

Bones of Contention in Multiple Myeloma

By Joseph Mikhael MD, MEd,
FRCPC, and Menaka Pai, MD

The Scientific Committee Session on Hematopoietic Growth Factors — Growth Factor Networks in Myeloma Bone Disease — will explore the rock-hard connection between myeloma and bony disease. Attendees will learn that bone disease is not just an unfortunate sequela of abnormal plasma cell production, but an integral part of its pathophysiology. Indeed, why do some patients with multiple myeloma (MM) have debilitating bony disease, while others have none? Understanding the mechanisms of bone disease in myeloma may indeed unlock some of the keys critical to battling this disease.

Dr. Kenneth Anderson from the Dana-Farber Cancer Institute will describe advances in our understanding of the bone marrow microenvironment. The field of oncogenomics, coupled with models of the myeloma cell in its environment, has revolutionized the way we think of myeloma because it has facilitated identification of multiple novel targets. This has resulted in a series of directed therapeutic strategies that have had a profound impact on survival in patients with myeloma.

Dr. Roodman will focus on treatments directed not so much at the plasma cell itself, but its environment. The most critical cell in this arena is the osteoclast, the cell responsible for bone resorption. The osteoclast activity is attributed to painful, bony lesions, and it now appears that plasma cells feed off the byproducts of osteoclastic activity. The vicious cycle continues as stromal cells in the marrow release substances such as RANKL, MCP-1, and IL6 that promote osteoclast formation and myeloma cell survival. Some progress was made with the use of bisphosphonates and their ability to affect osteoclast activity; the future, however, may lie with newer, more selective agents that will be discussed. It also appears that many of the novel agents used in myeloma also interfere with osteoclast activity along with their more anti-myeloma direct effects — further evidence of the connection between the myeloma cell and its surroundings.

Dr. Mundy will describe the specific role of bortezomib in the myeloma bone microenvironment. As a first in class proteasome inhibitor, bortezomib has had a remarkable response rate in patients with myeloma — especially in those with advanced disease, and in those with extensive bony involvement. This is in part due to its apoptotic effect on plasma cells, but may also be a function of its interaction with the bone. In particular, it promotes new bone formation, reversing the effects of osteoclasts. Furthermore, it may even be able to directly inhibit osteoclasts. To find out more of how it may do so, you will have to drag your bones to the session — you have two chances to make this session today, as it will be presented twice, at 7:30 a.m. and 2:00 p.m.