Long-Term Data Further Confirm SpaceOAR Hydrogel Quality of Life Benefits

Prostate cancer patients who received the SpaceOAR hydrogel before radiation therapy (RT) continue to report benefits five years after treatment, i.e., better urinary and sexual function, a new study reported. The study titled, “Quality of Life After Radiation Therapy for Prostate Cancer with a Hydrogel Spacer: Five-Year Results,” was published in the International Journal of Radiation Oncology: Biology, Physics.

“These long-term results further validate previous three-year data of the SpaceOAR System and highlight the long-term bowel and sexual quality of life benefits it can provide to prostate cancer patients who are treated with RT,” stated Michael Pinkawa, MD, PhD, radiation oncologist at MediClin Robert Janker Klinik in Bonn, Germany, and lead author of the study. The SpaceOAR system, developed by Augmenix, was designed to temporarily create a protective space between the prostate and the rectum wall. By pushing the tissues apart, the injectable solution reduces the amount of radiation that reaches the rectum, minimizing its potentially damaging effects. The spacer is stable for three months, after which it returns to liquid form and is absorbed by the body.

Recently, data from a three-year follow-up of a pivotal Phase 3 Trial (NCT01538628) showed that men who used SpaceOAR had decreased rectal toxicity and fewer declines in both urinary and bowel quality of life compared with the control group.

(Continued on page 5)

Axumin PET/CT Scans in Men with Suspected Recurrent Prostate Cancer May Change Treatment Plans

More than six out of 10 men whose doctors suspected their prostate cancer had returned due to rising PSA levels saw their treatment plans revised after scanned by PET/CT imaging with Axumin (18F-fluciclovine).

Results are from the Phase 3 FALCON trial (NCT02578940), whose findings were recently presented at the 2017 American Society for Therapeutic Radiology Oncology (ASTRO) Annual Meeting in San Diego by Eugene Teoh, MD, Oxford University Hospitals NHS Foundation Trust.

The presentation, Impact of 18F-fluciclovine PET/CT on clinical management of patients with recurrent prostate cancer: results from the Phase III FALCON trial reported that early and accurate localization of metastasis facilitates treatment, as the tumors are smaller in size and respond better to localized therapy.

Axumin, a 18F-fluciclovine injection, is a molecular agent used in positron emission tomography (PET) imaging in men with suspected recurrent prostate cancer. The suspicion is supported by high levels of PSA in the blood, following prior treatment. The US Food and Drug Administration (FDA) has approved this injection for use in PET imaging, but not for treatment planning in men with biochemical recurrence (BCR).

(Continued on page 5)
Predicting Probability of Lymph Node Invasion in Prostate Cancer Patients Undergoing Sentinel Lymph Node Dissection


Journal of Cancer 22 August 2017 [Epub]

Objectives: To update the first sentinel nomogram predicting the presence of lymph node invasion in prostate cancer patients undergoing sentinel pelvic lymph node dissection (sPLND), taking into account the percentage of positive cores.

Patients and Methods: Analysis included 1,870 prostate cancer patients who underwent radioisotope-guided sPLND and retropubic radical prostatectomy. PSA, clinical T (clinical tumor stage) category, primary and secondary biopsy Gleason grade, and percentage of positive cores were included in univariate and multivariate logistic regression models predicting lymph node invasion, and constituted the basis for the regression coefficient-based nomogram. Bootstrapping was applied to generate 95% confidence intervals for predicted probabilities. The area under the receiver operator characteristic (ROC) curve (AUC) was determined in order to quantify accuracy.

Results: Median PSA was 7.68 ng/mL (interquartile range [IQR] 5.5-12.3). The median number of lymph nodes removed was 10 (IQR 7-13). Overall, 352 patients (18.8%) had lymph node invasion. All preoperative prostate cancer characteristics differed significantly between lymph node-positive and lymph node-negative patients (P <0.001). In univariate analysis, the proportion of positive cores was the foremost predictor of lymph node invasion (AUC, 77%) followed by PSA (71.1%), clinical T category (69.9%), and primary and secondary Gleason grade (66.6% and 61.3%, respectively). For multivariate logistic regression models, all parameters were independent predictors of lymph node invasion (significant at P <0.001). The nomogram exhibited a high predictive accuracy (AUC, 83.5%).

