing loss
Case History (Before 2013):

- 19 mo left moderate hearing loss
- Saliva Cytomegalovirus (CMV) PCR- positive
- Neonatal Dry Blood Spot PCR- positive
- 6 week course of valganciclovir
- 20 mo bilateral profound hearing loss
- Bilateral Cochlear Implantation
- 4 ½ years old- struggling with speech and hearing
“New Current” Approach to Pediatric SNHL

History, physical examination, complete audiologic work-up

- Diagnosis apparent (syndrome, AD, trauma, meningitis)
  - Appropriate treatment

- Diagnosis uncertain (idiopathic)
  - CMV testing

  - Bilateral
    - GJB2 screen
      - Positive
        - Genetic counseling
      - Negative
        - Imaging
          - Preferential seating
          - Serial audiograms
          - Lab tests as indicated
          - ECG (if severe to profound SNHL)

  - Unilateral

- Imaging
  - FM, HA and/or CI
  - Preferential seating
  - Ophthalmology evaluation
  - Speech therapy
  - Audiology rehabilitation
The Role of Cytomegalovirus Evaluation in Pediatric Hearing Loss

SNHL Etiology Based on CMV, Imaging and Genetic Evaluation

Largest group with a known etiology 30%

N=83
CMV Testing Approach Prior 2013:

SNHL

History and Physical Examination, Audiologic Findings

Diagnosis Apparent

Idiopathic Diagnosis

CMV saliva or urine PCR assay

positive

Possible or Probable CMV induced SNHL (>3 weeks of age)

Definitive CMV induced SNHL

positive

Definitive CMV induced SNHL (<3 weeks of age)

DBS PCR CMV assay

negative

Possible or Probable CMV induced SNHL

Genetic testing, imaging, ophthalmology and EKG

positive

Genetic or inner ear dysplasia

negative

Idiopathic Diagnosis

Probable CMV induced SNHL

MRI brain AND temporal bone; serial audiologic testing

positive

Idiopathic Diagnosis

negative

Go to Idiopathic Diagnosis (asterisk)
CMV Testing Approach - NOW:

- Newborn Hearing Screen
  - Passed
  - Failed
    - CMV testing before 3 weeks of age
National Map for Hearing Targeted Early CMV Screening 2016:

CMV Legislation

From National CMV Foundation Website March 2016
Early Outcomes from Utah’s Hearing-Targeted Cytomegalovirus Screening Program

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Utah Early Hearing Detection and Intervention (EHDI)Director
Cytomegalovirus Public Health Initiative
Children’s Hearing Aid Program

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CMV Data Coordinator
Utah CMV Law
26-10-10 UCA, “Cytomegalovirus (CMV) Public Education and Testing”

• UDOH establish and conduct a public education program to inform pregnant women and women who may become pregnant about CMV (incidence, transmission, birth defects, diagnostic methods, preventative measures)

• Provide information to: child care providers, school nurses, health educators, health care providers, religious organizations offering children’s programs as part of worship services
Do U know about the risks of CYTOMEGALOVIRUS during pregnancy?

1 OF EVERY 5 children born with CYTOMEGALOVIRUS (CMV) will have PERMANENT DISABILITIES;

And yet,

MOST WOMEN ARE UNAWARE that CMV during pregnancy can harm their baby.

Know the Facts. Protect your baby.

Learn more at: HEALTH.UTAH.GOV/CMV
or FACEBOOK.COM/CMVUtah
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Utah CMV Law

26-10-10 UCA, “Cytomegalovirus (CMV) Public Education and Testing”

If a newborn infant fails the newborn hearing screening test(s)......

Medical Practitioner shall: Test the newborn infant for CMV before 21 days of age...unless the parent objects;

And provide to the parents information re: birth defects caused by congenital CMV and available methods of treatment.
26-10-10 UCA, “Cytomegalovirus (CMV) Public Education and Testing”

(continued)

**UDOH shall:**

- Provide information to the family and the medical practitioner (if known) information re: the testing requirements when providing results indicating that an infant has failed the newborn hearing screening test(s).
R398-4-3. Clarification of when a newborn fails a hearing screen.

