

Managing Hormone Sensitive, Non-Metastatic Relapse and Castrate-Resistant Metastatic Prostate Cancer

II. Advanced Prostate Cancer

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Exciting new drugs are in clinical trials which block metabolism of adrenal androgens into testicular androgens or block the effect of testicular androgens.

The 2010 NCCN guidelines were updated to simplify chemotherapy. Taxotere is used, and now Provenge is added as an option for men who are symptomatic or minimally symptomatic with good performance status.

Prostate cancer is believed to return when the androgen receptor which drives the growth of prostate cancer becomes hypersensitive to the circulating androgens that are very low in a castrated man. Prostate cancer not only allows this hypersensitivity, it makes its own testicular androgens from circulating weak adrenal androgens, and if these are blocked, prostate cancer may make testicular androgens maybe even from cholesterol.

There is no such thing as androgen independent prostate cancer; prostate cancer, with or without testicles, is still being driven by the male hormones, testosterone and DHT. Prostate cancer is most likely turning these weak androgens produced by the adrenal gland into DHT. When Lupron is used, adrenal androgens are turned into DHT; with abiraterone, DHT can be made from cholesterol.

Another alternative is to destroy the androgen receptor directly. Dominant negatives is an approach used to cause tumor volume to grow slower. Blood vessels which supply the prostate are unique in the body; they, too, make an androgen receptor protein unlike, for example, kidney. These blood vessels represent a potential target; by removing testosterone, these vessels die and expose antigens, thus activating the clotting system.

Thus, new agents which be appearing in the marketplace in the next year include abiraterone and MDV3100, along with new strategies in the next three to four years which target the ability of prostate cancer to make its own hormones, strategies which directly target the androgen receptor.