

Prostate Cancer Patients Maintain Bone Health with On-And-Off Therapy

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The growth of prostate cancer is largely dependent on male sex hormones called androgens, particularly testosterone. Many treatments for prostate cancer are aimed at dramatically reducing testosterone levels, thus slowing the growth of prostate cancer. However long-term androgen-deprivation therapy (ADT) is associated with a number of side effects, including skeletal, cardiac and diabetic complications, hyperlipidemia, sexual dysfunction and hot flashes. The increased rate of bone loss, and associated increased risk of fractures, has been a long-standing clinical concern for long-term quality of life. Furthermore, the rate of bone loss and risk of developing fractures increases with the duration of ADT treatment. There has been recent interest in using bisphosphonates and other factors to decrease the risk of osteoporosis and bone fractures in patients undergoing ADT, but many of these treatments remain under study.

Because of these side effects, as well as issues with the cost and efficacy of long-term ADT use, recent studies have compared the outcomes and side effects of intermittent androgen deprivation (IAD) to ADT. While the effect of IAD on long-term survival has been mixed, based on the patient population and disease stage examined, IAD has shown clear improvements in the quality of life among patients during treatment. Most notably, patients experience fewer sexual side effects and have improved quality-of-life during the off-treatment periods. To address the long-term effect of IAD treatment on skeletal health, Drs. Evan Yu and Tia Higano and colleagues in the Clinical Research Division, University of Washington and Seattle Cancer Care Alliance have examined the dynamics of bone mineral density (BMD) in men with non-metastatic, hormone-sensitive prostate cancer throughout a series of IAD treatment cycles. Fifty-six patients met the eligibility criteria for this study, including the presence of either locally advanced or biochemically recurrent prostate cancer following radical prostatectomy or radiation. Patients with biochemically recurrent prostate cancer were identified as those having at least two consecutive increases in the prostate-specific antigen (PSA) blood biomarker. Furthermore, men could not have detectable metastases.

To assess the long-term effects of IAD on bone health, the authors measured BMD at the spine and left hip using dual-energy X-ray absorptiometry at baseline prior to treatment, at the completion of nine months of ADT, and following a period off treatment. Patients also received CT scans and lumbar spine X-rays to detect bone fractures. Patients were maintained off ADT treatment as long as

they maintained low serum PSA (1-4 ng/mL based on disease history). Patients whose PSA levels increased, a possible sign of greater disease burden, were treated using additional rounds of ADT until the development of resistance to androgen depletion (median: 5.5 years, range: 1.1 to 13.8+ years). The majority of patients (56-80%) experienced BMD losses during the first ADT treatment round, however they also experienced significant recovery during the off-treatment period. Further rounds of ADT had less of an effect on BMD, with an eventual stabilization of bone density over time to a level just below baseline. However, these results were heterogeneous between patients, possibly due to differences in recovery time for hormone and bone levels between patients. Despite this, patients did not experience any fractures, with the exception of a compression fracture reported by one patient after a fall from a ladder. By comparison, of a cohort of similar patients who received continuous anti-androgen treatment, 3.9% of patients experienced fractures following three years of ADT.

This study demonstrates that prostate cancer patients with locally advanced or biochemically recurrent non-metastatic disease who receive IAD have generally stable bone health and are not at increased risk for bone fractures. Together with previous studies showing that men with non-metastatic, hormone-sensitive prostate cancer who are on IAD do not experience any significant increase in development of therapy resistance, this study suggests that IAD may be a clinically relevant treatment option for a defined subset of prostate cancer patients. A larger phase III trial of IAD versus continuous ADT would be beneficial to define bone health and fracture risk in individual patients during IAD, as well as verify that IAD has similar long-term effects on survival as ADT within men with locally advanced and nonmetastatic, hormone-sensitive prostate cancer.

[Yu EY, Kuo KF, Gulati R, Chen S, Gambol TE, Hall SP, Jiang PY, Pitzel P, Higano CS](#). 2012. Long-term dynamics of bone mineral density during intermittent androgen deprivation for men with nonmetastatic, hormone-sensitive prostate cancer. *J. Clinical Oncology* 30(15):1864-70.

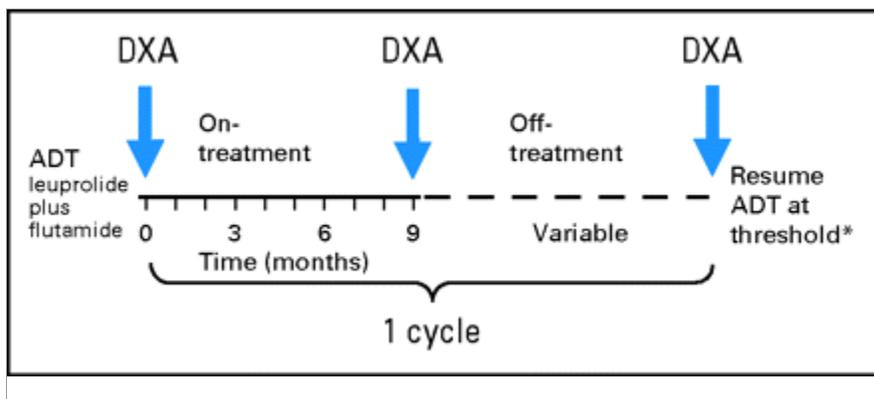


Image courtesy of the authors

Diagram of one full cycle of intermittent androgen deprivation followed by an off-treatment recovery period. DXA bone scans, as well as CT and X-rays, were completed throughout the study to monitor bone health and development of fractures.