The Oncology Center of Central Baltimore

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Introduction

Prostate cancer is the most second common cancer in males in the United States. The wider use and acceptance of screening has resulted in the earlier diagnosis of prostate cancer. New techniques of radiation have increased the types of treatment options available. Newer chemotherapy treatments have resulted in better palliation of symptomatic metastatic disease.

Our current newsletter will review the standards of screening for prostate cancer as well as some of the newer therapies for treatment. In clinical trials section, we have published a list of the currently available clinical trials at Union Memorial Hospital. We have also added a section listing current websites for information regarding treatment of prostate cancer.

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The Role of Chemotherapy in the Treatment of Prostate Cancer

The initial treatment of metastatic prostate cancer continues to be suppression of testicular androgen production. When patients with metastatic prostate cancer fail androgen ablation, chemotherapy becomes an option for treatment.

The initial experience with chemotherapy in the treatment of hormonal resistant prostate cancer had been disappointing. Response rates ranged from 10-20%.

An important trial in the treatment of hormonal resistant prostate cancer was a Canadian study published in 1996 comparing Mitoxantrone plus prednisone against prednisone alone. The study showed a modest improvement in survival, but more importantly it showed a significant improvement in the palliation of symptoms (pain) when chemotherapy was used compared to steroids alone. This was also confirmed by another randomized study by Calgb published in 1999.

Most recently, another class of drugs called taxanes, which target the micro tubular network, have been shown to be effective in the treatment of hormonal resistant prostate cancer. The taxanes include the drugs Taxol and Taxotere. These drugs have been used alone or in combination with another drug called Estramustine. They have produced response rates in the range of 40-60%.

We have been using the taxanes in the treatment of metastatic prostate cancer at Union Memorial Hospital for the past three years. The drugs are given as an outpatient weekly, over one hour. Many of our patients have experienced little to no side effects from the taxanes given in this manner. We have observed significant drops in the PSA levels as well as improvement in pain control. We have seen duration of responses ranging from six months to two years.

Although the ultimate value of these drugs in the treatment of prostate cancer remains to be completely defined, we are encouraged by the results and will continue to make available clinical trials for the use of chemotherapy in both early and late stage prostate cancer.

Websites Dealing with Prostate Cancer

WEBSITE	SIGN-ON	COMMENTS
NATIONAL CANCER INSTITUTE	cancernet.nci.nihgov	THE SINGLE BEST MAINTAINED RESOURCE FOR PHYSICIANS AND PATIENTS
PROSTATE CANCER INFOLINK	www.comed.com/prostate/	PATIENT FRIENDLY; EXCELLENT FIGURES
ASCO ONLINE	www.asco.org	PHYSICIAN ORIENTED, LATEST ABSTRACTS, LECTURES FROM WORLDWIDE CANCER RESEARCHERS
US TOO	www.ustoo.com	PROSTATE PATIENT ORGANIZED INFORMATION
CAP CURE	www.capcure.org/	FOUNDED BY MICHAEL MILKEN, THE LARGEST PRIVATE ORGANIZATION SPONSORING PROSTATE CANCER RESEARCH
PROSTATE CANCER HOMEPAGE UNIVERSITY OF MICHIGAN	www.cancered.mich.edu/prostcan/prostcan.html	ONE INSTITUTION'S VIEW ON TREATMENT OPTION, BUT WELL DONE

Journal Watch

In each issue of our newsletter we will highlight those oncology articles that appeared in the five major internal medicine journals over the preceding months. We hope that this will keep you abreast of changes that are occurring in the field.

1. Huntsman, David, et al, Early gastric cancer in young, asymptomatic carriers of germ-line e-caderin mutations, New England Journal of Medicine, June 21, 2001, Number 25 Volume 344 pages 1904-1909.
   Conclusions: Recommends genetic counseling and consideration of prophylactic gastrectomy in young, asymptomatic carriers of germ-lin truncating CDH1 mutations who belong to families with highly penetrant hereditary diffuse gastric cancer.