The newborn **must fail both hearing screens**, the initial hearing screen routinely done at birth **and** the subsequent follow-up screen **or if/when the initial failed hearing screen is obtained after 14 days of age** before the medical practitioner is required to test for CMV.
Utah Newborn Hearing Screening

INPATIENT

Hospital 10-12 hrs.

Before Discharge 24 hrs.

OUTPATIENT

10-14 Days
R398-4-4. Special populations of newborns.

In special populations of newborns where newborn hearing screening(s) cannot be accomplished prior to 21 days of age,

testing for CMV is left to the discretion of the medical practitioner(s) caring for the newborn.

Special population of newborns may include, but not limited to, premature or medically fragile newborns or newborns receiving on-going medical care.
Percent of Eligible Infants Tested for CMV
3 Years of Testing since the Mandate

- July-Dec 2013: 36%
- Jan-June 2014: 56%
- July-Dec 2014: 51%
- Jan-June 2015: 55%
- July-Dec 2015: 69%
- Jan-June 2016: 70%
Performance Variability
Performance Variability

CMV Testing by Hospital

- # Eligible
- # Tested
**REQUIRED CMV LAB TESTING REPORT**

For infants failing newborn hearing screening

**TO:** ___________ Clinic: ___________ Fax: ___________

**FROM:** ___________ Facility ___________ Fax: ___________

1. **Date Faxed:** ___________ (completed by NBHS screener, faxed to PCP AND documented in Hi*Track)

The following infant, who lists you as their Primary Care Physician, has **FAILED** the INITIAL newborn hearing screen and will **REQUIRE** a follow-up hearing screen **no later than 14 days of age**. Please encourage the family to keep the following re-screening appointment.

**FAILING INITIAL hearing screening**

<table>
<thead>
<tr>
<th>Infant’s Name</th>
<th>D.O.B.</th>
<th>Mother’s Name</th>
<th>Contact#</th>
<th>Follow-up Appt.</th>
</tr>
</thead>
</table>

2. **Date Faxed:** ___________ (completed by NBHS screener, faxed to PCP AND documented in Hi*Track)

*The following infant has **FAILED** the FOLLOW-UP (2nd) hearing screen. **CONGENITAL CMV testing is required BEFORE THE INFANT IS 25 days of age** per Utah Cytomegalovirus (CMV) Testing Mandate.

**FAILING follow-up hearing screening**

**CMV LAB TESTING NEEDS TO BE ORDERED BY PHYSICIAN** (Saliva/Urine)

<table>
<thead>
<tr>
<th>Infant’s Name</th>
<th>D.O.B.</th>
<th>Mother’s Name</th>
<th>Contact#</th>
<th>Diagnostic Appt.</th>
</tr>
</thead>
</table>

The following infant has **PASSED** the FOLLOW-UP (2nd) hearing screening. No further action is necessary.

<table>
<thead>
<tr>
<th>Infant’s Name</th>
<th>D.O.B.</th>
<th>Mother’s Name</th>
<th>Contact#</th>
<th>Date Passed</th>
</tr>
</thead>
</table>

3. **Date Faxed:** ___________ (PHYSICIAN enter lab results below and fax to (801) 584-8492)

**CMV LAB TESTING RESULTS MUST BE ENTERED BELOW AND FAXED TO Utah Department of Health Early Hearing Detection and Intervention (EHDI) at (801) 584-8492 WITHIN 10 DAYS OF RECEIPT.**

<table>
<thead>
<tr>
<th>Infant’s Name</th>
<th>D.O.B.</th>
<th>Date of CMV Test</th>
<th>Urine (U) or Saliva (S)</th>
<th>RESULT: Detected (+) or Not Detected (-)</th>
<th>N/A: Family DECLINED*</th>
</tr>
</thead>
</table>

*If family declines CMV testing, please have family fill out and sign the CMV Testing Declination Form (available at health.utah.gov/CMV) and fax it with this form.
REQUIRED CMV LAB TESTING REPORT
For infants failing newborn hearing screening

To: ___________  Clinic ___________  Fax ___________
From: ___________  Facility ___________  Fax ___________

1. Date Faxed: (completed by NBHS screener, faxed to PCP AND documented in Hi*Track):

   The following infant, who lists you as their Primary Care Physician, has FAILED the INITIAL newborn hearing screening and will REQUIRE a follow-up hearing screen no later than 14 days of age. Please encourage the family to keep the following re-screening appointment.

