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Treatment Trends For Multiple Myeloma –Options For Elderly Multiple Myeloma Patients

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Elderly people with multiple myeloma have better treatment options now than ten years ago. In the past decade, the introduction of thalidomide (Thalomid), Velcade (bortezomib), and Revlimid (lenalidomide) have improved patients' response to treatment and increased survival time, even when used without stem cell transplants.

In this article, Dr. Donna E. Reece, a physician and researcher at the Princess Margaret Hospital in Toronto, reviews the best ways to use new drugs to treat older patients who are ineligible for stem cell transplants.

Improving On The Standard Of Care From The '60s – Melphalan And Prednisone

Since the 1960s, doctors have been treating multiple myeloma patients with melphalan (Alkeran) and prednisone. Recent studies found that adding new drugs in combination with melphalan and prednisone improves results.

A Phase 3 trial published in the New England Journal of Medicine in August 2008 found that adding Velcade to melphalan and prednisone resulted in better responses and longer times before patients' myeloma progressed — 2 years compared to 16.6 months for people treated with melphalan and prednisone alone.

The study participants treated with Velcade, melphalan and prednisone were also more likely to have longer survival times. After 16 months, 87 percent of those participants survived, compared to 78 percent of participants taking only melphalan and prednisone.

The trial followed 682 people with multiple myeloma and had such great impact on the multiple myeloma research community that the National Comprehensive Cancer Network, a group of 21 United States cancer centers, considers treatment with melphalan, prednisone, and Velcade a "category 1 recommendation," meaning that the cancer centers unanimously agree that there is a high-level of evidence supporting the regimen.

Dr. Reece also reviewed recent studies that tested the addition of thalidomide to melphalan and prednisone. She found that all five studies reported better responses and longer times before myeloma progression for melphalan, prednisone, and thalidomide compared to melphalan and prednisone alone.

The most recent study, a Phase 3 trial presented to the American Society of Hematology last December, found 66 percent of multiple myeloma patients treated with melphalan, prednisone, and thalidomide reached partial response or better, compared to 47 percent of people treated with melphalan and prednisone. The difference in time before disease progression was 14 months versus 10 months.

However, three of the five trials Dr. Reece studied did not find significantly different survival times, so she wrote that thalidomide's ability to improve overall survival with melphalan and prednisone treatment is uncertain.

A New Idea — Thalidomide Or Revlimid Plus Dexamethasone

Dr. Reece found the continuous use of blood vessel-inhibiting drugs thalidomide or Revlimid plus dexamethasone (Decadron) to be a new trend in treating multiple myeloma. Several recent Phase 3 trials investigated this kind of treatment specifically in older patients. Many of these trials suggested that older patients cannot tolerate higher doses of dexamethasone.

One trial, published in the *Journal of Clinical Oncology* in May 2008, compared a thalidomide and dexamethasone therapy with a placebo and dexamethasone. Researchers looked at 470 multiple myeloma patients with a median age of 64.

Study participants taking thalidomide and dexamethasone had better responses than participants taking the placebo and dexamethasone. People treated with thalidomide and dexamethasone also had longer times until myeloma progression, one year and 10.6 months versus 6.5 months. However, more people taking thalidomide and dexamethasone treatment experienced severe side effects. Overall survival time was not studied.

Another trial, published in *Blood* in April, compared thalidomide and dexamethasone treatment with the classic melphalan and prednisone treatment in patients with a median age of 72. The study participants treated with thalidomide and dexamethasone had better responses. However, there was not a significant difference between the two treatments in time until myeloma progression, and the thalidomide-dexamethasone participants lived for 41.5 months compared to 49.5 months.

Older patients' low tolerance for higher doses of dexamethasone was underscored by a trial published in the *Journal of Clinical Oncology* in May 2008. Researchers found that after one year, 96 percent of their study participants taking Revlimid and low-dose dexamethasone survived, compared to 88 percent of study participants taking Revlimid and standard-dose dexamethasone. After two years, the numbers were 87 percent and 75 percent. The study investigated 445 people with a median age of 65.

Maintenance Therapy For Elderly Patients

Dr. Reece's review included one Phase 3 trial on maintenance therapies for older patients, published in the *British Journal of Hematology* in November 2008. Researchers treated 147

multiple myeloma patients, median age over 70, with thalidomide, dexamethasone, and Doxil (doxorubicin liposomal).

They then selected the 103 study participants who showed any response to treatment to receive maintenance therapy with either dexamethasone and thalidomide or dexamethasone and interferon-alpha, which can improve the body's response to infection and slow tumor growth. Sixty-three percent of the participants treated with thalidomide and dexamethasone lived to two years, compared to 32 percent of participants treated with interferon and dexamethasone.

"The superiority of any one novel regimen has not yet been demonstrated," Dr. Reece concluded, "and decisions for management are often made on individual . . . factors present in a given patient."

Nevertheless, the studies illustrate the increasing options for older myeloma patients. They also show that people undergoing any modern treatment often achieve good responses and usually enjoy two years before their myeloma progresses, which is a good improvement over the 60 percent response rate and 18-month response durations, as reported by the NCCN, from the days when melphalan and prednisone were the standard choice.