

MCN for Neonatology

West of Scotland

Neonatal Guideline



Cytomegalovirus (CMV) - Congenital infection

Introduction

Congenital CMV is the leading non-genetic cause of sensorineural hearing loss. Worldwide, the birth prevalence of CMV is estimated at 7 per 1000 births. Approximately 10% of infected newborns are symptomatic at birth and of those around half will have significant impairment in their neurodevelopment. Of infants who are asymptomatic at birth approximately 15% go on to have long term sequelae including sensorineural hearing loss in childhood.

Vertical transmission of CMV infection can be intrauterine, intrapartum, and postnatal. Intrauterine transmission is the most important route as it may result in major neurological sequelae. Symptoms of congenital CMV can range from mild transient symptoms to severe multi system dysfunction and death.

There is currently no universal screening program for CMV.

There is now sufficient evidence to recommend treatment of infants with symptomatic congenital CMV who have evidence of neurological involvement, as this may improve outcomes for hearing and neurodevelopment. The evidence is based on a course of IV ganciclovir or oral valganciclovir commencing within the first 4 weeks of life and it is therefore important to make an early diagnosis where possible.

Recent research suggests that the best outcomes result from a 6 month course of treatment when compared with earlier regimens which used a shorter course of 6 weeks. These guidelines have been updated to reflect the recent European consensus statement.

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1. Clinical assessment

CMV infection should be considered if there is:

- Blueberry muffin rash
- Petechiae or purpura
- Hepato or splenomegaly
- Prolonged jaundice or conjugated hyperbilirubinaemia
- Chorioretinitis
- Congenital cataracts
- Symmetrical IUGR (birth weight <-2SD for gestational age)
- Microcephaly (head circumference <-2SD for gestational age)
- Colitis or atypical necrotising enterocolitis
- Pneumonitis
- Sepsis like syndrome, especially if non-responsive to antibiotics
- Evidence of maternal infection in pregnancy
- Antenatally diagnosed ventriculomegaly/intracranial calcification
- Postnatally identified intracranial calcification (generally periventricular), or unexplained ventriculomegaly or other imaging consistent with CMV
- Seizures
- Maternal history of suspected CMV

It has been proposed that screening for CMV should be offered where a neonate does not receive a "pass" on their newborn hearing screen since formal audiology may not confirm hearing impairment in the appropriate timescale to benefit from valganciclovir therapy.

Such screening is under discussion with the Universal Neonatal Hearing Screening (UNHS) committee but is not current policy.

Laboratory tests may show:

- Thrombocytopenia
- Conjugated hyperbilirubinaemia
- Elevated hepatic transaminases

2. Diagnosis

The diagnosis of congenital infection is made by PCR testing of body fluids in the first 3 weeks of life but ideally within the first 2 weeks (Table 1). Urine and saliva have a high sensitivity and specificity and are the diagnostic gold standards. Blood PCR has a lower sensitivity and is more useful for monitoring disease activity.

Both urine and salivary swabs should be tested by PCR where CMV is suspected.

If CMV infection is diagnosed after 3 weeks of age it may be unclear whether the infection is congenital. It may be possible to clarify when the infection occurred by testing a bloodspot stored by the neonatal screening laboratory. This would require parental consent (*Appendix 1*). The sensitivity for bloodspot testing is variable and false negatives can occur.

Treatment may still be considered in infants with evidence of CNS involvement or who have severe focal organ disease, in whom the timing of infection is uncertain but this should be discussed with the paediatric infectious disease team.

Table 1 Diagnostic tests

Test	Information
CMV PCR in Urine	Can be a bag sample or obtained through cotton wool in the nappy
CMV PCR saliva swab	This should be taken at least 1 hour after breastfeeding. There are no restrictions in formula fed babies.
CMV PCR on dried blood spot specimen	This is used for diagnosis of congenital CMV if the infection is diagnosed initially after 3 weeks of age. NB. False negatives can occur.

3. Investigations

Blood tests

- FBC
- LFTs including conjugated bilirubin
- Coagulation - if evidence of hepatitis or hepatomegaly
- U&Es
- CMV viral load (0.5ml EDTA to virology)

In cases where there is uncertainty regarding the need for treatment and where there is involvement of an infectious disease specialist it may be helpful to arrange for maternal booking bloods to be checked for CMV IgM and IgG with avidity. A positive IGM and low IgG avidity indicates primary infection. First trimester maternal infection is associated with a higher risk of symptomatic infection and neurological sequelae. This information may be beneficial when counselling parents.