   **FAILING INITIAL hearing screening**

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<tr>
<th>Infant's Name</th>
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<th>Mother's Name</th>
<th>Contact#</th>
<th>Follow-up Appt.</th>
</tr>
</thead>
</table>

2. Date Faxed: (completed by NBHS screener, faxed to PCP AND UDOD, documented in Hi*Track):

   The following infant has FAILED the FOLLOW-UP (2nd) hearing screen. CONGENITAL CMV testing is required BEFORE THE INFANT IS 21 days of age per Utah Cytomegalovirus (CMV) Testing Mandate.

   **FAILING follow-up hearing screening**

   **CMV LAB TESTING NEEDS TO BE ORDERED BY PHYSICIAN (Saliva/Urine)**

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<th>Infant's Name</th>
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<th>Mother's Name</th>
<th>Contact#</th>
<th>Diagnostic Appt.</th>
</tr>
</thead>
</table>

   The following infant has PASSED the FOLLOW-UP (2nd) hearing screening. No further action is necessary.

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<thead>
<tr>
<th>Infant's Name</th>
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3. Date Faxed: (PHYSICIAN enter lab results below and fax to (801) 584-8492)

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</table>

*If family declines CMV testing, please have family fill out and sign the CMV Testing Declination Form (available at health.utah.gov/CMV) and fax it with this form.
Urban A (Year 3: 7/1/15-6/30/16)

- 1st CMV Fax
- 2nd CMV Fax
- %CMV Tested

<table>
<thead>
<tr>
<th>Year</th>
<th>1st CMV Fax</th>
<th>2nd CMV Fax</th>
<th>%CMV Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>7/1/15-6/30/16</td>
<td>95%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>
You are receiving this information because one of the children in your care has met CMV testing criteria. Please add "CC: UDOH CMV (Fax: 801-584-8492)" to your LAB REQUEST.

UCA 26-10-10 Cytomegalovirus (CMV) Public Education and Testing Law

(3) If a newborn infant fails the newborn hearing screening test(s) under Subsection 26-10-6(1)(a) Newborn Hearing Screening Law, a medical practitioner shall:

(a) test the newborn infant for CMV before the newborn is 21 days of age, unless a parent of the newborn infant objects; and

(b) provide to the parents of the newborn infant information regarding:

(i) birth defects caused by congenital CMV; and

(ii) available methods of treatment.

R098-4.5, Reporting requirements

Medical practitioners are required to submit results of the CMV testing to UDOH for each newborn under their care who is referred for CMV testing within 10 days of receiving results. (Fax: 801-584-8492)

Important CMV PCR Testing Information

- Many laboratories currently offer PCR-based CMV testing. Testing should be performed only on SALIVA (via OraCollect 100 swab) or URINE. At present, ARUP Laboratories is the only local facility that has a validated test for saliva. Saliva samples should be collected at least 90-120 minutes after breastfeeding to prevent false positives, as CMV can be present in breast milk.

- Each primary care provider should submit specimens through their normal laboratory testing mechanism. If the laboratory service does not normally use ARUP as the referring laboratory and the saliva test is desired, please specify the testing location as ARUP, and include test name and test code listed below. All laboratories have the ability to forward specimens to ARUP through their channels.

- Many Utah laboratories have validated qualitative CMV PCR assay testing on urine, including: LabCorp, Quest, PAMI, IHC, and ARUP. Viracor-IBT Laboratories has quantitative only.

- Pricing will vary depending on the laboratory and the specific hospital contract. Primary care providers will need to consult their affiliated hospitals or reference laboratories to obtain pricing information.

- The CPT code for CMV detection (qualitative) by PCR is 87496, and is covered by Medicaid and other insurances.

- An appropriate ICD-10 code would be 1091.90 (neonatal hearing loss).

