

To: Human Subjects Review Committee,
Fred Hutchinson Cancer Center

From: Dr. Robert A. Bruce April 19, 1983

Subject: Application H834-180R, Oncology Protocol #126

This application from Dr. Paul Martin and associates is to continue NCI supported pilot-study research initiated 5/1/81 on murine monoclonal anti-T cell antibodies to remove T-cells from donor marrow in allogenic marrow transplantations to reduce risk of graft-versus-host disease in marrow recipients. To date 9 patients have been enrolled in this protocol and allegedly no new or unexpected complications have occurred. Neither is there evidence of protection against graft-versus-host disease. Further studies on 12^{or} more suitable patients are proposed for the coming year. In vitro elimination of T cells will be accomplished by use of rabbit serum antibodies and complement. Any toxicity and anti-GVHD effects will be noted. Both protocol and informed consent are reported to be changed. But the incidence of adverse effects reported by letter to the FHCR Human Subjects Review Committee dated March 9, 1983 that monoclonal antibodies given in large doses for over 30 days to two patients resulted in death from unexpected lymphosarcoma-like B-lymphocytes. In one case B-cells appeared to be of host origin; in the other case they appeared to be of donor origin, possibly due to infection with Epstein-Barr virus. Criteria for continuation versus termination of this study are based upon statistical considerations and so stated in the application.

RECOMMENDATIONS: Approval, PROVIDED statistical criteria for decision to continue or to discontinue this study are rigorously followed. The informed consent should at the very least indicate that some unexpected adverse effects have occurred in occasional patients who received large doses of the monoclonal antibody material for several weeks. The risk of fatality from an additional malignant process in two out of nine patients studied to date can hardly be overlooked in the statement of potential risks. Whether this was due to infection or not unfortunate and unexpected consequences allegedly occurred.

at the time
of review
submitted

EMPHASIS PROVIDED

is later