Alpharadin (Radium-223 Chloride) Improves Overall Survival in Men with Metastatic CRPC

Early PSA Testing & Risk of Long-Term Death

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Doc Moyad’s “No Bogus Science” Column – “___ Dietary Supplement Fights/Kills Prostate Cancer? Should Doc Moyad Support It?”

**ALFARADIN (RADIUM-223 CHLORIDE) MEETS ITS PRIMARY ENDPOINT OF SIGNIFICANTLY IMPROVING OVERALL SURVIVAL IN A PHASE 3 TRIAL IN PATIENTS WITH CASTRATION-RESISTANT PROSTATE CANCER THAT HAS SPREAD TO THE BONE**

Results from the Phase 3 ALSYMPCA (ALPharadin in SYMptomatic Prostate CANcer) trial evaluating Bayer’s investigational compound, radium-223 chloride were announced, showing that the trial met its primary endpoint by significantly improving overall survival in patients with castration-resistant prostate cancer (CRPC) and bone metastases. Alpharadin is exclusively licensed from Algeta ASA.

Based on a recommendation from the Independent Data Monitoring Committee (IDMC) after a pre-planned interim analysis, the study will be stopped and patients on the placebo arm will be offered treatment with radium-223 chloride. Overall survival results were statistically significant – median overall survival was 14.0 months for radium-223 chloride and 11.2 months for placebo (2-sided P-value = 0.0022, HR = 0.699).

Complete study results will be presented at an upcoming scientific meeting.

Safety and tolerability of radium-223 chloride were consistent with previous (Continued on page 8)

**EARLIER PSA TESTING MAY PREDICT LONG-TERM DEATH RISK FROM PROSTATE CANCER**

A PSA test initially taken between age 44 and 50 years can predict the chance that a man will die from prostate cancer in the next 25 to 30 years, according to researchers at Memorial Sloan-Kettering Cancer Center, New York.

Findings presented at the 2011 American Society of Clinical Oncology (ASCO) Annual meeting, suggest that more than half of men could forego annual PSA testing and have just 3 PSA tests in their lifetime. Men between the ages of 44 and 50 years with higher PSA levels are at high risk for aggressive prostate cancer and should continue to receive PSA tests and screening as necessary, according to the study authors.

“This research helps us distinguish between those men who may benefit from regular PSA screening for prostate cancer and those men who may not need to be screened so frequently,” said lead author Hans Lilja, MD, PhD. “Instead of testing all men each year or every 2 years, screening and surveillance efforts can be focused on early detection of prostate cancer in those men who are found to be at high risk of death from the disease.”

The team analyzed archived blood samples from 12,090 men between 44-50 who provided blood between 1974 and 1986, and repeat samples from 4,999 of (Continued on page 8)

**SURGERY WORKS IN LOCALLY ADVANCED PROSTATE CANCER**

Men with locally advanced (cT3) prostate cancer had a 20-year diseasespecific survival of 81% following radical prostatectomy (RP), data from a large clinical series showed. The cohort had a progression-free survival (PFS) of 72% at 10 years and 61% at 20 years.

cT3 disease accounts for a small percentage of all prostate cancers. Though inferior to outcomes in patients with localized (cT2) cancer, findings suggest RP offers a reasonable therapeutic option having favorable long-term results for a group of patients with no clear standard of care, according to a presentation at the 2011 American Urological Association (AUA) meeting.

“Oneologic outcomes for men with clinical T3 disease remain favorable with long-term follow-up,” said Christopher Mitchell, MD, of the Mayo Clinic in Rochester, MN. “RP, as part of a multimodality treatment strategy for patients with cT3 disease, offers durable cancer control and survival rates at 20 years. The results compare favorably with current strategies combining external beam radiation therapy and hormones.” Despite a lack of Level 1 evidence from randomized, controlled trials, nonsurgical management of patients with unfavorable clinical features in the preferred treatment approach (Continued on page 8)
ACTIVE SURVEILLANCE PROGRAM FOR PROSTATE CANCER: AN UPDATE OF THE JOHNS HOPKINS EXPERIENCE

Tosoian JJ, Trock BJ, Landis P, et al
J Clin Oncol, E-pub 4 April 2011

Purpose: We assessed outcomes of men with prostate cancer enrolled in active surveillance.

