CMV (CYTOMEGALOVIRUS INFECTION)
Supporting information

This guideline has been prepared with reference to the following:

Luck SE, Wieringa JW, Blázquez-Gamero D et al. Congenital Cytomegalovirus: A European Expert Consensus Statement on Diagnosis and Management. Pediatr Infect Dis J. 2017;36:1205-13

Shah T, Luck S, Sharland M et al. Fifteen-minute consultation: diagnosis and management of congenital CMV. Arch Dis Child Educ Pract Ed. 2016;101:232-5

http://ep.bmj.com/content/101/5/232.long

Kadambari S & Sharland M. Congenital CMV: current and future research in the UK. 2013

https://cmvaction.org.uk/wp-content/uploads/2013/10/Audacity-Article.pdf

Kadambari, S, Williams, EJ, Luck, S. et al. Evidence based management guidelines for the detection and treatment of congenital CMV. Early Human Development 2011:87;723-8

European Congenital Cytomegalovirus Initiative. Rationale for treating neurologically symptomatic babies. (Recommendation 13). 2006

Ganciclovir/valganciclovir is of use in the treatment of congenital CMV infection?

Ganciclovir and valganciclovir are two of a number of agents (including cidofovir and foscarnet) having documented in vitro activity against CMV. Ganciclovir has, to date, been more rigorously evaluated for safety and efficacy in infants with congenital CMV infection (Jones, 2003).
Valganciclovir has only been the subject of two small randomised studies (Kimberlin 2008, Lombardi 2009). The pharmacokinetic parameters were found to be similar to Ganciclovir. A placebo-controlled, double blind, randomised study comparing 6 weeks versus 6 months with Valganciclovir is currently being carried out by the CASG. (Kadambari 2011)
Ganciclovir therapy has been associated with a high rate of complications. An open label, phase II trial in 47 symptomatic infants (Whitley, 1997) administered daily doses of 8 or 12 mg/kg in divided doses, 12 hrly for 6 weeks. Thrombocytopaenia occurred in 37 babies (78%) and neutropaenia in 29 (61%). Although levels of CMV in the urine decreased during the treatment period, they returned to near pretreatment levels when therapy was discontinued. Hearing improvement or stabilization occurred in 5 (16%) of 30 babies at 6 months or later.
A randomised controlled trial in 100 symptomatic infants (Kimberlin, 2003) administered 6mg/kg i.v. 12 hrly for 6 weeks vs no treatment. A large number of patients in this study were non-evaluable at follow-up, leaving 42 patients (25 in the treatment group and 17 controls). Twenty one (84%) of the treatment group had improved or maintained normal hearing at 6 months, vs 10 (59%) of the controls. Twenty nine (63%) of 46 patients in the treatment group had grade 3 or 4 neutropaenia during treatment vs 9 (21%) of 43 controls ($P < .01$).
A controlled Phase III study of symptomatic congenital CMV involving the CNS (Oliver, 2009) randomised 100 neonates to either 6 weeks of intravenous ganciclovir or no treatment. Denver developmental tests were performed at 6 weeks, 6 months, and 12 months. For each age, developmental milestones that > or =90% of normal children would be expected to have achieved were identified. The numbers of milestones not met ("delays") were determined for each subject. The average number of delays per subject was compared for each treatment group. At 6 months, the average number of delays was 4.46 and 7.51, respectively, for ganciclovir recipients and "no treatment" subjects ($p=0.02$). At 12 months, the average number of delays was 10.06 and 17.14, respectively ($p=0.007$). In a multivariate regression model, the effect of ganciclovir therapy remained statistically significant at 12 months ($p=0.007$).
A randomized controlled trial compared 6 weeks of valganciclovir therapy with 6 months of valganciclovir therapy (Kimberlin, 2015). The 6 month group had improved total ear hearing at 12 month follow up (73% vs. 57%, $P=0.01$) and 24 month follow up (77% vs. 64%, $P=0.04$). The 6 month group had better neurodevelopmental scores on the Bayley Scales of Infant and Toddler Development, third edition, on the language-composite component ($P=0.004$) and on the receptive-communication scale ($P=0.003$).

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Jones CA. Congenital cytomegalovirus infection. Curr Prob Pediatr Adolesc Health Care 2003;33:65-100

Kimberlin DW, Lin CY, Sanchez PJ, et al. Effect of ganciclovir therapy on hearing in symptomatic congenital cytomegalovirus disease involving the central nervous system: a randomized, controlled trial. J Pediatr 2003;143:16-25

Kimberlin DW, Acosta, EP, Sanchez, PJ, et al. Pharmacokinetic and Pharmacodynamic Assessment of Oral Valganciclovir in the Treatment of Symptomatic Congenital Cytomegalovirus Disease. J Infect Dis 2008:197:836-45.
http://jid.oxfordjournals.org/content/197/6/836.long

Kimberlin DW, Jester PM, Sánchez P et al. Valganciclovir for Symptomatic Congenital Cytomegalovirus Disease. New Eng J Med. 2015;372:933-43
http://www.nejm.org/doi/full/10.1056/NEJMoa1404599#t=articleTop

G. Lombardi, F. Garofili, P. Vilani et al. Oral valganciclovir treatment in newborns with symptomatic congenital cytomegalovirus infection Eur J Clin Microbiol Dis, 12 (28) (2009), pp. 1465–1470.

Oliver SE, Cloud GA, Sanchez PJ, et al. Neurodevelopmental outcomes following ganciclovir therapy in symptomatic congenital cytomegalovirus infections involving the central nervous system. J Clin Virol 2009;46 Suppl 4:S22-6
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2805252/

Whitley R, Cloud G, Gruber W, et al. Ganciclovir treatment of symptomatic congenital cytomegalovirus infection: results of a Phase II study. National Institutes of Allergy and Infectious Diseases Collaborative Antiviral Study Group. J Infect Dis 1997;175:1080-6
http://jid.oxfordjournals.org/content/175/5/1080.long

Evidence Level: II

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