

treatment is with another drug, sunitinib. Sunitinib has been approved for use in cancer, after failure of imatinib due to the tumor's resistance to imatinib (100). Hence, where a clinical study is to be conducted with imatinib, it is reasonable that the Clinical Study Protocol mandate that the subjects be treatment-naïve with regard to imatinib, to ensure that the tumors in the subjects have not already developed drug-induced resistance to imatinib.

d. Prior treatment with hormones as a basis for exclusion

Prostate-specific antigen (PSA) is a biomarker used in clinical trials (101) for prostate cancer, and it is used in routine screening of the general public for prostate cancer. Where men are treated with testosterone (for any reason), the result can be an increased expression of prostate-specific antigen (PSA) (102). Collette et al. (103) point out that expression of PSA is controlled, at the genetic level, where control is mediated by an androgen-responsive element. Alterations of serum androgen levels can provoke changes in PSA expression, where these changes are totally independent of burden of prostate tumors.

An increase in PSA that occurs by this mechanism does not indicate any increase in risk for prostate cancer.

Moreover, men diagnosed with metastatic prostate cancer are treated with leuprolide or goserelin, which reduce in testosterone expression (104). Leuprolide is an oligopeptide that is a hormone analogue (105). A consequence of this reduced expression of testosterone is a reduced expression of PSA. Because of the fact that hormones (and hormone analogues) can alter the expression of PSA, clinical trials for prostate cancer may exclude men who had been receiving hormones, or may stratify men into those who had been receiving hormones, and those who had not been receiving hormones (106). Another reason for excluding or stratifying men who had reduced testosterone levels is that reduced testosterone can impair the general quality of life of the men (thereby causing the study subjects to have two disorders, the prostate cancer and the testosterone-induced reduction in quality of life) (107).

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