For additional help: Utah EHDI (801) 584-8215 or health.utah.gov/CMV or smcvear@utah.gov

Revised 11.09.2015
Number of CMV Tests by Specimen Type

- Urine: 55%
- Saliva: 39%
- Blood: 6%

Blood - 6%, Saliva - 39%, Urine - 55%
Number of CMV Tests by Specimen Type

- URINE: 55%
- SALIVA: 39%
- BLOOD: 6%

Blood - 6%  Saliva - 39%  Urine - 55%
LAB Collection and Testing For
CONGENITAL Cytomegalovirus for PARENTS

Your infant meets criteria for Utah mandated congenital CMV testing by either:
- not passing their (first) hearing screening at 14 days of age or older
- not passing BOTH their first hearing screening AND their second (re-)screening.

1. A test sample will need to be collected BEFORE your baby is 21 days old:

<table>
<thead>
<tr>
<th>Urine</th>
<th>Saliva*</th>
<th>Blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR</td>
<td>Acceptable</td>
<td>NOT</td>
</tr>
<tr>
<td>Acceptable</td>
<td>2 hours or more after feeding</td>
<td>OR</td>
</tr>
<tr>
<td>Acceptable</td>
<td>2 hours or more after feeding</td>
<td>NOT</td>
</tr>
<tr>
<td>Acceptable</td>
<td>2 hours or more after feeding</td>
<td>UNAcceptable</td>
</tr>
</tbody>
</table>

   Either of these samples may be taken at your provider’s office or at the lab
   Please call your baby’s doctor to find out where you should go.
   Take this sheet with you when you have the sample collected.

   If a saliva sample is taken, the inside of your baby’s cheek will be swabbed. This must be done
   120 minutes after their last feeding as CMV could be present in breast milk.

2. CMV Detection by PCR CPT code 87496 (qualitative - preferred) or CPT code 84797 (quantitative) should be conducted.

3. Results should be sent to your baby’s requesting physician AND to the
   Utah Dept. of Health CMV Fax: 801-584-8492

If you have any questions, please call the Utah Dept. of Health at (801) 584-8215

*The saliva must be collected using an ORAcollect-H00 kit available from ARUP supply 440255.
False Positives

- 7/13 to 6/14: 7
- 7/14 to 6/15: 1
- 7/15 to 6/16: 1
Protocols - IP and OP < 14 days

- Infants who did not complete IP and OP within 14 days of birth were 88% less likely to have CMV testing completed!*
Babies that failed their IP screen and then went on to have **2 or more OP screens** instead of the recommended one OP screen were **55-60% less likely** to have CMV testing completed.
Percent of Babies with CMV Testing Who Passed the Second OP Screen

- 15% (7/13 TO 12/14)
- 31% (1/15 TO 6/15)
- 33% (7/15 TO 12/15)
- 51% (1/16 TO 12/16)
Out-of-Hospital Births
Percent of Out of Hospitals Births Tested for CMV

- 7/13 TO 12/14: 3%
- 1/15 TO 6/15: 13%
- 7/15 TO 12/15: 0%
- 1/16 TO 6/16: 25%

% Tested for CMV
Out-of-Hospital Births

- A total of 5 out of 87 or 5.7% of out of hospitals births were tested for CMV (First 24 months)

- It was encouraging to note that the percent of out of hospitals births tested for CMV improved from 3% in the first 18 months after the mandate to 13.6% in the last 6 months.
DOB 7/1/2013 to 6/30/2015
The First Two Years....

Total Number of Births: 103,868
- Total “Eligible”: 840
  - Less “Special Populations”
    - (1st NBHS after 21 days): 136

Eligible = 704* (7 per 1000)

* + # of babies with “potential eligibility” = 242 - 38 x 10% = 20 children
DOB 7/1/2013 to 6/30/2015: The First Two Years

- 704 Eligible Babies
  - 3/77 Out-of-Hospital Births had CMV testing
  - 94/244 “2+ OP rescreens” had CMV testing

- If remove the above two groups =
  - CMV testing 50% ➔ 74%
Trends (Infants without CMV testing 1/1/15 - 6/30/15)