Conclusion: The first update of the only available sentinel nomogram predicting lymph node invasion in prostate cancer demonstrates even better predictive accuracy and improved calibration. In addition, the percent of positive cores represents the leading predictor of lymph node invasion. This updated sentinel model should be externally validated and compared with results of extended PLN-based nomograms.

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and Prostate Cancer Risk: Results from the EPICAP Study


Cancer Medicine, 21 September 2017; [Epub]

Chronic inflammation may play a role in prostate cancer carcinogenesis. In that context, our objective was to investigate the role of nonsteroidal anti-inflammatory drugs in prostate cancer risk based on the EPICAP data. EPICAP is a population-based case-control study done in 2012-2013 (département of Hérault, France) that enrolled 819 men aged less than 75 years old, newly diagnosed for prostate cancer and 879 controls frequency matched to the cases on age. Face-to-face interviews gathered information on several potential risk factors including nonsteroidal anti-inflammatory drug use. Odds ratios and their 95% confidence intervals (CIs) were calculated using unconditional logistic regression models.

All nonsteroidal anti-inflammatory drug use was inversely associated with prostate cancer: Odds ratio 0.77, 95% CI 0.61-0.98, especially in men using nonsteroidal anti-inflammatory drugs that preferentially inhibit COX-2 activity (Odds ratio 0.48, 95% CI 0.28-0.79). Non-aspirin nonsteroidal anti-inflammatory drug users had a decreased risk of prostate cancer (Odds ratio 0.72, 95% CI 0.53-0.99), particularly aggressive prostate cancer (Odds ratio 0.49, 95% CI 0.27-0.89) and in men with a history of prostatitis (Odds ratio 0.21, 95% CI 0.07-0.59).

Our results are in favor of a decreased risk of prostate cancer in men using nonsteroidal anti-inflammatory drugs, particularly for men using preferential anti-COX-2 drugs. Protective effects of nonsteroidal anti-inflammatory drugs seems to be more pronounced in aggressive prostate cancer and in men with a history of prostatitis, but this needs further investigations to confirm.
Doc Moyad’s What Works & What is Worthless or “No Bogus Science” Column

“What! Melatonin Fights Prostate Cancer? What?”

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

Editor’s Note: Us TOO invites certain physicians and others to provide information and commentary for the Hot SHEET to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

There are several ongoing clinical trials of melatonin treatment along with conventional therapy for breast cancer, and now there is some shifting interest in testing melatonin against prostate cancer.1 In the meantime, be careful about the dose that you use for sleep and if you are a good sleeper, then you don’t really need melatonin.

Melatonin is an interesting dietary supplement, simply because it has a history of helping cancer patients with sleep issues or insomnia.2,3 However, not only regular melatonin, but alternative low-doses of other forms of melatonin have also been successful for insomnia. One example is Circadin, which is a prolonged-release melatonin given at a 2 mg dose. This product is available in other countries or online at www.circadin.com.

Many of the melatonin products that you buy at your local store are immediate release, which means that they work quickly and help you fall asleep but do not always help you maintain your sleep throughout the night. It is for this reason some folks do better with prolonged-release (or controlled-release) formulation of melatonin or do better if they just take melatonin when, or if, they wake up in the middle of the night.

Another major problem with melatonin is that some dosages recommended for sleep are borderline wacky! 10 mg? 15 mg? What? These higher dosages can cause you to feel drowsy and slow during the day and could even impact memory. Also, it can lower blood pressure somewhat, especially at higher doses when sleeping, which could be very problematic if you are already on blood pressure medications. It is for this reason that if you are having trouble sleeping then using a lower and more physiologic dosage such as 1, 2 or even 3 mg is more than enough and is safer.

Now, the final problem is that there are many studies touting the effects of melatonin on cancer. Although they are interesting, results from these studies are incomplete, so there is no reason to take a high dosage of melatonin. What are you going to do if in a year or so researchers find that high dosages of melatonin not only have toxicity, but could encourage tumor growth or even show that they simply do not work? The bottom line is that we do not have a good answer right now. So, when that is the case it is best to follow the Moyad Mantra, which is “Start Low, Go Slow and You Will Save Side Effects and Dough.”