Patients and Methods: Since 1995, a total of 769 men diagnosed with prostate cancer have been followed prospectively (median follow-up, 2.7 years; range, 0.01 to 15.0 years) on active surveillance. Enrollment criteria were for very-low-risk cancers, defined by clinical stage (T1c), prostate-specific antigen density <0.15 ng/mL, and prostate biopsyl findings (Gleason score ≤6, two or fewer cores with cancer, and ≤50% cancer involvement of any core). Curative intervention was recommended on disease reclassification on the basis of biopsy criteria. The primary outcome was survival free of intervention, and secondary outcomes were rates of disease reclassification and exit from the program. Outcomes were compared between men who did and did not meet very-low-risk criteria.

Results: The median survival free of intervention was 6.5 years (range, 0.0 to 15.0 years) after diagnosis, and the proportions of men remaining free of intervention after 2, 5, and 10 years of follow-up were 81%, 59%, and 41%, respectively. Overall, 255 men (33.2%) underwent intervention at a median of 2.2 years (range, 0.6 to 10.2 years) after diagnosis; 188 men (73.7%) underwent intervention on the basis of disease reclassification on biopsy. The proportions of men who underwent curative intervention (P = 0.026) or had biopsy reclassification (P < 0.001) were significantly lower in men who met enrollment criteria than in those who did not. There were no prostate cancer deaths.

Conclusion: For carefully selected men, active surveillance with curative intent appears to be a safe alternative to immediate intervention. Limiting surveillance to very-low-risk patients may reduce the frequency of adverse outcomes.

Presented in part at the 105th Annual AUA Meeting, 31 May 2010, San Francisco, CA

Surgery Delay in Men with Low Risk Prostate Cancer

J Urol 185: 2143-7, 2011

Purpose: Treatment options for patients with low risk prostate cancer include radical prostatectomy (RP), radiation therapy (RT), and active surveillance (AS). Among patients treated with RP, prior studies have demonstrated significantly higher biochemical progression rates with surgical delays of 6 months or greater. We determined the impact of surgical delay on RP outcomes specifically in low risk patients.

Materials and Methods: From our RP database we identified men who fulfilled the D’Amico low risk criteria (clinical stage T1c/T2a, PSA less than 10 ng/mL, and biopsy Gleason 6 or less). Pathological tumor features and biochemical progression rates were compared between men with and without surgical delay. We used Cox proportional hazards models to examine predictors of biochemical progression.

Results: Of 1,111 men who fulfilled the D’Amico low risk criteria, those with a surgical delay of 6 months or more were significantly older, had a higher proportion of African American men, and a lower proportion of clinical stage T2a (vs. T1). A surgical delay of 6 months or more was associated with a greater risk of high grade disease at prostatectomy (p = 0.001) and biochemical progression (p = 0.04).

The progression-free survival rate was significantly lower among men with a surgical delay. On multivariate analysis with prostate specific antigen and clinical stage, surgical delays of 6 months or more were significantly and independently associated with time to biochemical progression.

Conclusions: In men who met the D’Amico low risk criteria, a surgical delay of 6 months or more was associated with significantly worse RP outcomes, including more pathology upgrading and a higher rate of biochemical progression. Low risk patients choosing to defer initial definitive therapy should be counseled regarding the possibility of worse treatment outcomes at a later date.
NADIA® ProsVue™ – A New Prognostic Prostate Cancer Test

Test identifies men at greatly reduced risk of clinically documented prostate cancer recurrence following radical prostatectomy (RP)

Results of a multicenter clinical study of IRIS International’s proprietary prostate cancer test, NADIA® ProsVue™, in men after RP was presented at the 2011 Annual meeting of the American Urological Association (AUA). Principal investigator and lead author, Judd W. Moul, MD, presented the study results in a moderated poster session in Washington, DC.

This case-cohort study evaluated the prognostic capability of the Company’s proprietary ultrasensitive PSA test to identify men at a low risk for developing clinically documented cancer recurrence post-RP. The linear rate of change (slope) of ProsVue values over time was calculated for each of 304 study subjects (64 clinically recurring and 240 stable) using three successive PSA values determined from banked serum samples.

A slope cutpoint of 2.0 picograms (pg)/mL per month was used to divide patients into a “reduced risk” group (slope ≤ cutpoint) and “not at reduced risk” group (slope > cutpoint). Univariate and multivariate analyses compared ProsVue slope with traditional risk factors (pre-RP PSA level, pathologic stage and Gleason score [GS]) as predictors of clinical outcome.

