

“FLARE” – AN ANDROGEN DEPRIVATION THERAPY (ADT) SIDE EFFECT

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I have concluded that many physicians are unaware of the importance of preventing the effects that can occur with "flare." And other physicians remark that in their personal experience, none of their patients experienced the problem. Others elect to administer an antiandrogen at the same time as the LHRH injection. However, it makes sense that none of us wants to be among those patients who may experience the effects that can occur from "flare."

Below is the recommendation with reasonable explanation why it is important to prevent “flare” provided by Stephen B. Strum, M.D., FACP, Medical Oncologist Specializing in Prostate Cancer since 1983 and co-author with Donna Pogliano of what many of us consider our prostate cancer "bible," "A Primer on Prostate Cancer - The Empowered Patient's Guide." Please note that with the suggestion to be prescribed an antiandrogen to begin at least six days prior to a first injection of an LHRH agonist, that also means if returning to an LHRH agonist after an "off-phase".

“Frankly, I can't imagine the administration of an LHRH agonist like Zoladex without first pre-treating the patient with an anti-androgen to prevent flare. The LHRH product stimulates the release of LH which in turn stimulates the testicles to make testosterone. This stimulates PC growth as well as normal prostate cell growth. Such stimulation lasts for up to 2 weeks. WHAT SITUATION EXISTS IN MEDICINE WHERE WE STIMULATE CANCER GROWTH AND YET ACT SO NONCHALANTLY ABOUT DOING SO? This is utter nonsense and no man should receive an LHRH agonist without preventing flare, be it biochemical flare or clinical flare. Read about Flare in "A Primer on Prostate Cancer, The Empowered Patient's Guide" by Strum & Pogliano or in a past PCRI (Prostate Cancer Research Institute) issue of INSIGHTS (go to www.pcri.org and search under Insights).

Here are some additional thoughts about FLARE. The Importance of Preventing Flare: The anti-androgen should be administered at least 7 days prior to the LHRH agonist. This is done to prevent or diminish the effects of initiating the LHRH agonist which routinely results in release of LH, stimulation of gonadal testosterone and increased growth of PC with release of PSA. The cell populations that are stimulated involve both benign and malignant prostate cells. In patients with bulky disease that is compromising spinal cord, ureters, or seriously involving bone, this paradoxical stimulation at the start of LHRH therapy can result in medical emergencies such as spinal cord compression, ureteral blockade or severe increase in bone pain. Even in patients without bulky disease, we have detected increases in LH, Testosterone and PSA despite using 7 days of an anti-androgen. However, even though the PSA does increase, this effect is markedly dampened by the priming doses of anti-androgen which results in a fall in PSA within 24 hours. Therefore, the anti-androgen prevents testosterone released during the initial surge from the LHRH agonist from doing major damage. We call this biological flare as contrasted with clinical flare. Biological flare is characterized by an increase in LH, testosterone and PSA whereas clinical flare is associated with the same plus clinical symptoms of an increasing tumor mass.

Since there are studies showing that PSA in itself leads to tumor growth by cleaving Insulin Growth Factor 1(IGF-1) from Binding Protein 3 resulting in free IGF-1, a potent stimulator of tumor cell growth, we feel that any maneuver that will decrease PSA may be of benefit to the patient. PSA will also cleave the pro-molecule of urokinase plasminogen activator (uPA) to the high molecular weight uPA or HMW-uPA. uPA is made by the PC cell and also stimulates its own growth (autocrine effect). uPA dissolves bone matrix by its activating collagenase I and releases IGF-1 by cleaving IGF binding proteins 1 & 2. uPA also stimulates the osteoblast to grow and release other active growth factors. Anything that we can do to stop these autocrine and paracrine cycles may help the man with PC. Preventing tumor flare is therefore a good first step.”