2. Shapiro, C.L. et al, Drug therapy: side effects of adjuvant treatment of breast cancer, New England Journal of Medicine, June 28, 2001, Number 26 Volume 344
   Conclusion: Excellent review of the side effects in the adjuvant treatment of breast cancer.

3. Meijers-Heijboer, Hanne, et al, Breast cancer after prophylactic bilateral mastectomy in women with a BRCA 1 or BRCA 2 mutation, New England Journal of Medicine, July 19, 2001, Number 3 Volume 345 pages 159-164.
   Conclusion: In women with a BRCA 1 or BRCA 2 mutation, prophylactic bilateral total mastectomy reduces the incidence of breast cancer at three years of follow-up.

4. Bach, Peter, et al, The influence of hospital volume on survival after resection for lung cancer, New England Journal of Medicine, July 19, 2001, Number 3 Volume 345 pages 181-188.
   Conclusion: Patients who undergo resection for lung cancer at hospitals that perform large numbers of such procedures are likely to survive longer than patients who have such surgery at hospitals with a low volume of lung resection procedures.

5. Modan, Baruch, et al, Parity, oral contraceptives, and the risk of ovarian cancer among carriers and noncarriers of a BRCA 1 or BRCA 2 mutation, New England Journal of Medicine, July 26, 2001, Number 4 Volume 345 pages 235-240.
   Conclusion: The risk of ovarian cancer among carriers of a BRCA 1 or BRCA 2 mutation decreases with each birth but not with increased duration of use of oral contraceptives. These data suggest that it is premature to use oral contraceptives for the chemoprevention of ovarian cancer in carriers of such mutations.

6. Kreitman, Robert, et al, Efficacy of the anti-CD22 recombinant immunotoxin BL22 in chemotherapy-resistant hairy-cell leukemia, New England Journal of Medicine, July 26, 2001, Number 4 Volume 345 pages 241-247.
   Conclusions: BL22 can induce complete remissions in patients with hairy-cell leukemia that is resistant to treatment with purine analogues.

Prostate Cancer Screening

Prostate cancer is one of the most common cancers diagnosed in the United States. Although incidence rates are declining, it is estimated that prostate cancer was diagnosed in 180,400 men during the year 2000. It is the second leading cause of cancer mortality in men. The incidence of prostate cancer rises rapidly in men after the age of 50. Since the introduction of Digital Rectal Exam (DRE) and PSA screening for the detection of prostate cancer, there has been an increase in the diagnosis of cancers that are still confined to the prostate. It appears logical to conclude that this would result in more cures and therefore reduced mortality from the disease.

This reasoning is, of course, simplistic and perhaps why screening for prostate cancer is fraught with controversy. Proponents of screening argue that the detection of cancers early results in curative options and a decrease in mortality. This may be borne out by the fact that even though the incidence of prostate cancer increased markedly in the 80's with the introduction of screening, there was not a concomitant increase in mortality. Then why is screening not routinely recommended by all groups? The primary reason for this is that the PSA test is prone to high rates of false positive results. Among older men with benign prostatic hypertrophy, the specificity of the PSA test with the traditional cut off value of 4 ng/ml may be as low as 54%. There is also the concern that PSA screening may detect indolent prostate cancers that may never become clinically significant during the person's lifetime. This would result in unnecessary morbidity from treatment of these cancers.

Patients who should be screened for prostate cancer:

1. Screening should only be done if the life expectancy is greater than 10 years.
2. Patients should be willing to undergo biopsies if the PSA is elevated and accept definitive therapy if a diagnosis of cancer is made.

Current recommendations for screening are:
(AUA, ACS Guidelines)

1. ***Average Risk Patients***

Annual DRE and PSA screening beginning at 50 years of age.

High Risk Patients

This category includes African-Americans and males with a strong family history of prostate cancer. For such patients, annual PSA and DRE are recommended beginning at age 45.

Future Developments:

Since the specificity of the PSA test is low, methods have been devised to try and improve its specificity. The PSA velocity is the rate of change in the PSA level. A value of more than 0.75 ng/ml per year is more suggestive of prostate cancer, but to obtain a reasonable estimate, these levels need to be measured three times at least a year apart.

