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THE POTENTIAL USE OF CELL-MEDIATED IMMUNOTHERAPY FOR TREATMENT OF GASTROINTESTINAL MALIGNANCIES

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Despite major progress in early diagnosis and treatment, most metastatic gastro-intestinal tumors (GIT) remain incurable. Based on the feasibility of allogeneic lymphocytes to eliminate otherwise resistant hematological malignancies, we developed new strategies for cure of cancer based on administration of intentionally mismatched donor lymphocytes. Instead of durable engraftment of donor's lymphocytes following induction of transplantation tolerance following engraftment of donor's stem cells following stem cell transplantation (SCT), a simple outpatient procedure was developed based on the use of non-engrafting donor lymphocytes (NED), activated *in vitro* prior to and following cell infusion with low dose interleukin 2 (IL-2) that activates both T and natural killer (NK) cells. When NED is applied at the stage of minimal residual disease (MRD), elimination of cancer can be accomplished within days before consistent rejection of NED. Anti-cancer immunotherapy can be amplified by adding monoclonal or bispecific antibodies (BSA) to target killer cells against residual malignant cells. In contrast to graft-vs-host disease (GVHD) following SCT, no such risk exists using NED because of consistent rejection of NED within a few days. As such, using allogeneic targeted activated cancer killer cells (ATACK) represents a simple cost-effective anti-cancer procedure that at the stage of MRD can result in cure. Applying ATACK using BSA, results in induction of long-lasting anti-cancer immunity because Fc of binding of BSA to patient's dendritic cells and induction of memory T cells against recurrent disease. For inoperable hepatoma, transplantation tolerance can be accomplished by combined administration of donor's bone marrow and liver allograft, avoiding the need for life-long immunosuppressive treatment and elimination of extra-hepatic disease can be accomplished by immunotherapy using activated donor lymphocytes. Based on pre-clinical animal data and pilot clinical trials, using non-engrafting ATACK may represent a novel method for the treatment of GIT best applicable at the stage of MRD.

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