In univariate analysis, a ProsVue slope >2.0 showed a hazard ratio (HR) of 18.3 – a 94.5% reduction in risk for men with a ProsVue slope ≤2.0. Multivariate analysis including traditional risk factors showed a HR of 9.8 – an 89.8% reduction in risk for men having a ProsVue slope <2.0. Of traditional factors, only pathologic GS was a significant predictor with a HR of 5.4 – an 81.4% reduction in risk for men having a GS <6.

Dr. Moul, Director of the Prostate Cancer Center and Division Chief of Urology at Duke University Medical Center, noted that clinical management post-RP necessarily involves individualized programs based on risk for recurrence. In general, traditional risk factors do not have strong predictive value for individual men, even when used in combination. He said improved tools for risk stratification are needed to estimate survival, determine if secondary therapies are necessary and define intensity of follow-up.

Dr. Thomas Adams, PhD, IRIS Chief Technology Officer, added, “Compared with Gleason score and traditional factors in the multivariate analysis, ProsVue slope was the strongest independent predictor in the model. Due to its high sensitivity, we believe NADIA ProsVue provides information previously unknown in post-RP patients.”

César Garcia, IRIS’ Chairman, President and CEO added “Any predictive diagnostic which could avoid unnecessary treatment will prove helpful to patients, the medical community and the health-care system.”

Study sites were Duke University Medical Center, Durham, NC; Eastern Virginia Medical School, Norfolk, VA; Memorial Sloan-Kettering Cancer Center, New York, NY and University of Washington Medical Center, Seattle, WA.

Presented 17 May 2011 at the 2011 Annual AUA meeting, poster MP61

Exelixis Drug Shown To Control Solid Tumors

Tumor control high for liver, Prostate and ovarian cancers; Effect on bone metastases “unprecedented”

Exelixis Inc.’s experimental cancer drug cabozantinib was shown in a mid-stage trial to help control advanced prostate, ovarian and liver cancers. The drug was also found to fully or partly eliminate cancer that had spread to the bone in patients with breast and prostate cancer and melanoma, according to the American Society of Clinical Oncology (ASCO), which featured the data ahead of its 2011 Annual Meeting in June.

“Cabozantinib, also known as XL184, is an oral drug designed to block the pathway that tumors need to form new blood vessels – the same target as drugs like Roche’s Avastin – as well as MET, another driver of tumor formation that is found in certain thyroid tumors.

The Phase 2 study included 483 patients with advanced, progressive solid tumors. Patients received cabozantinib over 12 weeks. Those responding stayed on the drug; patients with stable disease were randomized to cabozantinib or placebo; and patients whose cancer worsened were removed from the trial.

In the pre-publication data released, there were 398 evaluated patients with all types of cancer, of whom 9 percent experienced partial tumor shrinkage. But the rates of cancer stabilization were much higher – 76 percent of liver cancer patients, 71 percent of prostate cancer patients and 58 percent of ovarian cancer patients saw their tumors either shrink or remain unchanged.

Also, 59 of 68 patients with bone metastases (mostly from prostate cancer, but also from breast cancer and melanoma) had either partial or complete disappearance of cancer on bone scans. The effects were associated with improvement in pain, a reduction in narcotic requirements and improvement in anemia.

The most common serious side effects in the trial were fatigue and hand/foot tenderness. Drug dosage was reduced in 41 percent of patients due to side effects and 12 percent of patients were removed from the trial for adverse events.

Reuters, 18 May 2011
Targeted prostate biopsies that use a fusion of multiparametric magnetic resonance imaging (MRI) and ultrasound can produce a significantly higher yield and might be a replacement for traditional systematic biopsies, according to the results of a study presented at the International Society for Magnetic Resonance in Medicine (ISMRM) 19th Annual Meeting and Exhibition.

MRI can identify cancer in more than half of men whose initial biopsy is negative, but direct MRI-guided biopsy is not universally available— even to radiologists, said lead investigator Daniel Margolis, MD, assistant professor of radiology and co-director of prostate MRI at the David Geffen School of Medicine at UCLA. Blending of ultrasound guidance with MRI targeting could bypass this problem and accelerate the adaptation of targeted biopsy, he said.

The study enrolled 54 consecutive patients with both an abnormal PSA level and digital rectal exam who underwent multiparametric MRI—a blend of diffusion-weighted MRI, dynamic contrast-enhanced MRI, and traditional T2-weighted MRI—to identify targets for biopsy. Targets were chosen by an experienced uroradiologist on the basis of a decreased T2 signal, abnormal dynamic contrast-enhanced MRI, or apparent diffusion coefficient.