Lumbar puncture is no longer a first line investigation, however in a small minority of cases it may aid treatment decisions. In cases where there is uncertainty advice should be sought from a paediatric infectious diseases specialist (ID).

Neuroimaging

Congenital CMV can manifest with intracranial calcification, periventricular cyst, subependymal pseudocyst, germinolytic cysts, white matter abnormalities, cortical atrophy, migration disorders, cerebellar hypoplasia and/or lenticulostriate vasculopathy. A cranial ultrasound should be performed looking for intracranial abnormalities in all infants with confirmed congenital CMV. MRI should subsequently be performed in all symptomatic infants and in asymptomatic infants with any intracerebral abnormalities detected on cranial ultrasound.

Ophthalmological assessment

Ophthalmological assessment should be performed in all infants with congenital CMV at the time of diagnosis. Retinal scarring, strabismus, chorioretinitis, optic atrophy, cataracts and cortical visual loss may be seen in symptomatic infants.

Audiological assessment

A baseline audiological assessment should be performed on all infants with congenital CMV. Hearing loss can be progressive or late onset so ongoing screening is required as outlined in the follow up section.

4. Who should we treat?

Severe symptomatic CMV:

- central nervous system involvement (abnormal neurological or ophthalmological examination), microcephaly, evidence of CMV on neuroimaging such as periventricular calcification*, isolated sensorineural hearing loss (SNHL)**

**If there are abnormalities on neuroimaging which are of uncertain association with cCMV, further discussion should be had with ID and radiology*

***the treatment of isolated SNHL is controversial and has not been evaluated in RCTs*

Treatment would usually be offered to infants of >32 weeks gestation and >1800g birthweight presenting in the first 30 days of life and only after a risk versus benefit discussion with the family.

Treatment should also be considered in:

- Acutely unwell infants with evidence of severe single organ disease or multisystem involvement (significant hepatitis with marked hepatosplenomegaly, marked bone marrow suppression, pneumonitis, colitis)

The evidence is limited for use in this group and duration of treatment should be discussed with an infectious disease specialist

Moderate CMV is defined as babies with persistent abnormal liver function or haematological abnormalities (>2 weeks duration) or more than 2 signs or symptoms associated with "mild" disease such as petechiae, mild hepatomegaly or splenomegaly, small for gestational age without microcephaly and transient transaminitis or haematological abnormalities. There is no consensus on the treatment of these babies and they should be considered on a case by case basis after discussion with an infectious disease specialist. Parents should be made aware of the limited evidence and the potential risks of treatment.

The Kimberlin trial, from which the evidence of treatment is based, treated children with symptomatic congenital CMV with and without CNS involvement (Kimberlin *et al.* 2015). The beneficial effects of antiviral therapy in terms of long term hearing function were more marked in children with baseline CNS involvement although the number recruited with mild congenital CMV was very small.

Treatment should not be offered to babies with asymptomatic CMV or mild disease (1 or 2 transient or clinically insignificant signs or symptoms)

Post natal infection, pCMV, does not normally cause significant problems in term infants but may do so in extremely preterm infants. Opinion suggests treatment should be considered in infants with severe symptoms (see section on postnatal CMV in extremely preterm infants) in discussion with the paediatric infectious disease team prior to commencement for an individualised treatment plan.

5. Treatment

Oral valganciclovir is first line treatment and IV ganciclovir should only be used if oral medication is not tolerated or if there is severe disease and absorption is uncertain

5 a) Acutely unwell infants with severe focal or multisystem disease

Ganciclovir 6mg/kg twice daily by intravenous infusion (central line)

Change to oral valganciclovir 16mg/kg twice daily (unless renal impairment) when the infant is on approximately 50% enteral feeds.

Patients on oral valganciclovir have fewer side effects (neutropenia) than patients on ganciclovir and this switch will obviate the need to maintain central venous access

Course Duration: 6 months

5 b) Well infants with evidence of CNS involvement

Valganciclovir 16mg/kg/dose twice daily by mouth (unless renal impairment)

OR

Ganciclovir 6mg/kg twice daily by intravenous infusion via central line (if nil by mouth) changing to valganciclovir when the infant is on approximately 50% enteral feeds.

