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Treatment Trends For Multiple Myeloma –Autologous Stem Cell Transplants (from The Myeloma Beacon)

July 2009 issue of Current Opinion in Hematology

Many important advances in the treatment of multiple myeloma have been made in recent years. In the July issue of Current Opinion in Hematology, Dr. Donna E. Reece of the Princess Margaret Hospital in Toronto, Canada reviewed the current approaches to treating newly diagnosed multiple myeloma patients. This article focuses on Dr. Reece's findings about autologous stem cell transplants.

Autologous stem cell transplantation – the process of collecting stem cells and returning them to the same individual – following chemotherapy is a common treatment option for newly diagnosed myeloma patients. Stem cell transplantation replaces the stem cells destroyed during the chemotherapy treatment, leading to higher response rates and longer survival.

In her review, Dr. Reece covered ongoing research on the steps taken before, during, and after transplant treatments. These steps include pre-transplant induction therapies, which serve as the first step in reducing cancer cells; high-dose treatments, which prepare the body for the transplant; the use of two transplants instead of one; and after-transplant maintenance therapies.

The Importance Of Improving Induction Therapies

Multiple myeloma researchers are becoming increasingly aware of the importance of complete response, which is a standardized measure that uses bone marrow and immunofixation tests to determine how well patients respond to treatment. Complete response is emerging as an important predictor of progression-free survival and longer overall survival.

Most studies look at the relationship between response and overall lifespan after treatment. However, it may also be important to reach complete response after induction therapy (and before the autologous stem cell transplant). Those who reach complete response after induction therapy may achieve greater overall survival after their entire course of treatment.

Thus, doctors hope to further develop multiple myeloma treatment by improving, and therefore increasing complete response to, induction therapies. Reece cited two Phase 3 clinical trials reported last year that compare different induction regimens.

One, presented to the American Society of Clinical Oncology, found that a Velcade (bortezomib) and dexamethasone (Decadron) induction regimen helped more people reach complete or very good partial response than did a commonly-used regimen of vincristine, doxorubicin (Adriamycin), and dexamethasone. Sixty-eight percent of people treated with

Velcade and dexamethasone had a least a very good partial response, compared to 27 percent of people treated with vincristine, doxorubicin, and dexamethasone. The better responses persisted after the study participants received stem cell transplants.

The other trial, presented to the American Society of Hematology, found a Velcade, thalidomide (Thalomid), and dexamethasone induction regimen caused a very good partial response or better in 92 percent of the study participants. In comparison, Velcade and thalidomide without dexamethasone caused a similar response in 79 percent of participants.

New High-Dose Treatments

Researchers are also conducting clinical trials of high-dose treatments using newly-discovered drugs. A group of researchers in France found that Velcade and high-dose melphalan (Alkeran) make for a “safe and highly effective” preparatory treatment in a Phase 2 trial, which was presented to the American Society of Hematology in 2008. In another Phase 2 trial published in the same year, M. D. Anderson Cancer Center researchers found arsenic trioxide, ascorbic acid, and melphalan to be “safe and well tolerated.” Their work appeared in the journal *Biology of Blood and Marrow Transplantation*.

Tandem Autologous Stem Cell Transplants

Tandem autologous stem cell transplants, or two transplants performed within six months of each other, is a controversial potential treatment. Reece wrote that researchers are interested in tandem transplants because they can help people reach complete response at relatively low costs.

She highlighted two large, conflicting recent studies on the tandem autologous stem cell transplant treatment. One, published in the *Journal of the National Cancer Institute* in July, not only reported that the treatment reaped no benefit to overall survival, but also correlated the treatment with higher mortality rates due to complications with the transplants. Another study, published in the journal *Experimental Hematology* in 2008, found that second transplants improved lifespan.

After-Transplant Therapies

Several recent studies have found that thalidomide helps people achieve longer remissions, but they differ on whether the drug improves overall lifespan as well. A study published in the *Journal of Clinical Oncology* in March found that thalidomide combined with prednisone improved both remission durations and lifespan after stem cell transplants. However, two studies published in 2006 reported improved remission durations without improved lifespan: one from the *New England Journal of Medicine* and one from *Blood*.

Replacing Autologous Stem Cell Transplants With Chemotherapy

One of the newest and most debated issues in stem cell transplant therapy for multiple myeloma is whether drugs like Revlimid (lenalidomide), thalidomide, and Velcade can replace transplants altogether. In an interview with the Beacon, Dr. Robert Kyle, a leading multiple myeloma physician with the Mayo Clinic, identified the necessity of transplants as a major controversy in myeloma research.

Reece touched on the debate in her review, writing that there is no answer yet, “but it is to be hoped that future trials will address this important issue.”

Many studies have come out in recent years as researchers work to improve autologous stem cell transplant therapy and analyze the effects of new drugs. However, more testing is necessary before the new treatment ideas may become widely used or the standard of care for multiple myeloma.

Overall, Reece wrote that “a number of questions remain about the optimal strategy” for myeloma management.

However, the wealth of findings and advancements that appears in Reece’s review suggests that myeloma research is moving forward, exposing new directions for treatment.