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## **Approaches for inducing immunotolerance in clinical mismatched-haploidentical hematopoietic stem cell transplant (HSCT)**

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Several approaches other than conventional HSCT were adopted in mismatched-haploidentical HSCT since 1987 in our institute.

A total of 142 cases of hematological malignancies were studied. The sources of stem cells were either from bone marrow or peripheral blood or both. Most of patients were high-risk cases. Cord blood transplantation was not included in this study. However, in 14 cases treated with GIAC regimen cord blood were co-infused as a tolerance inducing cells.

14 cases received T-cell depleted bone marrow treated with immunotoxin consisted of anti-CD3 conjugated with ricin chain. 5 of 14 patients had survived without disease for more than 8 years.

Five leukemias in CR2 received reduced amount of haploidentical bone marrow together with autologous T-cell depleted bone marrow since 1991. They were all engrafted with haploidentical marrow, although chimerism was only partial and not sustained. There was no GVHD in all cases. One patient had repeatedly >40% of maternal chimerism as proven by FISH, had DFS for 13 years.

23 patients received infusion of fetal liver cell suspension. Incidence and severity of acute as well as chronic GVHD was significantly lower. 15 of 23 patients had DFS for more than years.

From 2001, 100 cases of mismatched-haploidentical HSCT had received GIAC regimen with simultaneous cord blood infusion in 14 cases. In the term "GIAC", "G" denotes G-CSF primed donor's marrow and peripheral blood; "I" denotes immunosuppressive therapy intensified and prolonged; "A" is ATG (from day -5 to -2); combination use of bone marrow and peripheral blood was represented by "C". Among 100 cases transplanted with this regimen 71 (71%) have been living. Incidence of acute GVHD (grade II-IV) in 1 and 2 loci mismatched recipients was around 15%. That in 3 loci mismatched was around 25%. The cumulative incidence of extensive chronic GVHD in 1-3 loci mismatched recipients were <30%. In 14 patients receiving co-transfusion of cord-blood acute GVHD lower.

In summary, haploidentical HSCT is clinically feasible. It can be performed without significant acute GVHD