Special MRI/ultrasound fusion software (Artemis, Eigen) was used to perform transrectal ultrasound-guided biopsies of the targets; standard systematic biopsies were performed at the same time.

Multiparametric MRI identified 86 suspicious targets in 49 patients, of which 61 targets (40 patients) were biopsied on the basis of the high probability of cancer. After the first 25 patients, parallax imaging was added to optimize target acquisition, said Dr. Margolis.

Overall, 14 of the 61 suspicious targets were positive (23%), but after parallax optimizing, 8 of 17 were (47%) were found to be positive, he said. Of the samples from 652 systematic biopsies and 150 targeted biopsies, 38 (5.8%) and 26 (17%), respectively, were positive; the difference was not significant (P = 0.14), reported Dr. Margolis.

However, after parallax optimization, the difference in positive cores reached statistical significance; 7.1% of the systematic biopsy and 37% of the targeted biopsy samples were positive (P = 0.04).

“MRI-ultrasound fusion targets additional cancers, compared with systematic biopsies, and may replace systematic biopsies—resulting in fewer total biopsies, improved yield, and improved confidence for patients with a small amount of low-grade cancer who opt for active surveillance,” said Dr. Margolis.

“We are hindered by our blindness in looking at prostate cancer,” said Anvar Padhani, MB, BS, FRCP, FRCR, moderator of the session, who is honorary senior lecturer at University College, London, and consultant radiologist at the Paul Strickland Scanner Centre, Mount Vernon Cancer Centre, in Northwood, Middlesex, United Kingdom.

“Systematic biopsies are non-targeted and so lead to underestimates of tumor aggressiveness and tumor staging. The multiparametric approach is clearly the way to go if we are going to improve men’s health in the future, he said.

Presented 9 May 2011 at the ISMRM 19th Annual Meeting and Exhibition; Abstract 52

Fusion of MRI and Ultrasound Boosts Prostate Biopsy Yield

SAVE THE DATES
August 19-20, 2011
Us TOO University Symposium Chicago, IL
Watch for more info at <www.ustoo.org>

Intermittent vs. Continuous ADT – A Phase III Study

Intermittent androgen deprivation therapy (IADT) not continuous ADT (CADT) should be considered routine care for advanced prostate cancer

Fernando M. Calais da Silva and co-investigators present updated results to evaluate if IADT is associated with a shorter survival time. They studied 766 men with locally advanced or metastatic prostate cancer who received 3-months of ADT induction. PSA decreased to <4ng/mL or to 80% below the initial value in 626 men who were then randomized. ADT consisted of daily cyproterone acetate (CPA) 200 mg and monthly depot LHRH analog injections during induction. Patients randomized to the IADT arm ceased treatment while those randomized to the continuous arm (CADT) continued receiving 200 mg of CPA daily and an LHRH analogue.

A total of 474 patients died and 90 were lost to follow-up. They found no difference in survival, p=0.61, with hazard ratio (HR) 0.96 (95% CI 0.80 to 1.14). There were 239 deaths with IADT and 235 with CADT. A slight excess of cancer deaths in the IADT arm (136 vs. 109) is balanced by a slight excess of cardiovascular deaths in the CADT arm (68 vs. 62), and deaths from other causes (58 vs. 41). The HR of a cancer death is 1.27 (95% CI 0.98 to 1.64), p=0.06 with IADT compared with CADT. For cardiovascular deaths, the HRs are 1.05 (95% CI 0.75 to 1.49), p=0.77, CADT compared to IADT and for other deaths, the HR for CADT compared to IADT is 1.38 (95% CI 0.93 to 2.06), p=0.11.

The extra 5 years of followup now means that the study has accumulated almost 3,000 person years at risk among the 626 randomized patients and median follow up is now 57 months vs. 51 months in the initial publication. They concluded that IADT should be considered for use in routine practice since it is associated with no reduction in survival, no clinically meaningful impairment in quality of life, better sexual activity, and considerable economic benefit.

