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VELCADE® Treatment Approaches

A Report of Findings from the 2013 Nurse Leadership Board Roundtable Meeting

December 6, 2013

New Orleans, Louisiana


INTERNATIONAL MYELOMA FOUNDATION
EDUCATION • RESEARCH • SUPPORT • ADVOCACY
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Overview

On December 6, 2013 in concurrence with the American Society of Hematology (ASH) Annual Meeting, members of the International Myeloma Foundation (IMF) Nurse Leadership Board convened to discuss treatment practices using VELCADE® in multiple myeloma (MM) patients.

Meeting objectives were specified as follows:

1. Review ASH abstracts relevant to VELCADE® therapy
2. Discuss current approaches to VELCADE® therapy
3. Discuss strategies for setting patient and caregiver expectations
4. Identify common barriers to continuing VELCADE® treatment
5. Share best practices to assess and manage side effects

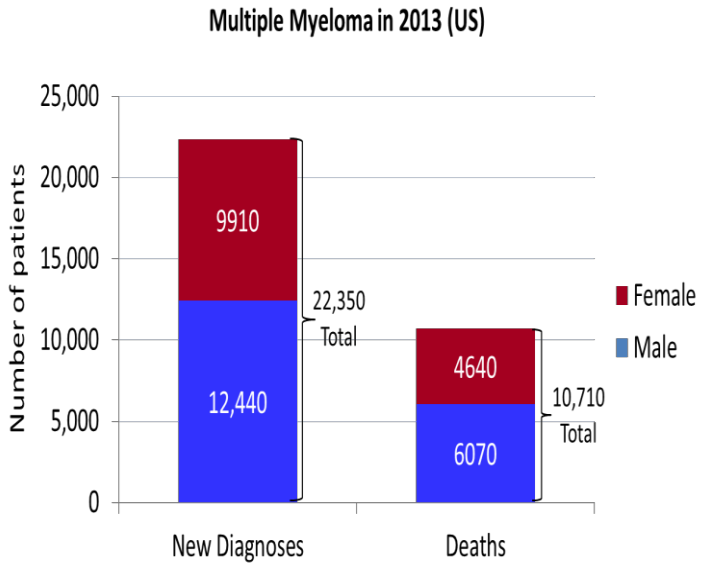
This report compiles key feedback from this meeting.

Introduction

Multiple myeloma is a neoplasm of plasma cells. Normally these cells produce antibodies that assist with the body's immune response. However, in the malignant state, the overproduction of abnormal plasma cells may cause secondary cytopenias and associated clinical sequelae. Excess protein secretion fosters dysfunction in other systems of the body such as the renal and neurologic systems.[1,2]

In 2013, it is estimated that approximately 22,350 patients will be diagnosed with MM and 10,710 individuals will die of the disease. (Figure 1). Men, individuals over the age of 65, and African Americans are at greater risk for developing MM.[3] Treatment is recommended for patients with active MM and end organ damage with the goals of achieving a complete response (CR) and enhanced quality of life. While treatment advances have contributed to the extended survival of MM patients, there currently remains no cure for MM and practitioners must manage patients through inevitable disease relapses and treatment toxicities.[1,4]

Figure 1.



VELCADE® is a proteasome inhibitor that was first approved for the treatment of MM in 2003. It is available in intravenous (IV) and, more recently, subcutaneous (SC) formulations that offer similar efficacy. However, data suggests that SC VELCADE® administration may be associated with less peripheral neuropathy.[5]

The IMF's Nurse Leadership Board is a group of nurses with expertise in MM with the mission of developing recommendations in nursing care for MM patients. Given recent data on the impact of VELCADE® dose intensity on survival and clinical insights related to VELCADE®-

associated toxicities, in conjunction with the ASH Annual Meeting on December 6, 2013, the IMF Nurse Leadership Board gathered to discuss VELCADE® treatment approaches. This report chronicles highlights and practice recommendations from that discussion.

Clinical Approaches to VELCADE® Use in Newly Diagnosed Multiple Myeloma (NDMM) Patients

The majority of members commented that approximately 30-60% of their practice is devoted to treating (NDMM) patients. Most members have open clinical trials at their institutions that target this patient population; however, they commented that the majority of trials are designed for patients with relapsed disease.

Impact of VELCADE® Treatment Duration/Dose Intensity on Outcomes

Roundtable leaders reviewed data from a sub-analysis of the phase III VISTA trial that compared efficacy in 170 patients who received a cumulative VELCADE® dose of < 39 mg/m^2 up to 54 months of therapy versus patients who received a cumulative VELCADE® dose of > 39 mg/m^2 (n = 170), as a part of a VELCADE®/Melphalan/Prednisone regimen. The study reported that higher cumulative doses of VELCADE® were associated with improvements in overall survival (OS) (60.4 months vs 50.3 months; *P* = 0.0356). It also reported that early VELCADE® discontinuation was associated with increased toxicity, particularly in elderly patients. Study authors proposed that a less intensive regimen could be utilized to maximize treatment durations and outcomes in these patients.[6] Roundtable leaders also shared data from a retrospective trial of 1058 treatment-naïve MM patients (TNMM) reporting that greater dose intensity was obtained with SC VELCADE®, due to fewer required dose reductions, than IV administration.[7]

Members commented that the data revealed by these studies reflect their clinical practice. In general, SC is the preferred administration modality for VELCADE® in their practices and they are witnessing increased use of SC administration in the broader clinical community. Most patients will start with a twice a week regimen, and then modulate to weekly dosing based on their disease response or the development of neuropathy. Patients with amyloidosis, elderly or frail patients, patients with insurance/financial challenges, and patients who live far away from the treatment center may be initiated on once weekly dosing.