Course Duration: 6 months

6. Treatment monitoring

Side effects of either preparation include bone marrow suppression – including neutropenia, thrombocytopenia, hepatotoxicity and anaemia. Neutropenia is the most important and most frequent side effect and may require reduction or cessation of therapy. It is usually reversible with reduction or brief cessation of therapy and is most common in the first 6 weeks of treatment. It is more prevalent in IV therapy (65% v 21%). Note that neutropenia also occurs in congenital CMV without treatment.

Hepatic involvement is more common after the fourth month but is usually mild and reversible on stopping therapy. Renal impairment may also be seen but is rare and reversible on stopping therapy.

Animal studies show reversible testicular damage and reduced sperm viability and there may be carcinogenic effects. These effects have not been shown in human studies but long term follow up data is lacking.

Oral treatment is generally well tolerated

The timings of treatment monitoring are different for the 2 groups of patients and depend on whether treatment is oral or IV.

Managing acutely unwell infants with multisystem involvement

For this group of patients it is important to achieve maximal suppression of viral load to control the clinical symptoms. This will require regular monitoring of viral load and may require adjustment of the dose of ganciclovir, or adjunctive therapy, if this goal is not achieved. This group will also be more vulnerable to the potential side effects as outlined above.

Monitoring

- FBC, U+E, and LFTs - 2-3 x /week for 3 weeks and at least once per week thereafter for the duration the baby is on ganciclovir. Once converted to valganciclovir follow well child monitoring.
- CMV viral load (0.5ml EDTA) – Day 3, then weekly through the course of treatment for the first 6 weeks then monthly (*this will depend on how unwell the child is and how important it is to maximally suppress*)
- Therapeutic drug monitoring is only required in the following circumstances
 - Failure of fall in viral load by 1-2 logs
 - Suspicion of toxicity
 - Abnormal renal function

It should also be considered in premature infants

Trough levels should be taken 1hr prior to administration. Peak levels should be taken 1 hr after the dose. Levels require 0.5 ml in Serum Gel or Plain Clotted tube. Results can take up to 1 week.

Action:

Neutropenia $<0.5 \times 10^9/L$ – Stop ganciclovir until recovery to $>0.75 \times 10^9/L$. Drug is then resumed at normal level. Repeat WCC at 3 days and 7 days and if level falls below 0.75 within 1 week reduce drug dose by 50% and continue.

Consider the use of granulocyte colony- stimulating factor in cases of persistent neutropenia.

Thrombocytopenia $<50 \times 10^9/L$ - Stop ganciclovir until recovery to $>50 \times 10^9/L$ and restart dose at previous level. If platelets were less than 10×10^9 at diagnosis, hold dose if level falls by 50%. Recheck FBC at 3 and 7 days.

Acute Hepatitis – This may be due to the disease itself or due to the ganciclovir therapy. Decisions about ongoing treatment will need to be made clinically (advice may be sought from the consultant in Virology or Infectious Diseases). In the Kimberlin study the treatment was stopped if the ALT rose to 10x the baseline level and only restarted when ALT fell to $< 5x$ the baseline level

Renal impairment - If there is evidence of worsening renal function (oliguria or rising serum creatinine) then the ganciclovir dose may require to be decreased as it is renally excreted. Therapeutic drug monitoring should be undertaken and dose adjusted according to levels. (Seek advice from pharmacy)

Failure of response to treatment– Blood CMV viral loads usually drop at least 1 and 2 logs during treatment. If no drop in viral load is seen with ganciclovir treatment, or if severe symptomatology persists, therapeutic drug monitoring should be undertaken as the drug dosage may need to be adjusted or an alternative treatment sought. In this instance there should be a discussion with both a consultant virologist and hospital pharmacist. There should be consideration of resistance testing. (see notes) Options may include

- Optimisation of serum ganciclovir levels Trough – 0.5 – 1.0 mg/L. Peak – 7-9 mg/L
- Viral Sensitivity Studies
- Adjunctive therapy with CMV specific Immunoglobulin

Managing well infant with CNS involvement but no systemic disease

As these infants are not systemically unwell the goal of treatment is not to completely suppress viral replication but rather to reduce the viral load during the period of treatment. It is therefore possible to complete their therapy as outpatients and less monitoring is required.

Monitoring

If the child is on IV ganciclovir follow monitoring schedule for unwell child.