Reported for UroToday by Christopher Evans, MD, FACS, Professor and Chairman, Department of Urology, University of California, Davis School of Medicine, 17 May 2011
Cells shed by a metastatic castration-resistant prostate cancer (CRPC) into blood may be a robust measure of how well treatment is working, a researcher said here. Working on a clinical trial of a new drug, the researchers found that the number of such cells in the blood predicted overall survival (OS), according to Howard Scher, MD, of Memorial Sloan-Kettering Cancer Center in New York, NY. If the finding is validated in future trials, the method could speed the development of new drugs, as well as aiding prognosis, Scher said at the annual meeting of the American Society of Clinical Oncology (ASCO). The analysis was planned as part of a phase III trial of abiraterone acetate (AA) which was approved in April to treat men with metastatic (CRPC) who have progressed on docetaxel (Taxotere®) treatment.

AA inhibits so-called CYP17 enzyme and prevents androgen synthesis by the tumor itself, one way by which prostate cancer escapes from drug therapy, Scher said. Essentially, he told reporters, “The cancers themselves learn how to produce their own androgens,” making hormone-blocking drugs less effective. The trial enrolled 1,195 patients with metastatic CRPC and randomly assigned them to get AA or placebo; all patients also got prednisone. Analysis showed a significant improvement in OS associated with the drug – a median of 15.8 vs. 11.2 months vs. placebo, Scher said. During the study, researchers measured circulating tumor cells (CTCs), using the Veridex Cell Search system, both at baseline and during therapy. The cells were part of a biomarker panel that included lactate dehydrogenase (LDH), PSA and alkaline phosphatase. The CTC count was unfavorable if the number from the cell search system was 5 or greater and favorable if it was below 5, he said.

AA treatment “converted” unfavorable counts in some patients to favorable ones as early as 4 weeks after starting therapy. The treatment effect was seen in up to 40% of patients, Scher said. In multivariate analysis, baseline CTC “conversion” with AA from unfavorable to favorable and LDH predicted OS.

An analysis adjusting for change in cell count almost completely eliminated any treatment effect, changing the hazard ratio from a significant 0.74 to a non-significant 0.97, Scher reported.

Men with metastatic CRPC are a “population in need of new therapies,” said Sonali Smith, MD, of the University of Chicago, who moderated a press conference where results were discussed. But, she added, there’s currently “no easy way” to predict who will do well.

“We’re all trying to hone in on a surrogate of survival,” she said, because determining OS in clinical trials “can take so long to assess. To have a biomarker that is very individualized within a patient and... to show that in a statistically significant way that this correlates with survival is very promising,” she said.

Abstract presented at the 2011 Annual ASCO meeting, abstract LBA4517

MedPage Today, 8 June 2011

**On your blog, Ask Dr. Myers, while answering a concern about post treatment incontinence, you said, “I am unimpressed by the male sling.” I believe that you are either misinformed about the state of technical improvement in the AdVance Male sling or are just sending a message. The AdVance male sling, properly prescribed after dynamic testing, inspection (cystoscopy) for uniform contraction and waiting at least one year has proven to be extremely effective in treating major incontinence. I refer you to the work done by Dr. Kurt McCammon at Sentara in Norfolk, VA. The surgery is simple but requires a deft hand and exact placement coupled with inactivity to ensure full healing after placement. I went from 100% incontinence after every treatment in the book including a million kegels, stim, etc. to 99.9% continent – from 6 to 12 diapers with pads per day to a single precautionary pad. To have you disclaim the effectiveness of the AdVance Sling is a significant disservice to chronic and severe sufferers.

I have obviously stirred up a hornet’s nest with my comments about this device. But I think you are making what I regard as a common mistake in logic by many patients. Because they did well, their treatment must be the treatment of choice. I would like to talk about how I see the issues as being more complex. You can evaluate a procedure several ways. One is by the success rate in the best of hands. Another is the average result across the nation in the community setting. Another way to look at it is in a worst case scenario. Suppose you had a surgery that prevented hair loss and 95% of the patients did just great, but 5% died during surgery. Well, I might think that hair loss is not such a bad thing and losing 5% of patients is an unacceptable price to pay despite 95% of the patients being happy.

With the muscle sling, I have two patients who have had severe lasting pain after the surgery. The most serious case involved a superbly trained surgeon who I think is excellent technically and who deeply cares for his patients. Pain was so severe that morphine-like drugs did not control the pain. The patient lost his business and became deeply depressed.

In fact, overall, the artificial urinary sphincter has been more successful and better tolerated. I think it is just a superior solution in every way. While you had a great experience and I personally think your surgeon is great at what he does, my patients have done much better when I have referred them for an artificial urinary sphincter.

