

Advanced Stage Disease

Protocols for Advanced Prostate Cancer and/or Local Failure After Radical Prostatectomy

Isaac Powell, MD

I. Case Presentation

This is a case scenario of a patient with local spread outside of the prostate gland with or without positive surgical margins after radical prostatectomy and/or detectable PSA or a rising PSA after surgery. Advanced disease, T3/T4, where the cancer is outside the capsule, invading the seminal vesical, or invading the bladder floor, is what we're going to address in this particular discussion. We look at PSA doubling time to evaluate prostate-specific survival, and it is very clear that the shorter the PSA doubling time, the worse the survival. Looking at it a different way, the shorter the PSA doubling time the greater the mortality from prostate cancer disease.

II. Randomized Study

We will look at a randomized, open label, multicenter, phase III, two-arm study of androgen deprivation with leuprolide, plus or minus docetaxel, a chemotherapeutic component for clinically asymptomatic prostate cancer subjects with a rising PSA following definitive local therapy, specifically prostatectomy.

Subjects had a rising PSA following radical prostatectomy, a PSA doubling time of less than or equal to nine months, a minimum PSA of one, and a testosterone of greater than or equal to 100 ng/ml. Arm A was docetaxel, which is the chemotherapeutic component, GnRH agonist, which is Lupron, and bicalutamide is Casodex. Arm B was the hormonal therapy only arm. The hypothesis of the study was that progression-free survival probability would increase from 55% to 65% at a minimum of 36 months.

Subjects in the group may have no radiographic findings that are clinically suspicious for metastatic disease, and salvage radiotherapy is allowable and encouraged where appropriate. The primary objective is progression-free survival within a period of 18 months of therapy and at least 18 months following therapy. Progression free survival is determined to be the time from a randomization to the first documentation of detectable PSA, radiographic progression or death. The secondary objective is to evaluate cancer-specific survival, to compare overall survival between the two treatment groups and molecular findings that may correlate with clinical outcomes.

III. Radiotherapy Protocol After Surgery (Closed)

The radiotherapy protocol after surgery study has been closed, but it is very important to discuss. It was an adjuvant radiotherapy protocol for T3 prostate cancer, and it has significantly reduced the risk of metastasis and improved survival. This study has been reported in the literature.

There were a total of 431 men with T3 prostate cancer who were randomized to radiation therapy or observation, and the primary study endpoint was metastasis free survival.

The conclusion was that adjuvant radiotherapy after radical prostatectomy for a man with T3 prostate cancer significantly reduces the risk of metastasis and increases survival.

IV. Lymph Node Metastasis

A study of hormonal therapy versus observation after surgery for node-positive prostate cancer has also closed and was reported several years ago but is important to know. In the immediate therapeutic group you, will see death from prostate cancer significantly less than the observational group, and it was statistically significant. Men who underwent therapy immediately clearly had a significantly better outcome than those who were observed and treated after the PSA began to rise. The P value was highly significant.

The conclusion was that locally advanced prostate cancer plus early aggressive combination therapy equal long-term survival and possibly “cure.”