Look, am I excited about melatonin for sleep and jet lag at lower dosages? Yes! Am I hopeful that higher dosages will be found to have anti-cancer effects? Yes! Would I recommend higher dosages right now beyond what is used for sleep? Nope! Do I like to ask myself questions in my own column? Yes!

(Continued on page 8)

Prostate Cancer Patients Unclear on Differences Among Treatments

Many men with localized prostate cancer don’t understand the differences between their treatment options, a new study suggests.

“Prostate cancer is the most common male cancer in Western Europe, but this study shows that men facing treatment have a poor understanding of how their treatment decision will affect their lives,” said Marie-Anne Van Stam of the University Medical Center, Utrecht from The Netherlands in an interview.

“This means that they are often not able to understand the differences in outcomes and side effects among the different treatment options, and end up making decisions on instinct.”

Options for treating prostate cancer that hasn’t spread include radical prostatectomy (RP), radiation therapy (RT) and active surveillance (AS), in which doctors monitor the cancer but don’t treat it unless it grows.

While RP is the most invasive approach, it does not reduce the risk of disease recurrence compared to RT. Men who undergo RP face a higher risk of urinary incontinence and erectile dysfunction, while RT is associated with bowel and urinary problems, the researchers reported online in BJU International.

Van Stam and her team analyzed questionnaires completed by 474 prostate cancer patients who had just received their treatment options from a urologist. Just over one-third of the men were aware that cancer recurrence was just as likely with RP as with RT, while 39% were aware that RP increased the risk of incontinence. Twenty percent knew that 10-year mortality is similar with AS, RT and surgery.

Forty-five percent of the survey respondents thought that men on AS always wound up receiving RT or another therapy later on. In fact, according to Van Stam, only half of patients on AS require definitive treatment. Men who spoke to a nurse specialist or radiotherapist in addition to the urologist, had a better understanding of the differences between treatments. “This finding encourages the incorporation of a nurse specialist and/or multidisciplinary consults in routine care,” Van Stam said.

“We don’t expect men to become prostate cancer experts; this is a once in a lifetime event,” she added.

“So the facts need to come from clinicians. However, we note, for example, that almost no clinical guidelines include a clear overview of the differences in the risks of side effects among treatments, or sections on communicating with patients, and this needs to change.”

Reuters Health
13 October 2017
Treatment with GnRHa and Orchiectomy Have Similar Cardiovascular Risk in Prostate Cancer

The risk of cardiovascular (CV) ischemic events may be increased among men with prostate cancer who receive androgen-deprivation therapy (ADT) by bilateral orchiectomy vs. men who receive gonadotropin-releasing hormone agonist (GnRHa) therapy (e.g., Lupron) according to data published online in the Journal of Clinical Oncology.

Recent evidence suggests that ADT may increase the risk of CV ischemic events such as myocardial infarction (MI, or heart attack) and ischemic stroke (IS), but the current data are inadequate for demonstrating whether bilateral orchiectomy or GnRHa therapy has worse long-term outcomes.

Researchers identified 14,715 men with prostate cancer from the Taiwan National Health Insurance Research Database, of whom 24.3% underwent bilateral orchiectomies and 75.7% received GnRHa therapy. The mean age at baseline was 75.4 years, and men treated with GnRHa were younger and had a greater number of distant metastases.

During 1.5 years of follow-up, men who had orchiectomy experienced a greater number of CV ischemic events compared with men receiving GnRHa therapy (hazard ratio [HR], 1.40; 95% confidence interval [CI], 1.04-1.88). The effect was more pronounced in men who were 65 years or older, were hypertensive, had a history of MI, IS, or coronary heart disease, and had a score of 3 or greater on the Charlson comorbidity index score.

At median follow-up of 3.3 years, both groups had similar risk of CV ischemic events (HR, 1.16; 95% CI, 0.97-1.38).

Data suggest CV risk is not significantly different between men who receive an orchiectomy or a GnRHa. The authors concluded that the findings provide “reassurance when considering a GnRHa as the method of ADT in prostate cancer patients.”

Cancer Therapy Advisor 3 October 2017

Genomic Testing for Localized Prostate Cancer—Where Do We Go From Here?

Stacy Loeb; Ashley E. Ross

Curr Opin Urol 27: 495-499, 2017

Purpose of Review: The goal of this article is to discuss current genomic testing options in localized prostate cancer.