**Ask Doctor Snuffy Myers**

Get connected to other men and family members dealing with a prostate cancer diagnosis at: http://ustoo.inspire.com

**Mark Your Calendars**

The dates have been selected for the 2011 Prostate Cancer Conference. Presented by the Prostate Cancer Research Institute (PCRI), their national annual Conference will be held in Los Angeles on September 9-11, 2011 at the Westin Los Angeles Airport Hotel. Visit <www.pcri.org> for more information.
In the past month, annual urology and cancer meetings took place with a long list of new studies presented on prostate cancer. One point to keep in mind while reading them is that many of the papers presented NEVER get published. For that reason, it is difficult to make strong recommendations based on the work presented. With that being said, there were several papers of interest.

**a1p1c1** We begin with important results presented from a phase III randomized study using a new radioactive agent called Alfaradin. In men with castration-resistant prostate cancer (CRPC) metastatic to bone, those getting Alfaradin had a significantly longer survival by almost 3 months vs. placebo. Side effects were not reported in the abstract. This result may lead to the drug’s eventual US approval. If that occurs, it will crowd the field of therapy options for men with progressive CRPC. Questions to address include if it should be given before or after Provenge and chemotherapy treatments and if Alfaradin will add to second-line hormonal response.

**THE BOTTOM LINE:** Men with progressive CRPC may benefit from the many new developments in the past few years. This is just one more that offers a potential survival benefit but presents a new challenge of deciding which drug should be given first, second and third.

**a2p1c2** There is growing recognition that only a small percentage of men are likely to benefit from screening is leading doctors to search for more selective ways to test only those at risk. The study from MSKCC suggested that men classified as low risk based on a PSA level at age 44-50 that is below the median value (half of men are below and half are above the median value) had a very low risk of dying from their disease. The abstract does not give the median PSA value. Although the conclusion suggests men should be tested earlier than age 50, the study was not designed to find out if doing that testing will save lives.

**THE BOTTOM LINE:** The design of this study cannot tell us if there is a true benefit from testing men at an earlier age.

**a3p1c3** Treatment for men with locally advanced prostate cancer remains an ongoing topic of debate. Is radical prostatectomy (RP) appropriate with subsequent RT if needed or should RT combined with androgen deprivation therapy (ADT) be a better choice? Unfortunately, no prospective, randomized studies are available so we continue to rely on uncontrolled studies and all their inherent shortcomings. The Mayo Clinic report found a high progression free survival rate at 20 years in a large series of men treated by RP. Although results appear similar to RT plus ADT, many men had additional therapy that was not standardized. Furthermore, no quality of life (QOL) information is available.

**THE BOTTOM LINE:** Although RP remains an option for men with locally advanced disease, what we really need to objectively compare RP plus secondary therapy to RT alone or combined with ADT is a prospective, comparative study of their effects on QOL with these different approaches. Until then, the relative value of RP compared to therapy alternatives remains difficult to determine.

**a4p2c2** Active surveillance (AS) results are provided in 2 reports with apparently contradictory findings. Tosoian and co-workers from Johns Hopkins Hospital reported results at 2, 5 and 10 years after diagnosis in men with very low risk disease. By 10 years, only 41% remained untreated. It appears that the majority of men underwent treatment because of disease reclassification. Some readers may view results in a positive way and others as negative. The positive finding is that no one had died of prostate cancer with this approach, so far. The negative finding is that nearly 2/3 of the AS group needed treatment by 10 years.

**a5p2c3** Results from a second report by O’Brien had negative results. Men delaying treatment by at least 6 months had a higher-grade tumor at the time of RP and a higher rate of biochemical progression vs. men that underwent immediate therapy.

**THE BOTTOM LINE:** Is AS safe or not? Until definitive data is available from a randomized trial, case series offer the best available information for men considering this approach. These 2 studies provide different answers to this question. Which answer is correct? At this time, no conclusion is possible. Men should recognize that both active treatment and AS have pros and cons and each man must participate in such decisions BECAUSE we do not yet have the necessary information to know what is the best course of action.

**a6p3c1** Several papers provide information about local therapy. The report about the NADiA ProsVue test has the potential to impact on post-RP patient management. The report found that men with a low rise in the value of this test were highly unlikely to progress following RP and this test result was a stronger predictor than other risk assessment tools such as Gleason score. The value of this report is that men were followed for several years after surgery.

