Bone Lesions in Hormone Refractory Prostate Cancer (HRPC)

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Despite the long-term efficacy of androgen deprivation (AD) therapy in patients with advanced prostate cancer, most patients eventually develop resistance to this therapy and develop hormone-refractory prostate cancer (HRPC). Recently, randomised studies have demonstrated that patients with HRPC may experience delays in disease progression and derive survival benefits from either secondary hormonal approaches or chemotherapy with taxanes. As a result, clinicians now face a dilemma regarding the timing and selection of secondary approaches.

For many patients who experience disease progression after androgen-deprivation therapy, however, chemotherapy may not be immediately indicated. Such cases include those individuals with hormone-refractory disease in the absence of clinical metastases, and those with asymptomatic metastatic disease, for example. As a result, clinicians treating patients with hormone-refractory disease must weigh the benefits of earlier chemotherapy against its risks, and may consider other therapies such as secondary hormonal approaches before initiating chemotherapy. Furthermore, the limitations of chemotherapy for prostate cancer are being clarified and include a lack of standard second-line therapy as well as uncertain benefits for those with non metastatic disease.

The bone provides a fertile soil to the prostate seed, resulting in the osteoblastic metastases that are pathognomonic for the disease.

The propensity of prostate cancer cells to metastasise to bone is leading to the design of novel therapies targeting both the cancer cell as well as the bone microenvironment. Tumor cells in the bone interact with the extracellular matrix, stromal cells, osteoblasts, osteoclasts, and endothelial cells to promote tumor-cell survival and proliferation leading to a lethal phenotype that includes increased morbidity and mortality for patients with advanced prostate cancer. Several strategies are being developed that target these complex tumor cell–microenvironment interactions and target the signal transduction pathways of other cells important to the development of metastases, including the osteoclasts, osteoblasts, and endothelial cells of the bone microenvironment. Current and new therapies in metastatic prostate cancer will comprise a multitargeted approach aimed at both the tumor cell and the tumor microenvironment.