Recent Findings: There are multiple genomic tests currently available for men with localized prostate cancer. Prolaris, OncotypeDx, and Decipher can all be tested using biopsy tissue. Prolaris and Decipher are also available for men undergoing radical prostatectomy to predict subsequent disease progression.

Summary: The Prolaris cell cycle progression score measured on biopsy predicts the risk of prostate cancer death in 10 years with conservative management, whereas, the primary endpoint for the OncotypeDx genomic prostate score is the risk of adverse disease at radical prostatectomy. Decipher measures genome-wide RNA expression, and its Genomic Classifier signature was initially designed to predict the risk of metastasis for:

Retreatment with Radium-223: First Experience from an International, Open-Label, Phase I/II Study in Patients with Castration-Resistant Prostate Cancer and Bone Metastases

Sartor O, Heinrich D, Mariados N, et al.

Annals of Oncology, 1 October 2017 [E-Pub]

Six Radium-223 injections at four-week intervals is indicated for men with castration-resistant prostate cancer (CRPC) and symptomatic bone metastases. However, patients usually develop disease progression after initial treatment. This prospective Phase I/II study assessed safety and efficacy of retreatment with up to six additional Radium-223 doses.

Patients had CRPC and bone metastases and six initial Radium-223 injections with no on-treatment bone progression; all had subsequent radiologic or clinical progression (after treatment stopped). Other drugs were allowed at investigator discretion, but men receiving chemotherapy and/or initiating abiraterone or enzalutamide were excluded. The primary endpoint was safety; additional exploratory endpoints included time to radiographic bone progression, time to total alkaline phosphatase and PSA progression, radiographic progression-free survival, overall survival, time to first symptomatic skeletal event (SSE), SSE-free survival, and time to pain progression.

Among 44 patients, 29 (66%) received all six retreatment injections. Median time from end of initial Radium-223 treatment was six months. Forty-one (93%) reported more than one treatment-emergent adverse event. No grade 4-5 hematologic (blood cell) treatment-emergent adverse events occurred. Only one (2%) patient had radiographic bone progression; eight (18%) had radiographic soft tissue tumor progression (three lymph node and five visceral [internal organ] metastases). Median times to total alkaline phosphatase and PSA progression were not reached and 2.2 months, respectively. Median radiographic progression-free survival was 9.9 months (12.8-month maximum follow-up). Five (11%) men died and eight (18%) experienced first SSEs. Median overall survival, time to first SSE, and SSE-free survival were not reached. Five (14%) of 36 evaluable patients (baseline worst pain score ≤7) had pain progression. After two years of follow-up, 28 (64%) patients died, and the median overall survival was 24.4 months.

Re-treatment with a second course of six Radium-223 injections after disease progression is well tolerated, with minimal hematologic toxicity and low radiographic bone progression rates in this small study with limited follow-up. Favorable safety and early effects on disease progression indicate that Radium-223 re-treatment is feasible and warrants further evaluation in larger prospective trials.

Join Us for a Special
Us TOO Prostate Cancer Panel Discussion and Webcast on
Advancing Prostate Cancer

Monday, November 6
5:45-7:30 pm (CT)
For more information or to register, visit:
Axumin PET/CT & Prostate Cancer Treatment
(Continued from page 1)

With this in mind, researchers aimed to assess the impact of PET/CT imaging with Axumin on clinical management choices for men with recurrent prostate cancer.

The FALCON trial, sponsored by Blue Earth Diagnostics, was a British-based, prospective, multi-center and open-label study testing the addition of Axumin PET/CT imaging to standard diagnostic techniques.

Researchers recruited men with recurrent prostate cancer being considered for curative intent salvage therapy. The team then compared their intended management plans, before and after Axumin PET/CT scan.

In a pre-planned analysis of the first 85 men, researchers found that 52 men (61.2%) had their clinical management changed after the Axumin PET/CT imaging results were added to the diagnostic work-up.

Among the 52 men, 13 (25%) changed from salvage treatment to watchful waiting, 18 (34.6%) had their salvage treatment revised to systemic therapy, and 21 (40.4%) had their previously planned radiotherapy field modified.

Thanks to its successful results, Blue Earth Diagnostics has announced a halt to patient recruitment.