- FBC, LFTs and U&E weekly for the first 4 weeks and then monthly until end of treatment
- Viral load fortnightly for 4 weeks and then monthly
- Weight and review of dosage at time of blood sampling

If viral loads are increasing check for compliance and then consider resistance testing. If the child is difficult to bleed the priority should be FBC followed by biochemistry followed by viral loads.

Drug levels are not required for valganciclovir

Actions

Neutropenia $<0.5 \times 10^9/L$ – Stop valganciclovir until recovery to $>0.75 \times 10^9/L$. Drug is then resumed at normal level. Repeat levels at 3 days and 7 days and if level falls below 0.75 within 1 week reduce drug dose by 50% and continue.

Thrombocytopenia $<50 \times 10^9/L$ – Stop valganciclovir until recovery to $>50 \times 10^9/L$ and restart dose at previous level. If platelets were less than 10×10^9 at diagnosis hold dose if level falls by 50%. Repeat FBC at 3 and 7 days.

Acute Hepatitis – This may be due to the disease itself or due to the therapy. Decisions about ongoing treatment will need to be made clinically (advice may be sought from the consultant in Virology or Infectious Diseases). In the Kimberlin study the treatment was stopped if the ALT rose to 10x the baseline level and only restarted when ALT fell to $< 5x$ the baseline level

Renal Impairment – If there is evidence of worsening renal function (oliguria or rising serum creatinine) then the valganciclovir dose may require adjustment. Consider reducing to once daily dosing until renal function improves. In severe renal impairment the drug should be stopped. For further advice on dosage adjustment in renal impairment refer to monograph.

Viral Load – The aim with this group of patients is to reduce the viral load by 1-2 logs. Dose adjustments are not required to achieve further suppression if this goal is achieved. If no response is seen advice should be sought from the consultant Virologist or Infectious Disease specialist

Notes

As the drugs are renally excreted drug levels often fall during therapy due to newborn renal maturation increasing drug clearance. This is a problem with ganciclovir rather than valganciclovir as oral bioavailability increases in early infancy which “compensates” for increased drug clearance therefore making valganciclovir a more stable method of treatment.

Resistance due to gene mutations can occur in CMV. Treatment failure and the emergence of some resistant mutations have been associated with the use of valganciclovir and ganciclovir. If persistent high levels of viraemia are seen, advice should be sought from a consultant virologist to consider performing resistance assays for common gene mutations, and alternative treatment.

Managing postnatally acquired (pCMV) in extremely premature infants

Systematic reviews report that symptomatic pCMV occurs in 0% to 34% (median 3.7%) and severe sepsis like syndrome (SLS) occurs in 0% to 13.8% (median 0.7%) of babies < 32 weeks who are infected postnatally with CMV). Of note a small study limited to babies of 22-24 weeks gestation showed a 65% rate of acquisition of CMV in these most immature infants.

Maternal Breast milk is the usual source of infection in pCMV. Whilst limited CMV is found in colostrum, CMV DNA is found in maternal breast milk with peak concentrations at 4-8 weeks of lactation before falling in swiftly in concentration.

No recommendation to pasteurise milk in this scenario or for this group of babies in general, given the well-recognised benefits of non-pasteurisation.

When to consider pCMV

Demographic of premature infants most at risk of pCMV

- <32 weeks
- <1500grammes
- Receiving maternal breast milk (mothers seropositive CMV)
- 4-6 weeks of age

Clinical Features/laboratory markers to support a diagnosis of pCMV in this group of babies

- Sepsis like Syndrome with negative blood cultures and marginally persistently raised CRP despite antibiotic therapy
- Worsening respiratory status/pneumonitis on CXR/lung USS
- Evidence of marrow suppression specifically fall in platelets
- Developing neutropenia (particularly < 0.5/mm³)
- Deterioration in LFTs with raised transaminases
- Colitis /NEC concerns without pathogenic X-ray findings of NEC

How to investigate for pCMV.

It is vital to include appropriate clinical details when postnatal CMV is being considered. Ensure that '*possible postnatal CMV pneumonitis in unwell ventilated neonate*' or '*possible disseminated postnatal CMV in sick premature infant*' is included in the clinical details of *all* samples requested. Without this clinical information samples may be rejected by the virology laboratory. Please email the virology laboratory (west.ssvc2@nhs.scot) to alert them when samples are coming.

