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Invited Plenary Abstract
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Cancer + Bone - new frontier in drug discovery in oncology

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Inhibitors of bone resorption have changed the way in which we think about cancer bone disease, clarified our understanding of the interactions that occur between cancer cells and osteoclasts in the bone microenvironment, and become major drugs in the field of oncology, with sales in the range of $3 billion dollars US and increasing. Bisphosphonates are the drugs most commonly used, and are likely to dominate this field for the next few years until approval is obtained for other agents that specifically interfere with RANK ligand effects on osteoclasts. However, with the widespread use of resorption inhibitors, new issues arise. The most prominent at this time is the issue of osteonecrosis of the jaw (ONJ), which appears to be predominantly bisphosphonate associated and was unknown as a complication 5 years ago, despite widespread use of these drugs in patients with cancer for almost 30 years. Our field's approach to the ONJ issue has been slow, and as a result there is danger that overreaction to its possibility as a side effect may lead to patients not being treated with these agents when they need them as life saving therapeutics. An interesting question unanswerable at present is whether ONJ is a specific association of bisphosphonates, or whether it is a complication of osteoclast inhibition by any means. Resorption inhibition invariably reduces tumor burden in bone, independent of the mechanism. This has important implications for the management of patients with advanced cancer, and emphasizes the importance of this form of therapy directed at the host in patients with widespread metastatic disease. The reduction in tumor burden is due to impaired release from remodeling bone of factors that promote tumor growth and aggressive behavior, such as TGFb. These issues and others relevant to cancers that metastatize to bone will be reviewed during this presentation.