OPTIMAL TIMING OF CHEMOTHERAPY IN MEN WITH HORMONE REFRACTORY PROSTATE CANCER

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LAY ABSTRACT

STUDY PURPOSE

Prostate cancer is the most common cancer in men, with more than 200,000 new cases of prostate cancer diagnosed every year (American Cancer Society 2005). For those diagnosed with localized disease, the five year relative survival rate is 100%. However, for men with metastatic disease the prognosis is more dismal. While most patients with metastatic prostate cancer initially respond to hormone therapy, the response is temporary, lasting only for a median of 18 to 24 months. Until recently, there was no role for chemotherapy for these patients given the lack of proven benefit and the known toxicities. Mitoxantrone plus corticosteroids were approved for palliative use after three different studies showed symptomatic improvement with these regimens[1-3]. There was, however, no increase in survival. In 2004, the TAX 327 and SWOG 99-16 studies changed the role of chemotherapy for patients with hormone refractory prostate cancer by demonstrating for the first time a survival benefit with docetaxel based chemotherapy regimens [4,5]. Finally there are therapies to offer patients with hormone refractory prostate cancer; however; it still remains an incurable disease. Questions still remain about the appropriate time to use this new intervention. TAX 327 and SWOG 99-16 treated both symptomatic and asymptomatic patients with hormone refractory prostate cancer. This study will compare the use of docetaxel and prednisone at the time of initial PSA relapse with delayed chemotherapy until there is clinical evidence of disease progression. The primary endpoint will be survival; secondary endpoint is quality of life.

STUDY SUBJECTS AND METHOD OF RECRUITMENT

Men with metastatic prostate cancer, either at diagnosis or after progression from localized disease will be recruited through advertisements and by referral from their primary care doctor, urologist, or oncologist.

STUDY PROCEDURE

This is a single center, randomized study. Patients will be treated with docetaxel infusion every three weeks with daily oral prednisone either at the time of PSA relapse or delayed until the time of clinically evident disease. Follow up examinations will be performed every three months.

ISSUES

None

A. Study Design and Statistical Analysis

(Calculations for 80% power, p=0.05)
Unpaired t-test
n(number in each group) $= 1+16\ (\text{standard deviation}/\text{effect})^2$

= 1+16 (7.5/2.4)2
= 157.25

B. Study Procedure

This is a single center, randomized study. Patients will be treated with docetaxel infusion every three weeks with daily oral prednisone either at the time of PSA relapse or delayed until the time of clinically evident disease. Follow up examinations will be performed every three months.

Dose Modifications

In the case of toxicity, the appropriate symptomatic treatment will be administered. For Grade 3 and Grade 4 toxicities, treatment will be withheld until the toxicity resolves to Grade 1 or less, and will then be restarted. If treatment is withheld for longer than 3 weeks the patient will be withdrawn from the study. In the case of hypersensitivity reactions docetaxel will be discontinued permanently without rechallenge.

Duration of Therapy, Monitoring and Response Assessment

Patients will be treated with up to ten cycles (as permitted by toxicities). They will be followed every three months until death to assess duration of response, adverse events, and survival. PSA will be measured every 4 weeks, while CXR, CT Scan or MRI of measurable lesions will be performed every 8 weeks (bone scan every 12 weeks).

C. Medical Device

Chemotherapeutic agents will be obtained from the pharmaceutical company.

D. Study Questionnaires

FACT-P quality of Life questionnaire
www.regenstrief.org/loinc/meetings/20030620/20030620/20030620_Handout5.pdf

E. Study Subjects

Eligibility Criteria

In order to be eligible, patients had to have histologically confirmed adenocarcinoma of the prostate, and have relapse after treatment with hormonal therapy. Patients will be excluded if they have prior history of systemic chemotherapy, any prior malignancy (except adequately treated basal cell or squamous cell skin cancer, adequately treated stage I or II cancer from which they were currently in remission and has been disease free for at least five years).

No investigational drugs will be allowed within 4 weeks of study entry. Patients were required to be recovered from all surgeries and infections, and, in the opinion of the investigator, not have any significant active disease process that would interfere with protocol treatment or survival. All patients will sign a written informed consent. A total of 400 patients will be recruited.

Baseline Radiologic and Laboratory Assessments
All patients will have a CT scan of the abdomen and pelvis within 28 days of study entry and a bone scan within 42 days of study entry. Baseline laboratory tests will include PSA, CBC with differential, basic metabolic panel, and liver function tests.
Patients will need a WBC ≥3500/μl or ANC ≥ 1500/μl, bilirubin ≤ the upper limit of normal, creatinine ≤ 2.0mg/dl, platelets ≥ 100,000/μl, ALT/AST < 2.5x upper limit of normal to be eligible for enrollment.

F. Recruitment of Subjects
Men with diagnosed metastatic prostate cancer who have undergone hormone therapy (either medical or surgical) and have PSA relapse will be eligible for recruitment.

G. Potential Conflict of Interest
None

H. Location of Study
Patients will receive chemotherapy in an outpatient infusion center.

I. Potential Benefits
Potential benefits include prolonged survival, prolonged remission from disease, and improved quality of life.

J. Alternative Therapies
Alternative therapies include the current standard of care which is medical or surgical castration followed by chemotherapy when disease ceases to respond to hormonal therapy.

K. Compensation to Subjects
Patients will receive financial compensation for their participation in this study.

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