- CMV PRC from saliva swab/Urine as above
- Blood for viral load (0.5ml EDTA)
- +/- Blind Broncho-alveolar lavage (BAL) to support evidence of pneumonitis
- CXR/AXR
- Distinguishing from congenital CMV after 21 days of life is crucial in making diagnosis of pCMV
- Testing dried blood spot (see appendix requires parental consent and specialised analysis in Edinburgh). Clarify and ensure DBS being sent is one obtained during first week of life. The result can take several weeks.

How to treat

Involve ID colleagues at the earliest opportunity .The indication for treatment in symptomatic pCMV is to suppress active viraemia and prevent destructive end-organ disease rather than to alter the course of a chronic infection

Full parental discussion, as there have been no RCTs of treatment in pCMV, case reports/case series to date only

Side effects of treatment /long term (section below)

Anti-viral treatment

Ganciclovir IV via central access if unable to tolerate feeds 6mg/kg twice daily

Then

Valganciclovir 16mg/kg twice daily if/when able to tolerate feeds, transition when on >50% enteral feeds and tolerating

No requirement for drug level monitoring

Monitoring

At least weekly FBC and differential

- pause if neutrophils < 0.5 until >0.75
- There may be a role for GSCF in cases where there is deemed a balance of benefit to continue treatment for severe symptomatic disease in presence of neutropenia as a consequence of treatment. Needs individual discussion with ID and Pharmacy colleagues to balance risk benefit.
- At least weekly LFTs
- Weekly viral loads

Length of Treatment

- Treatment in two weekly blocks
- Informed by weekly viral loads (perform start of each working week to enable management planning)
- Continue with further two weeks of treatment if viral load remains detectable
- Case reports suggest 4-8 weeks of treatment required
- Full viral load suppression leads to resolution of symptoms
- Inability to suppress viral load after 8 weeks treatment needs discussion with ID colleagues and consideration of immunodeficiency

Follow Up

- Consensus from multiple population based cohort studies that no association between pCMV and sensorineural hearing loss. Ensure routine audiology checks pre discharge from neonatal care.
- Neurodevelopment FU- already standard in this group of high risk infants
- Ensure term corrected cranial USS, low threshold for additional MRI at term
- Ensure ophthalmological examination has taken place specifically for retinitis in addition to routine ROP screening

7. Counselling of parents

There is evidence that anti-viral treatment is beneficial in improving, preventing deterioration or maintaining hearing in some cases of congenital CMV. The benefits however are moderate and the drug is unlicensed and requires significant monitoring. A full discussion should be had with parents prior to commencing treatment regarding the risks and benefits including unknown risks of carcinogenic effect and reduced fertility. There is a lack of long term follow up information and parents should be made aware of this. Documented written consent (*Appendix 2*) should be obtained from the parents and each child should have a written treatment plan (*Appendix 3*). The greatest evidence currently is for 6 months of treatment in CNS disease however should parents wish to consider a shorter treatment length (e.g. 6 weeks) this should be discussed and documented. Parents must be aware that 6 weeks of treatment is associated with non maintenance of effects.

8. Infection control

Standard precautions of using gloves and apron when examining, caring or handling body fluids should be undertaken for any infant with congenital CMV. Infection control should be contacted if more advice is required.

9. Follow up

General practitioners should be contacted prior to discharge to be informed of the diagnosis and treatment plan. A copy of the treatment plan should be sent with the discharge letter. The discharging team should check that the GP is happy to continue to prescribe valganciclovir for six months.

All infants (regardless of treatment and including asymptomatic children) should be referred to audiology for follow up hearing surveillance. They should be seen every 3-6 months for the first year, then every 6 months until 3 years of age and then yearly until 6 years old.

All infants, regardless of treatment, require long term neurodevelopmental follow up with an initial assessment at 6 months of age. Follow up should be for a minimum of two years. Infants with hearing impairment or other neurodevelopmental impairment should be referred to community child development services.

Initial ophthalmology assessment is required at diagnosis to evaluate the presence of retinal scarring. Asymptomatic newborns do not require further examinations. However, symptomatic newborns should have annual ophthalmology assessment until the age of 5 years to detect the presence of delayed or progressive chorioretinitis.

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Consent form for the retrieval and use of the residual dried bloodspot specimen

Please fill in the details below as discussed with your clinician/healthcare professional;

CHILD'S NAME

CHILD'S CHI NUMBER IF KNOWN.....

CHILD'S DATE OF BIRTH.....