PSA circulates both free and bound to macromolecules. The ratio has been used to stratify cancer risk. A low free PSA to total PSA ratio may be more suggestive of prostate cancer.

As physicians, it is our responsibility to make all men between the ages of 50-75 years aware of the availability of screening and to counsel them appropriately.

Screening Recommendations as per ACS and AUA

(American Cancer Society, American Urological Association)

Low Risk	High Risk
Yearly DRE, PSA starting at 50	Yearly DRE, PSA starting at 45

Prostate Brachytherapy Now Available at Union Memorial Hospital

Prostate brachytherapy or radioactive seed implants have increasingly become an accepted part of the treatment armamentarium to patients with prostate cancer. While the concept of implanting radioactive material into the prostate is a rather old one, dating back to the early 20th century, it has not been until recently that refinements in the procedure have made it clinically useful. This improvement has been the direct result of better dosimetry and has led to improved cure rates and much less toxicity. The use of ultrasound guidance and pre-planning of the implant as pioneered at the Seattle Prostate Institute are responsible for this superior outcome. Prostate Brachytherapy is used as both monotherapy and in conjunction with external beam radiotherapy and/or androgen suppression depending on clinical parameters.

Both the urologist and radiation oncologist share selection of patients for prostate brachytherapy. Patients who are ideal candidates for monotherapy must have organ-confined disease and preferably low PSA's and Gleason scores with moderate to low volume prostate glands. These patients are typically treated with radioactive Iodine-125 seeds designed to deliver 14,500 centiGray or rad over the life of the implant. The seeds' radioactivity decays in the prostate and are permanent once they are placed in the gland.

Patients with large glands, PSA's 10-20, and Gleason scores 7 and above, are usually treated with a combination of hormonal manipulation and external beam radiotherapy. In this setting androgen suppression begins 8 weeks prior to beginning external beam radiation therapy. Radiotherapy is limited to 5 weeks instead of the typical 8 weeks of treatment. These implants are performed with Palladium-103, which delivers the radiation dose somewhat more quickly. The dose of radiation is reduced in this setting to 10,000 centi-Gray or rad over the life of the implant.

Patients must be able to undergo anesthesia to have this procedure (either general or spinal). A treatment planning ultrasound is done several weeks before the implant is performed. This allows the radiation oncologist and physicist to plan where the sources need to be placed to deliver the dose of radiation desired and to avoid critical structures such as the bladder and rectum. Once the treatment plan is determined, the patient is taken to the OR and placed under anesthesia. The ultrasound probe is reinserted and the planning images are reproduced. The needles are then placed delivering the radioactive seeds. The entire procedure usually lasts about 2 hours. Patients are discharged to home after several hours in the recovery room. Side effects are usually minimal and most often involve voiding immediately after the procedure. Catherization for no more than 24 hours is rarely needed.

Results of Brachytherapy at 10 and 15 years are similar to surgical and external beam radiation therapy data using the Seattle method. Literature and more information can be obtained by contacting the Union Memorial Radiation Oncology Center at 410-554-4400.

Clinical trials

We continue to actively support a variety of clinical trials at Union Memorial Hospital. This chart highlights the Genitourinary protocols we are currently involved in.

A complete list of protocols is available to you by contacting the Oncology Center or downloading them from our website: www.oncologycenter.org.

Clinical Trials Program at Union Memorial Hospital for Prostate Cancer				
PROSTATE	s9921	ADJUVANT ANDROGEN DEPRIVATION VS CHEMOTHERAPY IN HIGH RISK PROSTATE CANCER PATIENTS FOLLOWING RADICAL PROSTECTOMY	ACTIVE	1
PROSTATE	s9916	DOCETAXEL, ESTRAMUSTINE VS MITOXANTRONE AND PREDNISONE FOR ADVANCED HORMONE REFRACTORY PROSTATE CANCER PHASE THREE	ACTIVE (NEW)	
PROSTATE	INTERNAL	THALIDOMIDE FOR ANDROGEN-INDEPENDENT PROSTATE CANCER AND RISING PSA ONLY	ACTIVE (NEW)	