- 34% were not recommended for CMV testing after failing (1st) OP screen and were brought back for a second OP screen
- 18% had co-morbid condition of chronic otitis media with or w/o CL/P - under care of ENT (54% of > 90 day dx)
- 14% of parents did not follow-through with CMV testing
- 13% were homebirths
- 10% wrong PCP in HiTrack (fax sent to wrong MD)*
- 5% PCP didn’t feel CMV testing necessary
- 3% had first NBHS after 14 days
- 3% had other etiologies (LVA, cochlear malformations, family hx of HL)
313 Eligible Babies

- 4/22 Out-of-Hospital Births had CMV testing
- 71/106 “2+ OP rescreens” had CMV testing

If remove the above two groups = CMV testing 69.5% ➔ 82%
The following reasons for not having CMV testing done on 98 of the babies born from 7-1-15 to 6-30-16 are as follows:

- 30% had 2 OP screens with a pass on the second.
- 13.5% had comorbid condition of COM with or without cleft lip and palate and were often under the care of an ENT.
- 11.5% of the doctors did not complete testing (fax was sent but just filed in the chart and doctor never saw it, sent to ENT, waiting for the results of the 2nd OP or diagnostics.)
- 11% were homebirths.
- 8% of parents did not follow through with recommended test.
- 7% of babies whose first screen was after 14 days and failed were not referred for testing.
- 7% of the faxes were not received at the doctor’s office.
- 5.5% reasons for not testing could not be determined.
- 4.5% of parents declined testing.
DOB 7/1/2013 to 6/30/2015: The First Two Years....

Eligible Babies: 704

<table>
<thead>
<tr>
<th>Criteria</th>
<th># of Babies</th>
<th>CMV Testing</th>
<th>Not Tested</th>
</tr>
</thead>
<tbody>
<tr>
<td>IP Refer + OP Refer</td>
<td>351</td>
<td>230 (66%)</td>
<td>121</td>
</tr>
<tr>
<td>Refer &gt; 14 days</td>
<td>93</td>
<td>17 (18%)</td>
<td>76</td>
</tr>
<tr>
<td>IP Refer -&gt; Evaluation/HL</td>
<td>16</td>
<td>9 (56%)</td>
<td>7</td>
</tr>
<tr>
<td>IP Refer + 1st OP Refer</td>
<td>244</td>
<td>94 (39%)</td>
<td>150</td>
</tr>
<tr>
<td>TOTAL</td>
<td>704</td>
<td>350 (50%)</td>
<td></td>
</tr>
<tr>
<td>Eligibility Group</td>
<td>1st and 2nd Year</td>
<td>3rd Year</td>
<td>Comparison</td>
</tr>
<tr>
<td>----------------------------</td>
<td>------------------</td>
<td>----------</td>
<td>------------</td>
</tr>
<tr>
<td></td>
<td>Tested/Total Infants</td>
<td>% Tested</td>
<td>Tested/Total Infants</td>
</tr>
<tr>
<td>IP Refer and OP Refer</td>
<td>230/351</td>
<td>66%</td>
<td>122/163</td>
</tr>
<tr>
<td>Refer &gt; 14 Days</td>
<td>17/93</td>
<td>18%</td>
<td>8/26</td>
</tr>
<tr>
<td>IP Refer à Eval.</td>
<td>9/16</td>
<td>56%</td>
<td>11/18</td>
</tr>
<tr>
<td>IP Refer and 1st OP Refer</td>
<td>94/244</td>
<td>39%</td>
<td>71/106</td>
</tr>
</tbody>
</table>
Percent of babies tested for CMV by 21 days has increased over time from 74.5% (234/314) in the first 2 years to 80% (78/98) in the first 6 months of the third year and 84% (97/116) in the last 6 months of the third year.
<table>
<thead>
<tr>
<th>Infants 7/1/2013-6/30/16</th>
<th>Identified by Mandate n=19</th>
<th>Symptomatic* n=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Hearing</td>
<td>47%</td>
<td>80%</td>
</tr>
<tr>
<td>Hearing Loss</td>
<td>53%</td>
<td>20%</td>
</tr>
<tr>
<td>Laterality</td>
<td>Unilateral - 60%</td>
<td>Unilateral - 0%</td>
</tr>
<tr>
<td></td>
<td>R- 50% L- 50%</td>
<td>Bilateral - 100%</td>
</tr>
<tr>
<td></td>
<td>Bilateral - 40%</td>
<td></td>
</tr>
<tr>
<td>Type</td>
<td>SNHL - 80%</td>
<td>SNHL - 50%</td>
</tr>
<tr>
<td></td>
<td>CHL -10%</td>
<td>Mixed - 50%</td>
</tr>
<tr>
<td></td>
<td>Mixed -10%</td>
<td></td>
</tr>
<tr>
<td>Degree by Ear</td>
<td>Mild-Moderate 21%</td>
<td>Mild-Moderate - 25%</td>
</tr>
<tr>
<td></td>
<td>Moderate-Severe - 29%</td>
<td>Moderate-Severe- 75%</td>
</tr>
<tr>
<td></td>
<td>Severe-Profound - 50%</td>
<td></td>
</tr>
</tbody>
</table>
Completion of Diagnostics <90 Days
Before and After the Mandate

