New Developments in Multiple Myeloma Management

by James R. Berenson, MD

Positive results from numerous clinical trials have led to a rapid increase in the therapeutic options now available to effectively care for people with multiple myeloma. New therapies such as bortezomib (Velcade®) and lenalidomide (Revlimid®) have moved their way out of the laboratory and into routine clinical practice. Other drugs that have been FDA approved for some time, thalidomide (Thalomid®) and arsenic trioxide (Trisenox®), have been reintroduced in new combinations showing excellent activity against MM, while others such as samarium153-lexidronam (Quadramet®) have shown promise in early clinical trials when used in combination therapy.

These drug therapies, both alone and in conjunction with the established modalities, have become more targeted in their therapeutic effects, and when used in combinations, lower doses can be very effective. **As a result, people with MM are receiving therapies that, not only are producing higher response rates, but also, with these lower dose therapies, are associated with improved quality of life.**

Thalidomide has been found to be effective as an anti-MM agent in one-third of people with myeloma, but produces higher response rates when combined with steroids. Although two recent randomized studies show that response rates are higher and the time to progression of the myeloma is longer with the combination compared to steroids alone, there was no improvement in survival.

Recent reports also suggest that patients may respond well to less thalidomide as well as less steroids when both drugs are used together, and that this lower dose combination produces decreased side effects. Two recent studies show that the addition of thalidomide to conventional (oral melphalan and prednisone [MP]) or high-dose therapy with double transplants improves response rate and achieves a longer time to progressive disease, but again without an improvement in survival. In contrast, a French study compared MP with and without thalidomide among elderly patients ages 65 to 75 years and found a superior overall survival in the thalidomide arm compared to people who did not receive thalidomide, and even to another group in the study that received high-dose therapy without thalidomide.

Lenalidomide is an analog of thalidomide with more potent anti-MM effects in the laboratory, and it has recently been FDA approved in combination with dexamethasone to treat relapsed or refractory MM based on the results of two randomized trials. These studies demonstrated significant improvement in response rate, time to progression, and overall survival among people who received lenalidomide combination with dexamethasone compared to those receiving dexamethasone alone.

Because significant toxicity in the combination treatment may also result from the steroids, the Eastern Cooperative Oncology Group compared standard-dose vs. low-dose dexamethasone with lenalidomide in people with newly diagnosed MM. Patients had reduced side effects, including smaller numbers of patients with high glucose levels, infections, and blood clots. Recently, this trial was closed because of a superior overall survival in the low dose dexamethasone arm. Many other lenalidomide combinations are now being evaluated, although the marrow suppressive effects of this agent may limit its ability to be used with cytotoxic chemotherapeutic agents.

Bortezomib is a drug already approved for use in people with relapsed MM. It has been evaluated with MP as first-line treatment for MM in elderly people and showed a high response rate in a recently published Spanish study. Researchers have evaluated the combination of bortezomib with vitamin C and low-dose melphalan in newly diagnosed MM based on the promising results of this combination in MM patients with relapsed or refractory disease. They are hopeful that this non-thalidomide, non-steroid containing front-line regimen will represent a safe, well tolerated, and active therapeutic option for newly diagnosed patients.

Bortezomib has also shown promise when used in combination with pegylated liposomal doxorubicin and results recently reported from a large randomized Phase III study showed the superiority of this combination as compared to treatment with single-agent bortezomib.

A relatively newer drug being studied in combination with bortezomib is samarium153-lexidronam. This agent is a bone-seeking radioactive compound approved for reducing bone pain for people with bone cancer. Based on laboratory studies suggesting the enhanced effectiveness of the combination of this radioactive agent with bortezomib, clinical trials are underway and early results are promising.

Different combinations of these new agents are also being evaluated in many clinical trials. It is likely that these agents will not only show promise as single agents, but also be tested with other already proven anti-MM agents. These newer therapeutic options will hopefully not only prove to be more effective, but will also allow people to live more active and fulfilling lives as well.

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Editor's Note: *Dr. James Berenson is the medical and scientific director of the Institute for Myeloma & Bone Cancer Research (www.imbcr.org). He has authored and co-authored many books, articles, and abstracts in medical journals and has served as a member, advisor, or director of over 40 organizations.* ■