A Study of Adoptive Invariant Nature Killer T Cell Therapy for Relapsed/Advanced Hepatocellular Carcinoma (HCC)

NCT03175679

March 1, 2017

Background

Invariant Natural Killer T (iNKT) cells activated by a specific glycolipid antigen (a-galactosylceramide) show strong antitumor activity against malignant tumor through producing high levels of cytokines, such as IFN-γ and IL-4. iNKT cells and their frequencies are abundant in the liver, but defect in malignant tumor development. We did a phase I dose escalation study with autologous in vitro expanded iNKT cells in advanced hepatocellular carcinoma (HCC).

Objectives

Inclusion criteria included diagnosed of HCC by CT or MRI, BCLC B/C stage, age 18 to 80 and predicted life span of 12 weeks or more to complete the study and follow-up. Exclusion criteria included uncontrolled systemic diseases, central nervous system metastases or other tumor, unstable immune system disease, positive HIV, syphilis or immune deficiency disease and known hypersensitivity immunotherapy and related drugs. All patient understood and voluntarily signed the informed consent.

Method

Patients underwent leukapheresis to collect circulating iNKT cells, which were isolated using a monoclonal antibody (6B11) against the invariant TCR-α chain expressed by iNKT cells and expanded in culture over 14 days. The expanded cells were harvested and divided into 3 doses. The expansion rates of iNKT cells in enrolled patients before and after

cultivation were analysed by flow cytometry analysis. Realtime-PCR was conducted to compare the mRNA level of Th1 and Th2 cytokines before and after iNKT cultivation.

Stuty design

Patients were intravenously doped with different doses of autologous iNKT cells, 3 infusions per course. Dosages were escalated from 3×10^7 cells/m^2 to at least 9×10^7cells/m^2. Tegafur will be given twice per day for 2 weeks after apheresis. Human IL-2 will be given during 5-14 days after iNKT cells infusion. Subjects were monitored for 4 weeks post-infusion to make sure the safety of this therapy. The laboratory safety tests and physical examination were carried out at 2nd week, 4^{th} week, 8th week and 12th week after iNKT infusion. All subjects were followed every 3 months until the disease progressed.

Statistical Analysis Plan

Means and standard deviations was used to analyze difference of expansion rates of iNKT cells and mRNA level of Th1 and Th2 cytokines in enrolled patients before and after cultivation, differences were considered significant for $p < 0.05$.