

DES/Diethylstilbestrol

Compiled by Charles (Chuck) Maack – Prostate Cancer Activist/Mentor

DISCLAIMER: Please recognize that I am not a Medical Doctor. I have been an avid student researching and studying prostate cancer as a survivor and continuing patient since 1992. I have dedicated my retirement years to continued research and study in order to serve as an advocate for prostate cancer awareness, and, from a activist patient's viewpoint, to voluntarily help patients, caregivers, and others interested develop an understanding of prostate cancer, its treatment options, and the treatment of the side effects that often accompany treatment. There is absolutely no charge for my mentoring – I provide this free service as one who has been there and hoping to make your journey one with better understanding and knowledge than was available to me when I was diagnosed so many years ago. Readers of this paper must understand that the comments or recommendations I make are not intended to be the procedure to blindly follow; rather, they are to be reviewed as my opinion, then used for further personal research, study, and subsequent discussion with the medical professional/physician providing your prostate cancer care.

The subject of Diethylstilbestrol (DES) comes up every so often. It certainly is an inexpensive form of treatment. But with any medication the patient should be aware of effects that might (not necessarily will) occur. Regarding the use of Diethylstilbestrol (DES) - Per Medical Oncologist. Stephen Strum: "It is important to be aware that with oral DES you do need anticoagulation - not with aspirin but with either Coumadin or low molecular weight heparin (I've been told that when prescribing DES, some physicians include aspirin in company with either of these anticoagulants). You also need to address the issue of gynecomastia with either RT to the breast tissues or the use of Tamoxifen at 10mg per day or possibly double that dose. You would certainly need to be under the direction and observation of your physician with this medication." And a physician posting to the ProstateProblemsMailList (PPML), Luis Garcia-Bunuel, commented "Coumadin, cautiously dosed (possibly also at only 1mg, since there have been reports that even 2 to 3mg dosages have had thrombotic effects), will make blood less coagulable, helping to prevent blood clots. Too much coumadin will cause unstoppable bleeding and death." So, friends, if interested in DES as your ADT treatment, be sure you find a Medical Oncologist who is knowledgeable in its use and will provide close monitoring. Better safe than sorry.

Please be sure to determine the cost of the accompanying anticoagulant to DES, either Coumadin, its generic warfarin, or low molecular weight heparin, and whether your health insurer covers the major cost of either of these anticoagulants

The use of transdermal estradiol (TDE) patches or gel also requires the close attention of a physician knowledgeable in this treatment option since TDE requires close monitoring and titrating for most effective dosage. An interesting article can be viewed here: <http://tinyurl.com/cmagaau>

A bit more explanation regarding diethylstilbestrol here: <http://tinyurl.com/mtvw16j>

Diethylstilbestrol/DES is a reasonable form of treatment, though many physicians continue to avoid prescribing because of the history of deep vein thrombosis/DVT that has accompanied DES. May I suggest that if prescribed and noticing any areas of swelling, tenderness or discoloration on the skin, that the treating physician should be notified immediately – as well as have him examine for the same at each appointment. The reasoning is that these are signs of possible blood clotting and the sooner this is determined or ruled out, the better. If any such signs do appear, you may be experiencing blood clotting. Take a read of this paper to be “up on” understanding should this occur:

<http://www.mayoclinic.com/health/deep-vein-thrombosis/DS01005/DSECTION=tests-and-diagnosis>

or try <http://tinyurl.com/m66w6x4>

Estrogens have significant effects on the prostate cancer cell. Estradiol has been shown to localize irreversibly to the nuclear membrane of the tumor cell within 2 hours of exposure. DES, a nonsteroidal estrogen, has been shown to inhibit RNA polymerase activity in prostatic tissue and inhibit DNA synthesis in both benign and malignant prostate tissue. All estrogens also exert a competitive inhibitory effect on androgen-dependent cancers by suppressing LH secretion at the level of the pituitary-testicular axis.

Until the advent of LHRH agonists, estrogens and DES were extensively used in the treatment of advanced prostate cancer. In the initial Veterans Administration Cooperative Urologic Research Group (VACURG) studies, DES was found to be as effective as orchiectomy for prostate cancer, but at a dose of 5 mg/day, carried a

significant risk of cardiovascular morbidity. More recently, single and cooperative group studies have evaluated the effectiveness of DES at dosages of 3 and 1 mg per day. Both dosages were found to be as effective as the 5 mg/day dosage with considerably fewer cardiovascular toxicities. Although serum testosterone levels were not consistently suppressed to castrate levels using the 1 mg/day dose, this dosage showed an equivalent anticancer effect compared to the 5mg/day dosage. It should be noted that the regression of metastatic disease can occur without maximal suppression of serum testosterone levels.

In a past study, Jazieh et al, reported results using oral DES treatment in 14 patients with progressive AIPC. DES was given at a dose of 1 mg 3 times a day along with routine anticoagulation with warfarin (Coumadin®). In this study, 9 (64%) patients responded with a greater than 75% decline in baseline PSA. PSA levels normalized in 5 (36%) patients, however, 2 of these patients may have had an antiandrogen withdrawal response. In patients with symptomatic disease, 50% showed improvement with DES treatment. The median duration of response was 8 months (range 2-24 months) and the median time to reach a PSA nadir was 3 months (range 1-10 months). There were no cardiovascular or thrombotic (blood clotting) events reported.

In another study, Smith, et al reported results of a phase II study of DES at a dose of 1 mg/day in 21 patients failing ADT. All patients were withdrawn from antiandrogen therapy and started DES at PSA progression. LHRH agonist therapy was stopped simultaneously. In this study, response, defined as a > 50% decline from baseline PSA, was seen in 9 (43%) patients. In 13 patients who failed only one hormonal therapy, responses were seen in 8 (62%) patients. In the 13 patients who failed more than one prior hormone treatment, a response was seen in only 1 (13%) of 8 patients. Duration of response was not reported. Sixteen patients remained alive after a median follow-up of 82 weeks with a 2 year survival rate of 63%. Therapy was generally tolerated well. Nineteen (90%) patients complained of nipple tenderness, but none discontinued therapy because of this side effect. Three (14%) patients developed gynecomastia (breast enlargement) and one (5%) patient developed deep venous thrombosis.

Important is finding a Medical Oncologist who is experienced in the prescribing of Diethylstilbestrol/DES.