Rather than initiating conversations with NDMM patients about duration of therapy, members rather focus conversations on duration of response, maintaining response, and reminding patients that MM is a chronic illness associated with ongoing treatment.

They tell patients that “efficacy of SC VELCADE® is shown to be as good as the IV administration in recent studies with NDMM patients, with decreased neuropathy.” They emphasize to patients “the longer you remain on effective treatment including VELCADE®, the better your potential to keep your disease under control.” They associate treatment with a marathon, not a sprint, stating that strategies to reduce treatment-related toxicity may allow patients to receive greater amounts of therapy over time.

Furthermore they communicate with patients from the outset that MM is a chronic disease and that therapy is continued over extended

periods of time to provide optimal responses. Treatment breaks are individualized based on how each patient is responding to and tolerating treatment. Maintenance therapy, or continued treatment using a less intensive regimen, is commonly recommended for patients with higher risk MM following an autologous hematopoietic stem cell transplant.

Members acknowledge that there is still much to learn about the impact of maintenance therapy on long-term safety and disease control. One member expressed concerns about the development of secondary malignancies with long-term melphalan use; another commented that while VECADE® may offer increased disease control throughout maintenance, Revlimid/Dexamethasone (RD) maintenance may be more convenient. The Nurse Leadership Board eagerly awaits maturation of data from several trials that are currently investigating different maintenance strategies and their impact in MM.

Choice of Therapy and Adverse Event Management

Roundtable leaders also reviewed data comparing the safety and efficacy of Cyclophosphamide/VELCADE®/Dexamethasone (CyBorD) with VELCADE®/Revlimid®/Dexamethasone (VRD) in NDMM patients, as well as data examining the incidence of neuropathy and cardiac failure in patients treated with VELCADE®.[8-10]

CyBorD, RD, and VRD were mentioned by members as preferred first-line treatment choices for their NDMM patients. Therapy selection is determined by disease cytogenetics, patient comorbidities, patient age, and patient preferences. VELCADE®- based regimens are usually chosen because of their association with a rapid depth of response. Younger/fitter patients, patients with more aggressive disease, patients with renal disease, and patients who may have challenges adhering to oral regimens are often prescribed VELCADE®. However, VELCADE® may not be the first choice for treatment in patients with pre-existing neuropathy (eg, diabetic neuropathy). Members agreed that CyBorD and VRD offered comparable efficacy and toxicity. One member commented that she has witnessed slightly increased rates of diarrhea with VRD than CyBorD in her patient population.

Members commented that they have not observed a greater number of cardiac events in VELCADE®-treated patients than what is seen in other patient populations, noting that MM patients are often elderly with comorbidities such as hypertension and diabetes that can complicate cardiovascular health. They advise patients to be aware of signs and symptoms of cardiovascular changes and to alert the medical team if they notice anything unusual.

While cardio-toxicity does not particularly pose a challenge in patients receiving VELCADE®, members mentioned that in addition to neuropathy, gastrointestinal disturbances such as diarrhea and constipation, do present as challenges to some VELCADE®-treated patients; particularly those who are elderly.

Members expressed concern that not all patients are initiated on prophylactic acyclovir and emphasized the need for this therapy in all VELCADE® patients to reduce the incidence of herpes zoster infection. They also noted the importance of advising patients not to take herbal supplements because of the uncertainty associated with how these products will interact with VELCADE®.

Members then shared strategies that they have employed to maintain patients on VELCADE®, including adverse event management and travel assistance. These strategies are outlined in Figure 2.

Figure 2.

Strategies Employed to Maintain Patients on VELCADE®
Side Effect Prevention and Management
Fatigue: Offer VELCADE® dose reductions
Neuropathy: Closely watch for development of neuropathy and chronicle progression; offer VELCADE® dose reduction and interruption; manage pain, as needed; consider Cymbalta® keeping side effects of this therapy in mind
Treatment Fatigue
Offer patients a brief break from therapy, if their disease is under control, or change their dosing schedule such that maintenance dosing is reduced to every other week
Encourage regular exercise to maintain strength and endurance. Consider physical therapy consultation to outline a program specific to the patient's health and underlying disease. Communicate to patients that as nurses you are with them, a part of their team, and will work together with them to keep them on therapy
Transportation Challenges
Utilize VELCADE® transportation assistance or assistance from the American Cancer Society
Time Constraints During Office Visits; or for Patients With Long Commutes
Consider performing labs only once per cycle (instead of every visit) for patients on long-term therapy with stable counts
For patients who travel to academic centers for treatment, collaborate with the providers in their local community to offer weekly maintenance with follow up at the academic center once per cycle

Closing Statements

Overall, members felt that the selected abstracts from ASH 2013 offered valuable insight, and thought that it would be beneficial for more practitioners to be made aware of these data. They encouraged nurses to identify any barriers that patients may have to remaining on therapy (eg, adverse events, transportation challenges) and work with patients closely to ensure that those barriers are eliminated. They emphasized the need for additional data regarding MM maintenance strategies, and called for education that assists patients with not only understanding their disease, but also understanding the meaning of their laboratory results and how to determine response.

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