- Before the Mandate (2 years prior to the Mandate):
  - 56.00%
  - 7/1/11 - 6/30/13

- After the Mandate (24 months after the Mandate):
  - 77%
  - 7/1/13 - 6/30/15

DX by 90 days/all babies who needed DX
Completion of Diagnostics <90 Days
7/1/13 – 6/30/15

- Did not undergo CMV testing: 61.50%
- Did have CMV testing completed: 87%

DX by 90 Days/All Babies Who Needed DX
In the first two years of CMV testing 85% of the babies with SNHL were tested for CMV.

Diagnostic Test Results and CMV Testing for the Third Year

<table>
<thead>
<tr>
<th>Results of Dx Eval</th>
<th>Number</th>
<th># Tested for CMV</th>
<th>% Tested for CMV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neural</td>
<td>1</td>
<td>1</td>
<td>100%</td>
</tr>
<tr>
<td>SNHL</td>
<td>47</td>
<td>42</td>
<td>89%</td>
</tr>
<tr>
<td>Mixed</td>
<td>8</td>
<td>10</td>
<td>80%</td>
</tr>
<tr>
<td>Conductive</td>
<td>65</td>
<td>51</td>
<td>78%</td>
</tr>
<tr>
<td>Normal Hearing</td>
<td>73</td>
<td>56</td>
<td>77%</td>
</tr>
<tr>
<td>Undetermined</td>
<td>15</td>
<td>11</td>
<td>73%</td>
</tr>
<tr>
<td>Eval. In Process</td>
<td>27</td>
<td>18</td>
<td>67%</td>
</tr>
<tr>
<td>Declined</td>
<td>2</td>
<td>1</td>
<td>50%</td>
</tr>
</tbody>
</table>
Percent of CMV Testing for excluded NICU Babies

31% 40% 42% 50%

7/13 TO 12/14 1/15 TO 6/15 7/15 TO 12/15 1/16 TO 6/16
CASE PRESENTATION

- Full-term WBN
- Healthy pregnancy and delivery and post
- No risk factors
- Only abnormality was failed NBHS
- CMV testing criteria met and done - +cCMV
- 1 month: ID consult - HUS -> imaging ordered
- ABR: No responses bilaterally
- ENT consult with Dr. Park
- MRI: abnormal white matter signal intensity with cysts and periatral anterior temporal lobe white matter
- ID: VGC x 6 mos
- 6 mos: CI evaluation
- Neuro: Rolling, sitting, transfer objects, no seizures, normal kidney and liver function
Three Years

- 155,769 live births
- 1188 eligible - 171 special populations = 1017 CMV testing eligible
- 663 infants tested = 65%
- 12/1017 parents declined = 1%
- 19/663 positive = 3%
Number of cCMV Babies Identified by the Mandate

- July-Dec 2013: 5 babies
- Jan-June 2014: 3 babies
- July-Dec 2014: 8 babies
- Jan-June 2015: 1 baby
- July-Dec 2015: 1 baby
- Jan-June 2016: 1 baby
Study Design:

