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Keeping Cancer At Bay: Long-term Therapy In The Fight Against Multiple Myeloma

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There is no known cure for multiple myeloma, so its diagnosis means high-dose chemotherapy followed by repeated treatments with each relapse of the cancer - a watch and wait approach. A new approach of providing patients with continuous therapy to keep the cancer at bay was explored by a team of international researchers from France, Switzerland, and Belgium; their findings will be published in the November 15, 2006, issue of *Blood*, the official journal of the American Society of Hematology.

"We have been anxiously waiting for the results of this study in the multiple myeloma community, as the issue of maintenance therapy has never been resolved," said Joseph Mikhael, MD, a hematologist at the Princess Margaret Hospital in Toronto. "The results are impressive in favor of ongoing treatment of patients with multiple myeloma, and are quite likely going to change the standard of care."

In multiple myeloma, an overgrowth of abnormal cells in the bone marrow leads to the painful destruction of bone. In this study, pamidronate, a drug often used early in the treatment of multiple myeloma to help protect against bone damage, was for the first time studied as a maintenance therapy. Its use alone was compared against its combination with thalidomide, a drug known to inhibit the growth of myeloma cells. A third set of patients in the study did not receive any maintenance therapy, the current standard of care in this disease.

A total of 597 patients participated, and measures of success included the likelihood of the cancer coming back, the risk of an adverse skeletal event (such as a bone lesion), and the patients' overall survival probability. Using these measures:

-- The results of using pamidronate alone compared with going without maintenance therapy were similar. The three-year probability of the patients remaining relapse-free was 38 percent without maintenance therapy and only somewhat better - at 39 percent - with pamidronate alone. The addition of thalidomide significantly improved these odds to 51 percent.

-- The use of pamidronate did not decrease the number of bone events as anticipated, and there was no significant difference in the number of these events between the three treatment groups.

-- The chance of overall survival four years after study enrollment in the pamidronate-thalidomide group was 87 percent. Patients in the pamidronate-alone arm had a 74 percent survival probability compared with those not receiving therapy at 77 percent.

Thalidomide, however, is not for everyone. The drug was originally dosed at 400 mg per day, but after 15 months, the median dose was decreased by half because of drug-related toxicity. Thalidomide was discontinued in 39 percent of the patients taking the drug due to side effects such

as numbness, tingling, or pain in the hands and feet, fatigue, and constipation. In contrast, only 4 percent of patients discontinued pamidronate.

Patients most likely to benefit from the addition of thalidomide to maintenance therapy were those whose responses to the original chemotherapy were not as successful, and those who did not have a chromosome 13 deletion, an abnormality found in about 15-20 percent of patients with multiple myeloma and one that is associated with a poorer prognosis.

"Thalidomide shows great promise for keeping multiple myeloma in check after chemotherapy," said Michael Attal, MD, PRD, lead author of the study and Head of the Department of Hematology at Hôpital Purpan in Toulouse, France. "If measures can be taken to mediate the toxicity of the drug, or if only those who would get the most benefit from it are treated, this could be an effective long-term therapy for many patients."

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The **American Society of Hematology** (<http://www.hematology.org>) is the world's largest professional society concerned with the causes and treatment of blood disorders. Its mission is to further the understanding, diagnosis, treatment, and prevention of disorders affecting blood, bone marrow, and the immunologic, hemostatic, and vascular systems, by promoting research, clinical care, education, training, and advocacy in hematology.

Blood, the official journal of the American Society of Hematology, is the most cited peer-reviewed publication in the field. Blood is issued to Society members and other subscribers twice per month, available in print and online at <http://www.bloodjournal.org>.

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