**THE BOTTOM LINE:** If validated, The ProsVue test might help identify which men should get immediate radiation (RT) and which men could defer that decision. The problem is that the test is performed over the course of one year while the best information to date has shown that some men benefit from RT if it is given within 6 months of RP. Further analysis and more results may help refine potential for using this test.

**a8p4c1** Improving detection was the focus of a paper combining the use of MRI and prostate ultrasound (TRUSP). They found that using the 2 together provided better prostate cancer detection than simply performing targeted prostate biopsies. Not enough information is provided, however, about the type, severity and risk posed by the additional cancers detected with this approach to permit a critical assessment.

**THE BOTTOM LINE:** Adding MRI to TRUSP may detect more cancers but it would greatly increase cost. It is not clear if the additional cancers detected are truly life-threatening. At this time, data are insufficient to recommend routine MRI along with TRUSP for men undergoing prostate biopsy.

**a9p4c3** Men with advanced disease continue to benefit from many new developments. The value of intermittent ADT... (Continued on page 7)
DOCTOR CHODAK’S BOTTOM LINE (Ref Key: article #, page #, column #) (Continued from page 6)

(IADT) has been assessed against continuous ADT (CADT) by two long-term, prospective, randomized studies. An update from a Spanish study found no difference in overall survival between the 2 groups. Based on their results, the authors conclude that intermittent ADT should be considered for routine practice.

There are several concerns about this study and its conclusions. First, men on IADT were more likely to die from prostate cancer but less likely to die from cardiovascular disease or other causes. Cyproterone acetate was used in this study as the antiandrogen and a large meta-analysis found that the use of this drug leads to an increased death rate from non-cancer causes. That may explain why the overall survival was similar in the 2 groups, which probably would not have occurred if a safer antiandrogen had been used. The reason the men on IADT had a lower cardiovascular death rate might be because they had a shorter duration of exposure to cyproterone acetate.

THE BOTTOM LINE: Although IADT may offer some men a better QOL, this study shows that it also is associated with a greater risk of dying from prostate cancer. An alternative conclusion from this study is (1) IADT is not as good against prostate cancer as CADT and (2) cyproterone acetate is not the right drug to be used when delivering combined androgen blockade.

a10p5c1 This paper has the potential to change the process of getting new treatments approved for prostate cancer. At present, the FDA only recognizes survival as an acceptable end-point for studies involving new therapies. An analysis of the Abiraterone study looked at the ability of circulating tumor cells (CTC) to predict the long-term outcome from the disease. A favorable CTC was less than five cells. Men that converted from an unfavorable to a favorable CTC had a better response to the therapy.

THE BOTTOM LINE: Although more studies are needed, this is a new marker that could reliably predict who is benefiting from a treatment and could have a huge impact on shortening the time it takes to evaluate new therapies.

DOC MOYAD’S WHAT WORKS & WHAT IS WORTHLESS COLUMN, ALSO KNOWN AS “NO BOGUS SCIENCE” COLUMN

“_____ dietary supplement fight/kills prostate cancer! Is Dr. Moyad is an idiot for not supporting this supplement?!”

Mark A. Moyad, MD, MPH
University of Michigan Medical Center, Department of Urology

Bottom Line: If someone tells you a dietary supplement works against prostate cancer, but they cannot show you ANY research in humans with prostate cancer please ask them what it is also like to personally know “Big Foot”, the “Loch Ness Monster”, and where you can still find Elvis living in the US.

Every week someone emails me, or a person I know with cancer, and tells me/ them that _____ (fill in the product name) dietary supplements definitely treat prostate cancer! And, when I review the data on this supplement it has not actually been tested in men with prostate cancer! So, how do they know for sure that this supplement works in men with prostate cancer? They cannot know for sure because the answer is not known, so what is wrong with saying that or stating this fact (“I don’t know”). And, if someone still wants to try this supplement despite not having clear answers to whether it helps, harms, or does nothing then I believe that is a personal choice. I get letters or comments by some folks that are really mad because they say I am just making a supplement look bad because I do not like it?! This notion that I just want to make some supplements look bad is as ridiculous as a random person in the US getting a dirty text message or photo from say a congressman from New York they have never physically met (Oops…bad analogy folks!)! Seriously though, it is ridiculous because no one that I know in prostate cancer wants to make dietary supplements look good more than myself. Yet, I know (after 25 years of working in this business or at least arguably the longest of anyone full time in prostate cancer history) that the way to bring respect to my field or discipline is to be the biggest critic of my own area of medicine (diet and dietary supplements). Otherwise, we will never legitimize this area of medicine. If a surgeon or radiation oncologist states that their treatment is the only legitimate treatment that helps prostate cancer it does not take long for the B.S. meter to go off! Yet, this is no different for dietary supplement “experts!” I like surgeons and oncologists that understand the benefits and limitations of their treatments.

