O-25	CYTOMEGALOVIRUS PREVENTION in BONE MARROW TRANSPLANTATION

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Human cytomegalovirus (HCMV) infection and disease remains a major cause of morbidity and mortality after bone marrow transplantation. Major advances have been made in preventing HCMV infection and disease through two different approaches. One approach is the strategy of preemptive therapy in which patients are given ganciclovir when HCMV infection is first identified. Treatment is continued for a variable period of time, usually after loss of detection of virus of for several months after initiation. An alternative strategy is the use or prophylactic ganciclovir therapy in which prophylaxis is given to all patients at risk of HCMV disease from time of engraftment up to 3-4 months post transplantation. Each strategy has advantages and disadvantages and there is no evidence for the clinical superiority of one over the other. Problems seen with ganciclovir prophylaxis has been the development of drug related toxicity, in particular neutropenia. Furthermore, the use of ganciclovir prophylaxis has been associated with HCMV disease which occurs late post transplant, i.e. after the first 6 months. One problem with the preemptive strategy has been lack of sensitivity in detecting viral replication, with subsequent development of HCMV disease. A recently completed comparative trial has examined the use of prophylactic valacyclovir for prevention of HCMV infection and disease compared to ganciclovir prophylaxis. Results show equivalence and may indicate another alternative agent for use.

The use of more sensitive tests such as HCMV PCR of antigenemia may improve the outcome but probably will not eradicate all HCMV disease. HCMV disease, especially pneumonitis, has not responded well to treatment with antivirals alone. While treatment with ganciclovir and immunoglobin improves outcome, there is still a substantial mortality which ranges between 30-70%. Gastrointestinal involvement with HCMV in the BMT patient has also not responded well to antiviral treatment. It is therefore imperative to prevent HCMV infection before it develops into disease.

Future posible strategies include the use of adoptive transfer of CD8- HCMV-specific cytotoxic T lymphocytes clones derived from the donor marrow or boosting donor or patient immunity wing subunit anti-HCMV vaccines such as gB or pp65.