“In line with our mission to develop and commercialize innovative PET imaging agents for cancer, the FALCON study was designed to assess the utility of fluciclovine (18F) PET/CT scan in providing meaningful information for physicians, with the hope that it may benefit men with recurrent prostate cancer,” Jonathan Allis, CEO of Blue Earth, said in a press release. “We look forward to announcing full results of the FALCON study in a future peer-reviewed publication.”

Added Abhishek Solanki, assistant professor of radiation oncology at Chicago’s Loyola University: “Currently approved imaging procedures have limitations in identifying the sites of recurrence of prostate cancer after definitive treatment, which can make decision-making difficult when assessing men with BCR. Newer imaging techniques, such as fluciclovine (18F) PET/CT, may provide actionable information to guide management.”

Prostate Cancer News Today 2 October 2017

SpaceOAR & Quality of Life Benefits
(Continued from page 1)

Now, researchers at the RWTH Aachen University Department of Radiation Oncology in Germany evaluated the quality of life changes up to five years after prostate cancer RT.

The study included 114 men, 54 of whom received the hydrogel prior to prostate cancer RT. Participants were surveyed for quality of life measures at baseline, at the last day of RT, and at two, 17, and 63 months after RT.

One and a half years after receiving RT, more men in the control group (32%) reported bothersome bowel symptoms than in the hydrogel group (6%). The benefits were sustained for over five years, with only 5% of the hydrogel-treated patients reporting bothersome bowel symptoms compared with 14% in the control group.

Moderate to large bowel urgency were also less frequent in the SpaceOAR group at both 1.5 and five years (0% vs. 13%, and 0% vs. 14%, respectively).

During the study, five men in the control group required invasive bowel procedures to manage adverse bowel symptoms vs. one patient treated with SpaceOAR.

SpaceOAR also was associated with better sexual function five years after RT. Men treated with SpaceOAR were eight times more likely to have an erection sufficient for intercourse vs. men in the control group.

“This five-year data confirms previously reported three-year outcomes from our randomized, multi-center trial and continues to build a growing portfolio of studies supporting the use of SpaceOAR hydrogel spacing during RT for prostate cancer,” said John Pedersen, CEO of Augmenix.

Prostate Cancer News Today 11 September 2017

The Influence of Prednisone on the Efficacy of Cabazitaxel in Men with Metastatic Castration-resistant Prostate Cancer (mCRPC)


Journal of Cancer, 22 August 2017 [E-Pub]

Background: Cabazitaxel is a second-generation taxane that is approved for use with concomitant low-dose daily prednisone (a corticosteroid) in mCRPC after docetaxel failure. So far, the role of daily corticosteroids in improving cabazitaxel efficacy or ameliorating its safety profile has not been fully investigated, so we compared outcomes of men receiving cabazitaxel with or without corticosteroids in a retrospective single-institution cohort of mCRPC patients.

Patients and Methods: Medical records of deceased men with documented mCRPC treated with cabazitaxel following docetaxel between January, 2011 and January, 2017 were reviewed at the single participating center. Patients who were receiving daily doses of systemic corticosteroids other than low-dose daily prednisone or prednisolone (≤10 mg a day) were excluded. The primary end-point of this analysis was overall survival (OS). Secondary end-points were exposure to cabazitaxel as well as incidence of grade 3-4 adverse events. Univariable and multivariable Cox proportional hazards regression was used to evaluate prednisone use and other variables as potentially prognostic for overall survival.

Results: Among 91 men, 57 received cabazitaxel and low-dose prednisone and 34 men did not. The median OS of the population was 9.8 months (interquartile range [IQR], nine to 14). Men receiving prednisone had an OS of nine months (IQR, eight to 12) vs. 14 months (IQR, 9.4 to 16.7) for men not treated with prednisone. Approximately 45% of men had a >30% PSA decline at 12 weeks. Prednisone use was not significantly prognostic for OS or PSA decline ≥30% rates on regression analyses. Importantly, a >30% PSA decline at 12, but not at three, six, and nine weeks, was prognostic for improved survival at multivariate analysis.

Conclusions: The data support the hypothesis that omitting daily corticosteroids in cabazitaxel-treated patients has no negative impact.

