

SCIENTIFIC ABSTRACT

Patients with newly diagnosed "poor prognosis" brain tumors and patients with recurrent brain tumors will undergo peripheral blood stem cell harvesting following G-CSF priming. 24×10^8 mononuclear cells (MNC)/kg will be collected by apheresis. CD34+ cells will be isolated utilizing the Isolex™ 300i system developed by Baxter Healthcare Corporation for the purpose of genetic manipulation of CD34+ cells from 12×10^8 MNC/kg. CD34+ cells will be transduced with the human O⁶-methylguanine DNA methyltransferase (MGMT) cDNA in the retrovirus construct, PGK-MGMT. Chemotherapy will consist of four courses of PCV (Procarbazine 150 mg/m²/d, days 1-7, CCNU 130 mg/m² on day 0, Vincristine 1.5 mg/m², day 0) given every 28 days. On Day 9 of the first course, 2/3 of the cell aliquots resulting from the transduction of CD34+ using the PGK-MGMT retrovirus will be infused. On Day 9 of the second and third course 4×10^8 MNC/kg untransduced cells will be infused. On Day 9 of the fourth course, 1/3 of the cell aliquot resulting from the transduction of CD34+ cells using the PGK-MGMT retrovirus will be infused along with 4×10^8 MNC/kg of untransduced cells. Following each course of chemotherapy, once the ANC has nadired and then risen to at least 1000/mm³, the presence and expression of the MGMT cDNA will be determined. Various safety testing will be done each time MGMT testing is done. Safety testing is discussed and described in detail in the body of the protocol.