IMF Hotline Coordinators Answer Your Questions

The IMF Hotline 800-452-CURE (2873) consistently provides callers with the best information about myeloma in a caring and compassionate manner. The Hotline is staffed by Nancy Baxter, Debbie Birns, Paul Hewitt, and Missy Klepetar. The phone lines are open Monday through Friday, 9 a.m. to 4 p.m. (Pacific Time). To submit your question online, please email TheIMF@myeloma.org

I am receiving VELCADE® as part of my treatment regimen. Is there a consensus among myeloma doctors on VELCADE dosing?

Bortezomib (VELCADE®) is an effective and widely used treatment for multiple myeloma. It can be given alone, in combination with dexamethasone, or in a variety of three- and four-drug combinations. Because of bortezomib's effectiveness, it is essential to ensure that patients are able to tolerate it well and not discontinue receiving bortezomib infusions because of side effects.

Peripheral neuropathy (PN) – which causes numbness, tingling, and/or sometimes pain in the hands, arms, feet, and/or legs – is a common problem among myeloma patients. Myeloma itself can cause PN, as can diabetes mellitus. Two of the most common novel therapies for myeloma, thalidomide (Thalomid®) and bortezomib, can also cause PN or worsen pre-existing PN. Because the goal of any treatment for myeloma is to attack the disease while preserving the patient's quality of life, it is important to be aware of this potential problem and to nip it in the bud before it becomes a debilitating and permanent condition.

At a meeting of the International Myeloma Working Group (IMWG) that took place in June 2010 in Barcelona, Spain, the myeloma experts who were gathered from around the world addressed many key questions, including, "How do we minimize the risk of neuropathy?" To answer this question, the experts examined important new clinical trial data that would enable them to draw up a guideline for bortezomib dosing with an eye to reducing the incidence of PN.

Clinical trials are the vehicle through which new drugs and drug combinations are tested, and are often also the means through which new dosing strategies are determined. Results of an Italian study group (GIMEMA) phase III randomized clinical trial, led by the University of Torino's Drs. Antonio Palumbo and Mario Boccadoro, that compared VMPT (VELCADE, melphalan, prednisone, and thalidomide) followed by VT maintenance, versus VMP followed by no maintenance, as first-line therapy in patients ineligible for stem cell transplant were presented at the December 2009 meeting of the American Society of Hematology (ASH) and at the June 2010) meeting of the American Society of Clinical Oncology (ASCO). During this trial, the study was amended to schedule bortezomib weekly (four doses weekly at a dose of 1.3 mg/m2 followed by one week of rest) instead of the traditional twice weekly schedule, in order to reduce the rates of PN. The study investigators, having analyzed the data from the completed trial, noted, "Compared to twice weekly, the weekly infusion of bortezomib significantly reduced the incidence of PN without affecting outcome."

In a phase III randomized study by the Spanish Myeloma Group (PETHEMA/GEM) that compared VMP versus VTP followed by maintenance with VT or VP as first-line therapy for myeloma, Dr. María Victoria Mateos of the University of

Salamanca, Spain, concluded that low rates of PN were observed after a modified bortezomib regimen that consisted of one 6-week cycle administered twice a week, followed by subsequent cycles in which bortezomib was administered in a weekly schedule (four weekly bortezomib doses at 1.3 mg/m2 followed by one week of rest).

Based on these trial results and the combined clinical experience of the IMWG experts, the IMWG concluded that weekly bortezomib dosing and earlier detection of PN are therapeutic options to minimize the risk of neuropathy. Specific guidelines for determining bortezomib dose, which will soon be published in an IMWG paper, are the following:

- Patients who have no PN can be treated with bortezomib in the traditional twice weekly schedule.
- Patients with low-level neuropathy (defined as "Grade 1" using the National Cancer Institute's common toxicity criteria: numbness, weakness, and/or loss of reflexes, but without any pain or loss of function in performing the activities of daily living) should be carefully evaluated by their physicians for the existence of PN risk factors and managed appropriately. Consideration should be given to administering bortezomib once weekly at a starting dose of 1.3 mg/m2.
- For patients treated with bortezomib who develop Grade 1 neuropathy who are experiencing pain, or those who have no pain but whose neuropathy limits their ability to perform daily living activities (Grade 2), consideration should be given to change bortezomib to a reduced dose of 1.3 mg/m2 once per week, as an alternative to the current package insert recommendation of reducing bortezomib dose to 1.0 mg/m2 twice weekly.
- Patients treated with bortezomib who have Grade 2 neuropathy with pain, or Grade 3, which is defined as severe pain, weakness, sensory alteration or numbness, and/or pain severely interfering with activities of daily living, and needing bracing or assistance to walk, should not be given bortezomib until their side effects improve. When the PN improves, consideration should be given to restarting bortezomib at 1.0 mg/m2 once per week (the current package insert recommendation includes restarting bortezomib at 0.7 mg/m2).

As always, we urge you to discuss this information with your hematologist/oncologist, and to report any and all symptoms of PN to your healthcare team AS SOON AS YOU EXPERIENCE THEM. Do not ignore any numbness, weakness, tingling, or pain you feel in your fingers, hands, arms, toes, feet, or legs. By reporting any and all symptoms as soon as possible, you enable your doctor to take prompt action to prevent what could become a debilitating and ongoing problem.