(Continued on page 8)
where new types of treatment are increasingly available as well,” he suggested.

A major tool for driving improvements in the quality of healthcare in recent years has been to give patients the choice over their healthcare provider, a move that has been accompanied by the centralization of specialist cancer services.

In the UK, this was expected to lead to patients being treated at their nearest hospital, following standard referral patterns, despite care being free at the point of access and patients having the right to choose any hospital that meets their needs. However, a previous study by the team revealed that around one third of men who underwent RP for prostate cancer were not treated in their nearest hospital and that the younger, fitter, and more affluent men were more likely to travel.

Researchers therefore conducted a population-based analysis of patient choice and hospital competition, obtaining individual patient-level data from the National Cancer Registration and Analysis Service for all men diagnosed with prostate cancer who underwent RP in the UK NHS between 2010 and 2014. These were linked at the patient level to the Hospital Episode Statistics database of all NHS hospitals in the UK, from which configuration changes in prostate cancer surgical units and examined the availability of robotic surgery during the study.

The team also determined each man’s residence. Men using their nearest center were defined as “core users,” and those who did not were defined as “bypassers.” For each surgical center, researchers calculated the number of men who had surgery elsewhere, despite it being their local hospital (“leavers”), and the number who had surgery there, although it was not their local center (“arrivers”). Finally, the spatial competition index (SCI) was calculated for each center to measure the degree of external competition, in terms of the demand for services and the availability of alternative hospitals.

The team identified 19,518 men who underwent RP between 2010 and 2014, of whom 19,256 were included in the analysis. Of the 65 surgical centers open in 2010, 23 (35%) gained patients and 37 (57%) lost patients during the study period, with five centers experiencing no net changes. In some cases, units performed 400 to 500 more procedures than they would have done had they operated only on local men, while some of those that lost patients performed 200 fewer procedures than expected. Ten (27%) of the centers were closed down during the study period because of the net loss.

Centers with a net gain were more likely to be established robotic centers than those with a net loss, at 43% vs. 5% (significantly different, P=0.0043).

The largest net gains and losses were seen in the most competitive areas. Established robotic centers were more likely located in the highest quartile of SCI scores: seven of 17 (41%) center were in the highest quartile vs. five of 48 (10%) centers in other quartiles (significantly different, P=0.0050).

Center closures were also more common in hospitals in the highest quartile of SCI scores than other quartiles, at six centers (35%) vs. four centers (8%) (significantly different, P=0.0081).

The team found large-scale adoption of robotic surgery during the study period, increasing from 12 (18%) of 65 centers in 2010 to 39 (71%) of 55 centers in 2014. The trend increased after the study period, reaching 42 (86%) of 49 centers in 2017.

Researchers write: “Both the closures and the rapid and unforeseen widespread adoption of robotic surgery effectively render commissioning guidelines – recommending phased introduction of robotic surgery for prostate cancer in NHS – obsolete.”

Dr. Aggarwal commented: “NHS choice and competition policy [are] based on the principle that men will travel to centers they think will provide the best service. “Closures were never intended to result from this, but the large number of men deciding to receive treatment elsewhere meant some centers faced risk of closures as they were no longer performing a sufficient number of procedures to sustain their service. However, since there are no publicly available indicators to help men judge the quality of prostate cancer surgery, they have to make choices based on other factors.”

“In this case, it appears that patients use the availability of robotic prostatectomy as an indicator of high-quality care, despite a lack of evidence of its superiority compared with open surgery.”

Medscape Oncology
10 October 2017

Long-Term Study Finds Low-Dose Brachytherapy Viable for Lower-Risk PCAs

Men with low-intermediate risk prostate cancer who receive low-dose permanent brachytherapy (BT), a type of radiation therapy (RT), have excellent outcomes in the long run, according to data recently presented at the American Society for Therapeutic Radiation Oncology (ASTRO) 2017 Annual Conference in San Diego, CA.

At nine years of follow-up, 11-14% of men treated with Iodine-125 (I-125) or Cesium-131 (Cs-131) BT had biochemical recurrence (BCR) based on a rising PSA.

BT is a relatively new cancer treatment where small radioactive seeds are implanted directly into a patient’s tumor. This ensures that RT is delivered specifically to a cancer site while sparing healthy surrounding tissues. Seeds used in BT may be composed of diverse radioactive compounds. Cs-131 seeds, in particular, have attributes that shorten treatment time and reduce common prostate side effects.