Asymptomatic cCMV Hearing Impaired Infants Randomized to Valganciclovir and No Treatment

- **Screening**
  - Key Inclusion Criteria:
    - CMV positive hearing impaired infants

- **Randomization**
  - Arm 1: VGC
  - Arm 2: Untreated Controls

- **Aim 1:**
  - Primary Endpoint (hearing)
  - 6 mo after VGC started

- **Aim 2:**
  - Primary Endpoint (safety)
  - 12 mo of age
Increasing the Detection Rate of the Symptomatic CMV Infected Infant:

- 10% fetal demise
- Prematurity
- Common features:
  - Hepatomegaly
  - Splenomegaly
  - Petechiae
  - Jaundice
  - Microcephaly
  - Chorioretinitis
  - Sensorineural hearing loss (50%)
Increasing the Detection Rate of the Symptomatic CMV Infected Infant:

• Minority symptomatic CMV cases diagnosed clinically!
• Vaudry et al., 2014; Townsend et al., 2011; McMullan et al. 2011
• <10% (Sorichetti et al. 2015)
6 Weeks vs. 6 Months Valganciclovir Hearing Outcomes @ Two year Followup

Kimberlin et al. NEJM 2015
### 6 Weeks vs. 6 Months Valganciclovir Bayley III Outcomes 24 mo.

<table>
<thead>
<tr>
<th></th>
<th>6 Week Therapy</th>
<th>6 Month Therapy</th>
<th>Adjusted P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive Composite</td>
<td>76.0±2.6</td>
<td>84.4±2.6</td>
<td>0.0236</td>
</tr>
<tr>
<td>Language Composite</td>
<td>72.5±2.9</td>
<td>84.6±2.9</td>
<td><strong>0.0037</strong></td>
</tr>
<tr>
<td>Receptive Communication Scale</td>
<td>5.2±0.5</td>
<td>7.3±0.5</td>
<td><strong>0.0027</strong></td>
</tr>
<tr>
<td>Expressive Communication Scale</td>
<td>5.5±0.5</td>
<td>7.3±0.5</td>
<td>0.0158</td>
</tr>
<tr>
<td>Motor Composite</td>
<td>74.1±3.2</td>
<td>85.5±3.3</td>
<td>0.0130</td>
</tr>
<tr>
<td>Fine Motor Scale</td>
<td>6.4±0.6</td>
<td>8.0±0.6</td>
<td>0.0566</td>
</tr>
<tr>
<td>Gross Motor Scale</td>
<td>5.3±0.5</td>
<td>7.0±0.5</td>
<td>0.0198</td>
</tr>
</tbody>
</table>

P-values < 0.0071 (=0.05/7) considered statistically significant using Bonferroni adjustment for multiple testing.
Utah NICU Targeted Approach:

- Abnormal head size (microcephaly [<10th %ile] OR macrocephaly [>90th %ile]) at birth
- Intrauterine growth restriction (weight <10th %ile for gestational age) at birth
- Hydrops
- Intracranial OR intraabdominal calcifications on first imaging exam
- Hepatomegaly OR splenomegaly (>1 cm below the right or left costal margin) in first 72 hours
- AST or ALT >100 U/L OR direct bilirubin >1.0 mg/dL in first 72 hours
- Petechiae at any time OR thrombocytopenia (<100,000/mm³) on ≥2 occasions in first 72 hours
- ‘Blueberry muffin’ appearance
- Neuronal migration disorders (e.g., polymicrogyria, lissencephaly, pachygyria, schizencephaly) on first imaging exam
- Unexplained brain lesions or neurologic findings
Utah NICU Targeted Approach:

• All NICUs in IHC/UU
• Urine PCR within first 3 weeks of life
• Positive CMV- peds ID, assessment for other signs CMV, ENT, ophthalmology
• One set of twins diagnosed within 1 week of implementation
Conclusion:

• Hopefully we will have an answer in about 5 years role VGC for asymptomatic CMV infected hearing impaired infants
• If there is a role, this result will drive the need for early CMV screening
• Targeted NICU screening- next step