Title	Donor Lymphocyte Infusion (DLI) for leukemia relapse: a revisit
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G-H-1

DONOR LYMPHOCYTE INFUSION (DLI) FOR LEUKEMIA RELAPSE: A revisit

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Background: The curative effect of bone marrow transplantation (BMT) is partly due to the graft versus leukemia effect. This can be augmented by DLI at leukemia relapse and induce sustained remissions.
Method: From 9/95-8/99, 18 cases (10 chronic myeloid leukemia (CML), 3 acute myeloid leukemia (AML), 4 acute lymphoblastic leukemia (ALL), 1 atypical CML) were treated. Their median age was 33 (range 18-49). Peripheral buffy coat (median 2.3 × 10^8/kg lymphocytes, range 0.13-12.2) apheresed from the previous donor was infused in 2 to 6 doses, with no graft versus host disease (GVHD) prophylaxis. For AML and ALL cases, chemotherapy was added for initial disease control.
Results: The overall complete remission (CR) & partial remission (PR) rate was 13/18 (72%). 8/10 CML cases (80%) achieved CR (including 6 molecular remissions), and 1 achieved near CR (90%Ph-ve). DLI induced molecular CR in one AML case, while 2 cases (1AML, ALL) were maintained in PR with isolated extramedullary disease (EMD). Both CML-BT and aCML cases did not respond. CR was not achieved in 4 cases relapsing <6month post BMT. Notably 8/9 cases failing to achieve sustained CR have EMD components. The median time of follow up of survivors was 22 mo. (range 1 to 48 mo.). The major side effects included self-limiting liver GVHD (n=5), severe skin GVHD (n=2), and herpes zoster virus/ cytomegalovirus reactivation (n=4).
Conclusions: DLI is a valuable treatment option for patients relapsing after BMT. Factors predictive of a successful response are: molecular relapse only, Ph+ve CML, relapse >1 year from BMT, no EMD, and preserved donor chimerism.

G-H-2

Ex Vivo Expansion of Peripheral Blood Haematopoietic Stem Cells: Preclinical Studies.

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Introduction. In autologous peripheral blood haematopoietic stem cell transplantation (aBMT), a period of severe neutropenia inevitably develops, owing to a deficiency of committed myeloid precursors that can give rise to mature neutrophils. Therefore, a combination of haematopoietic stem cells and more committed myeloid progenitor cells may overcome this problem, with the early haematopoietic recovery being mediated by more committed progenitors, and the long term haematopoiesis being maintained by repopulation with pluripotential stem cells. To test this hypothesis, we conducted preclinical studies to examine the expansion *ex vivo* of peripheral blood haematopoietic stem cells. Materials and methods. Circulating haematopoietic stem cells were collected with informed consent from patients undergoing stem cell mobilisation for aBMT. CD34 positive cells were isolated by positive selection with immunomagnetic beads coated with a monoclonal anti-CD34 antibody. The purity was verified by flow cytometry. Purified CD34 cells were plated at a concentration of 5,000 cells/ml/well, 10,000 cells/ml/well, and 20,000 cells/ml/well, in a stroma free suspension culture, supplemented with the haematopoietic growth factors interleukin-3 (IL-3), IL-6, stem cell factor, granulocyte colony stimulating factor, stem cell factor, and megakaryocytes growth and development factor, for 12-14 days. Parameters measured included the percentage increase in cell numbers, serial changes in surface antigen expression as defined by dual colour flow cytometric analysis, and clonogenic assays. Results. 4 cases were investigated. Cell number increased gradually until day 7, when dramatic increases in the rate of cell growth were observed (a mean increase of 90.8 fold at day 10). It was also observed that the fold increase of cells in cultures initiated with 5,000 cells/ml was higher than cultures initiated with 20,000 cells/ml. The number of granulocyte-macrohage colony-forming units (CFU-GM) paralleled nucleated cell production, peaking at day 10. Dual colour flow cytometry using antibodies to CD34, CD15, and CD11b evaluated the distribution and maturation stages of cells during culture. From days 9-14 there was emergence of a CD15+ CD11b+ population, indicating the maturation of cultured cells toward more mature neutrophilic forms. This was paralleled by a decrease of CD34+ cells, which dropped to only 1.6% of the starting number by day 14. Conclusion. At the end of a 14-day culture, cells produced were predominantly neutrophil precursors, and were developing normally as assessed by immunophenotype and CFU-GM assay. The results suggest that *ex vivo* expansion of haematopoietic stem cells could generate sufficient number of progenitors as a supplement to stem cell transplantation.