CHILD'S PLACE OF BIRTH.....

MOTHER'S NAME WHEN CHILD WAS BORN

MOTHER'S DATE OF BIRTH.....

HOME ADDRESS WHEN CHILD WAS BORN

.....

.....

I/we give permission for you to release the blood spot specimen from the above child for laboratory

investigations for

.....

NAME OF PARENT(S).....

PARENTAL SIGNATURE(S).....

DATE SIGNED.....

Appendix 2

Consent Form for treatment of valganciclovir or ganciclovir for congenital CMV

Child's Name:

CHI number:

Consultant Neonatologist:

Date:

I understand my child has been diagnosed with congenital cytomegalovirus and I wish them to receive ganciclovir/valganciclovir treatment for this.

I have received and read the parent information leaflet congenital CMV treatment

I understand the course of treatment is 6 months and requires regular blood tests and outpatient appointments as per my child's treatment plan.

I have received a copy of the treatment plan for my child

I understand the risks associated with treatment including potential long term risk as detailed in the parental information leaflet.

Name of doctor responsible for discussion with parents

Signature

Date

Name of parent out guardian

Signature

Date

Appendix 3

Treatment plan for valganciclovir

Name of Infant

CHI number

Responsible consultant

Congenital CMV infection confirmed

Urine date..... Saliva swab date

Newborn blood spot specimen (if applicable) date

Pre-treatment investigations completed

Investigation	Result
Full blood count	
U&Es	
Liver function	
Coagulation	
Viral load	
Ophthalmological assessment	
Hearing assessment	

Parental discussion by consultant completed

Parental information leaflet given

Consent form signed

Date of start of treatment

Date of end of treatment

First outpatient appointment given

GP contacted

Monitoring

Schedule	Date completed	Test	Results actioned	Weight	Dose adjustment
Week 1		FBC, UEs, LFTs			
Week 2		FBC, UEs, LFTs. Viral load			
Week 3		FBC, UEs, LFTs			
Week 4		FBC, UEs, LFTs, Viral Load			
Week 8		FBC, UEs, LFTs. Viral load			
Week 12		FBC, UEs, LFTs. Viral load			
Week 16 (month 4)		FBC, UEs, LFTs. Viral load			
Week 20 (month 5)		FBC, UEs, LFTs. Viral load			
Week 24 (month 6)		FBC, UEs, LFTs			N/A
Week 28 (month 7)		FBC, UEs, LFTs			N/A

Follow up

Outpatient appointment arranged

GP contacted and ongoing prescription arrangements made

MRI scan arranged

Audiology referral

Ophthalmology referral

Developmental clinic referral

Treatment plan for ganciclovir

Name of Infant

CHI number

Responsible consultant

Congenital CMV infection confirmed

Urine date..... Saliva swab date

Newborn blood spot specimen (if applicable) date

Pre-treatment investigations completed

Investigation	Result
Full blood count	
U&Es	
Liver function	
Coagulation	
Viral load	
Ophthalmological assessment	
Hearing assessment	

Parental discussion by consultant completed

Parental information leaflet given

Consent form signed

Date of start of treatment

Date of end of treatment

Reason for ganciclovir treatment

Monitoring

Treatment should be switched to valganciclovir when clinical improvement noted and oral medication tolerated. Monitoring schedule of valganciclovir should then be used for the remaining treatment.

Schedule	Date completed	Tests	Results actioned
Day 3		FBC, UE , LFT, viral load, ganciclovir levels	
Day 6		FBC, UE, LFTs.	
Day 10		FBC, UE , LFT, viral load, ganciclovir levels	
Day 13		FBC, UE, LFTs	
Day 17		FBC, UE , LFT, viral load, ganciclovir levels	
Day 20 (end of week 3)		FBC, UE, LFTs	
Week 4		FBC, UE , LFT, viral load, ganciclovir levels	
Week 5		FBC, UE , LFT, viral load, ganciclovir levels	
Week 6		FBC, UE , LFT, viral load, ganciclovir levels	

By week 6 most infants should be able to be converted to valganciclovir to complete 6 months of treatment. If the infant is not able to be converted to valganciclovir at this stage seek further advice from consultant virologist and paediatric infectious diseases team.

Date of conversion to valganciclovir

Follow up

Outpatient appointment arranged

GP contacted

MRI scan arranged

Audiology referral

Ophthalmology referral

Developmental clinic referral