For example, I have received letters recently that “curcumin” (a derivative of the spice “turmeric”) clearly fights cancer and I need to endorse it as a prostate cancer treatment? Yet, we do not have any legitimate human prostate cancer studies! There is an older 6-month study that shows that it does NOT reduce cholesterol (like some claim), and a newer study in pancreatic cancer that shows it can cause serious gastrointestinal problems at very high doses when combined with some types of chemotherapy. So, it does have limitations, but it also holds some promise. So, when some beneficial human studies in prostate cancer come along and/or some men get a real benefit from this product, and/or it is found to be relatively safe (heart healthy) as a supplement I will be the first to jump on this bandwagon! In the meantime, I can name over 100 supplements (I am not kidding) that look good against prostate cancer in a test tube or mouse or some laboratory, but I do not endorse them because they have not looked good or been tested in humans! Since, most of you reading this newsletter are humans (sorry Mickey Mouse, Old Yeller, Lassie, Benji, Clifford the Big Red Dog, the pig from Charlotte’s Web, Smokey the Bear, etc…) I would assume you now understand some of my philosophy that has helped me through the years accurately predict what really works and what is worthless for men with prostate cancer! Regardless, thanks for the therapy folks!

References:
Phase I and II trial outcomes and did not show any new or unexpected changes in the safety profile of radium-223 chloride. Common adverse events from the AL-SYMPCA trial included diarrhea, neutropenia, and thrombocytopenia. Radium-223 chloride is an investigational agent and is not approved by the US Food and Drug Administration, the European Medicines Agency or other health authorities.

We are pleased that radium-223 chloride met its primary endpoint of significantly improving overall survival in patients with CRPC and bone metastases, and are hopeful about the potential of radium-223 chloride for this patient population,” said Kemal Malik, MD, Head of Global Development and member of the Bayer HealthCare Executive Committee.

The company is evaluating the filing strategy for radium-223 chloride based on the IDMC’s recommendation to stop this study and will offer patients in the placebo arm active treatment with radium-223 chloride.

Bayer HealthCare news release, 6 June 2011

als 6 years later as part of the Malmö Preventive Project in Sweden. Blood samples from 1,167 60-year-old men involved in the Malmö project were also included. All men had never received any screening for prostate cancer.

Researchers analyzed each of the samples – in men ages 44-50, 51-55, and 60 – and determined that median PSA levels distinguished between low risk and high risk for developing aggressive prostate cancer. A PSA level below the median at age 44-50 was associated with a very low risk of prostate cancer death or metastasis within 15 years, although it did not rule out lifetime risk. By age 60, risk decreased to only 0.5% in those men with a PSA level below the median.

This study suggests that men should start the screening discussion with their physician at an earlier age and receive their first PSA test between the ages of 44-50 years. If at low risk, these men should receive a second test between 51-55 years, and if their PSA levels are still found to be low, they should receive their final PSA test at 60 years of age.

Modern Medicine, 2 June 2011

retrospectively review identified 7,883 men RP patients treated from 1987 to 1997, 4,812 (61%) with cT2 (localized) disease and 843 (11%) with cT3 disease. Median follow-up was 14.3 years. Primary endpoints were PFS, prostate cancer-specific survival (PCSS), and overall survival (OS) among patients with cT2 and cT3 disease.

cT3 patients had significantly more high-risk features than cT2 patients (higher pre-RP PSA, more final Gleason score ≥7, positive margins, seminal vesicles and lymph nodes(P<0.0001). cT2 patients had significantly better 20-year PFS, PCSS and OS.

Multivariate analysis revealed 5 factors predicting increased risk of metastases or local recurrence: pathologic GS ≥7, pre-RP PSA, positive surgical margins and seminal vesicles (P=0.033–0.004).

Mitchell acknowledged that the 76% rate non-standardized secondary therapies in their cT3 population was higher than than has been reported in other studies. Presented at the 2011 Annual AUA meeting, abstract 339, MedPage Today, 23 May 2011

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