

Northern New England Clinical Oncology Society

2006 Annual Meeting Abstract Submission

Contact Information

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Abstract (250 words)

Abstract Title:

Immunotherapy Immediately Following Transplantation for Multiple Myeloma: Early Recovery of Aggressive Cytotoxic Cells and Improved Immune Recovery

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Background:

Autologous peripheral blood stem cell transplantation (ASCT) is the standard of care for the treatment of multiple myeloma (MM), however a large percentage of patients relapse. Recent evidence shows an improved outcome if absolute lymphocyte count is increased immediately following transplant in patients with a hematologic malignancy.

Methods:

We designed a phase II trial evaluating the combination of SQ IL-2 and standard dose GM-CSF post-transplant for myeloma patients. Patients received melphalan 200mg/m² with GM-CSF (250mg/m²/d) beginning on day 5 post-transplant. IL-2 began on day 7 post-transplant and continued 5 days per week for 4 weeks. Peripheral blood samples were obtained at baseline (pre-transplant) and every week for 4 weeks post-transplant and were evaluated using flow cytometry and cytotoxicity/killing assays. Nineteen patients have been treated and 15 patients completed the full course of immunotherapy without complications. Dose Level 2 of IL-2 (1 x 10⁶ IU/m²/d) was not tolerated in 3 of 6 patients due to grade 3 or 4 fatigue and diarrhea (n=1) or supraventricular arrhythmia (n=2). Dose Level 1 of IL-2 (6 x 10⁵ IU/m²/d) was well tolerated by 12 of the remaining 13 patients. One patient was removed due to other medical issues (depression).

Results:

Level 3 or greater toxicities included nausea (n=5), diarrhea (n=3), anorexia (n=11), mucositis (n=9), not unlike commonly encountered toxicities during transplant. Engraftment of neutrophils occurred on day 13 (median; range 11-17) and platelets on day 17 (median; range 0-74). Absolute lymphocyte counts on days 10-15 following transplant were increased by 152% (mean; range 25-390%). Phenotype analysis showed a marked increase in the lymphocyte populations in the patients' peripheral blood within 3 weeks following transplant. CD3+ cells, a marker for all T cells, increased from 48% of all cells at baseline (day 0) to 81% (day 21; p = 0.01). CD4+ T cells increased from 22% to 47% (p = 0.05) and CD8+ cytotoxic T cells increased from 29% to 44% (p = 0.01). Natural killer cells (NK), designated as CD56+ cells, increased from 41% to 50% (p = 0.04). When analyzed for their killing ability, cytotoxicity of Day #21 lymphocytes from the patients' peripheral blood was strikingly increased at 74% compared to baseline (p = 0.01) when tested against a human myeloma cell line (RPMI 8226) using chromium release assays (E: T ratio = 100:1).

Conclusions:

These results demonstrate a tolerable regimen of immediate post-transplant immunotherapy with marked increase in the number and function of early cytotoxic effector T cells and NK cells. The enhanced immune recovery may translate into an improved outcome. Current research is elucidating the mechanism(s) of tumor cell killing *in vivo* and adding adoptive cellular therapy in a novel clinical trial.

Additional Information:

I agree to present my abstract if selected for presentation at the NNECOS Annual Meeting