(Continued on page 8)
Doctor Chodak’s Bottom Line


Editor’s Note: Us TOO has invited certain physicians and others to provide information and commentary for the Hot SHEET to enrich its content to empower the reader. This column contains the opinions and thoughts of its author and are not necessarily those of Us TOO International.

P1, “Long-Term Data…”

Which treatment is better for localized prostate cancer – radical prostatectomy (RP) or radiotherapy (RT)? Without a randomized study, it is not possible to answer this question. Until that occurs, men should be offered both, with a clear explanation of the odds of developing recurrent disease and side effects. The major side effects are bladder and sexual dysfunction for both treatments and additionally, bowel problems with RT. Suppose those side effects could be reduced following RT, would that shift the argument in favor of RT over RP? Importantly, SpaceOAR hydrogel injected into the space between the prostate and rectum does appear to lower side effects. Separating the two organs appears to provide some protection. Three-year data have already shown a benefit of this approach. Pinkawa, et al. present five-year data showing that the benefits are preserved, with a lower incidence of bowel urgency and an eight times lower incidence of erectile problems. These are very important findings and make a strong case for offering it to all men before external beam RT.

The Bottom Line: SpaceOAR is an approved therapy that significantly reduces the incidence of bowel urgency and erectile dysfunction after external beam RT and should be discussed with all men getting this treatment.

P1, “Axumin PET/CT…”

Managing a patient with a rising PSA after local therapy presents a major challenge. Studies of salvage local therapies have found that only a small percentage of men seem to benefit. This means that the therapy selected was incorrect, either because local recurrence was not present, distant disease was also present, or the therapy was ineffective. The study authors (Teoh, et al.) using 18F-fluciclovine PET/CT imaging provides encouraging data for a role using this test. The authors performed the test in 52 men and 31 had their planned therapies revised. This now sets the stage for well-designed therapeutic studies based on the findings. One study would be to include only men with positive findings limited to the prostate bed and another study is to include men with disease found elsewhere in the body. Either or both would help demonstrate if incorporating this test for men with a PSA recurrence is indeed worthwhile.

The Bottom Line: 18F-fluciclovine PET/CT imaging for men with recurrence after local treatment may help improve the selection of optimal therapy and avoid unnecessary treatment.

P2, “Nonsteroidal…”

Is there a role for NSAIDS in men with prostate cancer? That question, is addressed in part by Cénée, et al. who conducted a case-controlled study and found that men who had used an NSAID had a lower incidence of prostate cancer compared to men not using it. They also found the effect was greater in men with more aggressive disease. This analysis is similar to the ongoing debate about a protective effect of statins in prostate cancer. Unfortunately, in neither case is the evidence obtained from a randomized study. There are numerous potential explanations for these findings other than a true direct effect. Some questions needing answers are: how long was an NSAID being taken, what dose was used and at what interval, and over what period of time? For now, the information is interesting, but as the authors acknowledge, more data are needed from a well-designed study.

The Bottom Line: The use of an NSAID may offer a protective effect against prostate cancer, but many questions need answering before anything can be recommended.

P2, “Predicting Probability…”

Can a biopsy of only the sentinel lymph node accurately determine the presence or absence of lymph node metastases prior to RP? Kneib, et al. addressed this question. They did a guided biopsy of the sentinel node and then performed an RP and lymph node dissection. They found a number of factors to be independent predictors of positive lymph nodes. With all factors combined, they were able to identify 84% of the men with positive lymph nodes. Unfortunately, the authors did not tell us the false positive rate, which is critical to understand the trade off. A significant false positive rate can potentially lead to an incorrect decision to not offer a potentially curative RP. Another unknown is the impact of doing an RP when positive lymph nodes are present. Only one randomized study conducted years ago showed a survival advantage for early, continuous ADT after RP when positive nodes were present, but that study was small and is controversial. Also, many doctors still believe in removing the prostate, even if the nodes contain cancer. More data are needed to understand the role of sentinel node biopsy.

The Bottom Line: Performing a sentinel node biopsy may be helpful for sparing men an unneeded prostatectomy but more data are needed.

P4, “Treatment with…”

Prior studies raised a concern that ADT using an GnRHa increases the risk of cardiovascular (CV) events, even in men without a history of cardiac disease. Other uncontrolled studies found the incidence was lower after bilateral orchectomy, implying that surgical castration might be a better alternative. However, a large, retrospective study from Taiwan suggests that the CV risks are not limited to men treated with an GnRHa; it appears to occur with similar frequency following surgical castration after a median follow-up of 3.3 years. In contrast to previous studies, CV risk was greater during the first 1.5 years after orchietomy. A limitation with all of these studies is their retrospective design. Importantly, randomized studies conducted more than 20 years ago compared the two options and did not find a significant risk of CV morbidity in either group, although the studies involved far fewer men. Another, but larger randomized trial would be needed to make a true determination, something that is highly unlikely to be done.

The Bottom Line: An uncontrolled study suggests that orchietomy has similar CV risk as GnHRA, but only a large randomized study can verify if this is true.

(Continued on page 8)
Brachytherapy  
(Continued from page 6)

Results published in The International Journal of Radiation Oncology, Biology and Physics in August showed that men treated with Cs-131 recover urinary, bowel, and sexual function faster than with other BT radio-particles.

PCF researchers examined long-term effects of permanent BT using low-dose I-125, a common radio-particle, and IsoRay’s Cs-131 in men with low- to intermediate-risk localized prostate cancer. The study enrolled 140 men followed for a median of 95 months. Efficacy of both compounds was assessed by the incidence of BCR.

There was similar relapse-free survival in both groups: 89% vs. 85% in the I-125 and Cs-131 arms, respectively. Together with the prior data, findings support use of low-dose permanent BT to aid in treatment decisions.

Isotopes: A common radio-particle, such as Cs-131, is an approved particle, and 223 retreatment is reasonable and tolerable. A randomized trial is needed to demonstrate whether men will sufficiently benefit.

The Bottom Line: Radium-223 is an approved treatment for men with symptomatic bone metastases, but unfortunately, many men progress. A small study by Heinrick, et al. assessed effects of retreating men whose disease progressed after initial therapy. Most men tolerated a full treatment course. No grade 4 or 5 hematologic events occurred, but most men had unspecified side effects. Only 2% had disease progression during therapy, but over 60% of the men had died by two years. Importantly, retreatment with Radium-223 is possible and tolerable.

The Bottom Line: Omitting low-dose prednisone with cabazitaxel does not affect drug efficacy and could improve outcome but the results of the randomized study are needed to confirm if this true.

P5, “The Influence of...” is low-dose, daily prednisone needed when administering cabazitaxel for progressive, metastatic CRPC? Sonpavde, et al. attempted to address this question by retrospectively analyzing clinical data of men who had been treated with this drug. They found that the men not receiving low-dose prednisone had a longer overall survival than men who did receive the drug. Since the study was not randomized, no definitive answer is possible; however, a randomized study is currently underway.

The Bottom Line: Retreatment with Cabazitaxel is effective and safe, but a randomized study is needed to confirm if it is worthwhile.

Genomic Testing  
(Continued from page 4)

men with adverse disease at radical prostatectomy, and more recently, a biopsy version was released. Recently, Decipher signatures predicting prostate cancer cell line-age and postoperative radiation sensitivity have also been described. Any of these tests can be used by men with localized prostate cancer to provide additional prognostic risk stratification to aid in treatment decisions.

Doc Moyad’s Column  
(Continued from page 3)

References:

Doc Moyad’s Column  
(Continued from page 3)

References:

Doc Moyad’s Column  
(Continued from page 5)

References:

Doc Moyad’s Column  
(Continued from page 5)

References:

Doc Moyad’s Column  
(Continued from page 5)

References:

Doc Moyad’s Column  
(Continued from page 5)

References:

Doc Moyad’s Column  
(Continued from page 5)

References:

Doc Moyad’s Column  
(Continued from page 5)

References:

Doc Moyad’s Column  
(Continued from page 5)

References:

Doc Moyad’s Column  
(Continued from page 5)

References:

Doc Moyad’s Column  
(Continued from page 5)

References:

Doc Moyad’s Column  
(Continued from page 5)

References:

Doc Moyad’s Column  
(Continued from page 5)

References: