Men with advanced prostate cancer with a poor response to their first taxane-based chemotherapy regimen may benefit from switching to another, results of a small randomized trial showed.

“Nearly half of the men who did not achieve a ≥30% decline in PSA level while receiving either docetaxel or cabazitaxel achieved a ≥250% decline when they switched to the other drug,” said Emmanuel Antonarakis, MBBS, of Johns Hopkins University and colleagues in Baltimore.

“Overcoming primary (intrinsic) and secondary (acquired) resistance to taxane therapy remains a challenge in prostate cancer treatment, and several different mechanisms of taxane resistance have been proposed, many of which may operate simultaneously,” Antonarakis and colleagues wrote online in the Journal of Clinical Oncology.

“There is evidence to suggest that not all of the same resistance mechanisms apply to all taxanes. Therefore, the central clinical hypothesis of this study was that some patients with metastatic castration-resistant prostate cancer (mCRPC) with a suboptimal initial PSA decline with their first taxane can achieve a PSA response by an early switch to a second taxane before clinical progression.”

The phase II, noncomparative TAXYNERGY trial included 61 men with prostate cancer patients on active surveillance (AS) who have no cancer found on a confirmatory biopsy may be considered for a less rigorous AS regimen, according toinvestigators.

In a study of 224 prostate cancer patients managed with AS, investigators at Cleveland Clinic led by Ryan Berglund, MD, found that absence of cancer on a confirmatory biopsy is associated with a significant 49% decreased odds of grade reclassification and 68% decreased odds of volume reclassification compared with those who had a positive confirmatory biopsy.

“Overall, our findings suggest that very low-volume disease, reflected by a negative confirmatory biopsy, may be a strong prognostic indicator for slower-grade and volume reclassification, independent of age, PSA density, and stage,” Dr. Berglund’s group wrote in a paper published online ahead of print in the journal Urology. “It is possible that very low-volume of disease may exhibit a more indolent natural history.”

Investigators concluded that a less intense surveillance regimen may be considered for men with a negative confirmatory biopsy. Of the 224 men, 111 (49.6%) had a negative confirmatory biopsy. The remaining 113 men had stable disease on confirmatory biopsy. The median follow-up was 55.8 months.

“A typical AS regimen at Cleveland Clinic consists of: clinic visits every six to 12 months with PSA measurements and digital rectal examinations, a confirmatory biopsy within 12 months of..."
Radical Prostatectomy Innovation and Outcomes at Military and Civilian Institutions


Am J Manag Care 30 June 2017; Published Online

Objectives: Limited data are available regarding the impact of the type of healthcare delivery system on technology diffusion and associated clinical outcomes. We assessed the adoption of minimally invasive radical prostatectomy (MIRP), and whether this adoption altered surgical morbidity for prostate cancer surgery.

Study Design: Conducted retrospective review of administrative data from TRI-CARE, the healthcare program of the United States Military Health System. Surgery occurred at military hospitals, supported by federal appropriations, or civilian hospitals supported by hospital revenue.

Methods: We evaluated TRI-CARE beneficiaries with prostate cancer treated by RP between 2005 and 2009. MIRP was identified based on minimally invasive surgery billing codes. We assessed yearly MIRP utilization, 30-day postoperative complications (Clavien classification system), length of stay, blood transfusion, and long-term urinary incontinence and erectile dysfunction.

Results: A total of 3,366 men were treated by RP at military hospitals compared with 1,716 treated at civilian hospitals, with minimal clinicodemographic differences. MIRP adoption was 30% greater at civilian hospitals. There were fewer blood transfusions (odds ratio, 0.44; P < 0.0001) and shorter lengths of stay (incidence risk ratio, 0.85; P < 0.0001) among civilian hospitals, while 30-day postoperative complications, as well as long-term urinary incontinence and erectile dysfunction rates, were comparable.

Conclusions: Compared with military hospitals, civilian hospitals had a greater MIRP adoption during this time-frame, but had comparable surgical morbidity.

Takeaway points: This is a retrospective review of administrative data from TRI-CARE, the healthcare program of the United States Military Health System.

- Compared with 1,716 men in 767 civilian hospitals, 3,366 men underwent RP in 36 military hospitals.
- The adoption of MIRP was 30% greater at civilian hospitals.
- The 30-day postoperative complications, plus long-term urinary incontinence and erectile dysfunction rates, were comparable.
- Adoption of minimally invasive technology has not significantly improved surgical morbidity.
- This study suggests that adoption of technology may not always translate to an observable improvement in patient outcomes.

Prostate Cancer Screening Benefits Depend on Men’s View of Treatment Side Effects

The benefits of prostate cancer (PCa) screening are most evident in men with a family history of PCa, according to a study that simulated the benefits and harms of PCa screening under various circumstances.

Interestingly, while screening reduced the risk of dying from PCa, it had a negative impact on men without a known cancer risk, said the study, which appeared in the journal BMC Public Health.

“Therefore, there is no reliable method to distinguish clinically relevant from clinically irrelevant tumors,” Dr. Uwe Siebert, a professor at Austria’s Tyrolean Health and Life Sciences University (UMIT), said in a press release.

“In consequence, clinically irrelevant tumors may be treated, which unnecessarily exposes the affected patients to the unfortunately not uncommon long-term treatment complications such as erectile dysfunction (ED), urinary incontinence (UI) and bowel dysfunction,” added Siebert, who is president-elect of the Society for Medical Decision Making.

The study, Benefits and Harms of Prostate Cancer Screening — Predictions of the ONCOTYROL Prostate Cancer Outcome and Policy Model, attempted to tackle the issue of overdiagnosis and overtreatment — the main risk of PCa screening.

To assess its impact on quality of life, researchers analyzed what is called quality-adjusted life expectancy (QALE). The simulation showed that for men without a familial risk, screening reduced QALE, mainly if performed on an annual basis.

“Men at higher risk, depending on age, gained QALE. But how the risk of long-term treatment side effects was viewed affected how beneficial screening was in this group,” said Dr. Nikolai Mühle.

(Continued on page 7)
You should love a good placebo effect but you should also avoid a nocebo effect! So, this is another reason to avoid really negative people and really negative news! Keep it positive (but honest) and you may experience fewer side effects from many medications.

Ah, you’ve got to love a good placebo effect (from the Latin “I will please” – I know this is what it means in Latin because my parents MADE ME take three years of Latin classes – OMG-slow torture!). Placebo effects are well known in the area of pain reduction and even in the area of erectile dysfunction, prostate enlargement, and even hot flash reductions, where as many as one to two of out every three people report some real benefits just from taking a placebo when they thought they were taking a drug! Wow!

However, the little known evil twin/partner of the placebo effect also exists out there and it does not get enough attention. This is the Darth Vader to the Luke Skywalker or the Goofus to the Gallant or the Cain to the Abel or the Ohio State to the Michigan. Nocebo (from the Latin “I will harm” – I know this NOT from my Latin classes but Google), or the nocebo effect, basically refers to a harmful or negative impact a person experiences after taking something that does not really come with that impact. For example, you see a drug on TV that lists 20 side effects and you think you are experiencing one or many of those side effects even though you are not. However, the constant negative reminders of these side effects or even embellishment of them is enough to make you think you are experiencing the side effect.

So, researchers recently looked at an incredibly large randomized double-blind trial of low-dose atorvastatin (Lipitor®), the famous statin or cholesterol lowering drug vs. placebo and then they looked again at the study after it was non-blinded when everyone was then offered just the drug for several years so that patients and doctors clearly knew who was taking this drug. And, they found that the rate of muscle complaints significantly jumped in number after people found out what they were taking or, in other words, suggesting that nocebo came to town! So, the patients had no problem with the statin and no muscle issues, and then they find out they were actually taking a statin and then bam! Suddenly, muscle problems abound!?

This helps to explain part of the reason why you read about countless muscle issues with cholesterol lowering drugs despite placebo studies suggesting the rate of muscle problems are often similar to a placebo. This occurs with all types of low-dose drugs, in my opinion, and based on research from overactive bladder drugs to prostate enlargement drugs. This is also why avoiding overly-negative commercials or even extremely negative health care professionals and other negative people can help you, not only to keep your optimism, but also reduce your risk of nocebo from a variety of sources. So then you can instead experience more placebo!

By the way, as I was writing this column a commercial came on TV that said a drug I am interested in taking can cause diarrhea, anal leakage, erectile dysfunction, incontinence, and extreme noisy and malodorous flatulence. I decided NOT to try this drug because I already experience all of these symptoms every time they call me from Us TOO headquarters and tell me my column is late! Nocebo effect?!

Some Younger Men with Prostate Cancer Are Candidates for Active Surveillance

Slower Progression of Low-Risk Disease in Men Under 60

Younger age at diagnosis of low-risk prostate cancer was independently associated with reduced risk of disease progression in men managed with active surveillance (AS), researchers reported. Among 1,433 men with clinical low- and intermediate-risk prostate cancer, compared with the 58% of participants diagnosed when they were older than 60, those diagnosed at or before age 60 had a 7% reduction (55% vs. 48%) in the rate of progression (as assessed by biopsy-based Gleason score upgrade-free rates) during five years of AS (P<0.01), the authors wrote online in the Journal of Clinical Oncology.

“On Cox regression analysis, younger age was independently associated with lower risk of biopsy-based Gleason score upgrade (hazard ratio [HR] per one-year decrease, 0.97 [95% confidence interval (CI) 0.956 to 0.983]; P<0.01), which persisted in

Reference:
Genomic Test Can Predict Prostate Cancer Metastases After Surgery
But Test is Not Ready for Clinical Practice, Expert Warns

The genomic classifier test, Decipher, independently predicted metastases in men with prostate cancer following radical prostatectomy (RP), including nearly all clinicopathologic, demographic and treatment subgroups, according to a meta-analysis.

“The analysis of literature reports published from 2011 to 2016 showed that up to 16% of 855 men with a high-risk Decipher score >0.60 could benefit from the Decipher test,” reported Felix Y. Feng, MD, of the Helen Diller Family Comprehensive Cancer Center at the University of California San Francisco, and colleagues.

“After adjusting for clinicopathologic variables, Decipher remained a statistically significant predictor of bone, visceral, or lymph node metastasis per 0.1 unit (hazard ratio [HR] 1.30, P<0.001),” they wrote in the Journal of Clinical Oncology. “The C-index for 10-year distant metastasis of the clinical model was 0.76 and increased to 0.81 when Decipher was included,” they added.

“Although clinicopathologic variables perform reasonably well to predict who is at very low or very high risk of recurrence, Decipher independently improves upon this to further discriminate metastatic risk within these clinical risk groups,” the authors stated. “This observation has important implications for designing clinical trials for men with high-risk disease.”

Decipher, developed by GenomeDX Biosciences of Vancouver, is a 22-gene genomic classifier designed to aid in prognostication of patients who have undergone RP. While the authors noted that the use of Decipher could enrich a future study population for metastasis, they cautioned that more study is needed to determine how genomic testing can fit into clinical decision-making.

In an accompanying editorial, Anthony V. D’Amico, MD, of Brigham and Women’s Hospital and Dana-Farber Cancer Institute in Boston, agreed that caution is key, citing a number of uncertainties.

“ ‘It remains unknown whether the assessment of the time after RP when these patients were observed to develop metastatic disease was consistent,’ ” he said. “Other knowledge gaps include whether participants would have been considered high risk for metastases on the basis of clinical indices and how treatment affected the predictive value of their Decipher score,” he explained.

“The question of patient selection also needs to be determined, and whether genomic classifiers can provide information beyond that already provided by clinical predictors such as RP Gleason score, seminal vesicle invasion (SVI), and lymph node invasion (LNI),” he said.

“Future studies should look at use of the Decipher test in men who don’t have either a high-risk factor such as an RP Gleason score of 9 or 10, or a low-risk factor such as an RP Gleason score of 3+4,” D’Amico suggested.

“Guidelines for the type of scans and scanning frequency after PSA failure are needed, as are recommendations for adjuvant radiotherapy (RT) and/or androgen deprivation therapy (ADT) and the timing of salvage RT and/or ADT. “Until such information is available, it does not seem that the Decipher test is ready for use in clinical practice or to select men who are at high risk for developing metastatic prostate cancer for randomized post-RP adjuvant therapy trials,” D’Amico concluded.

Researchers analyzed five studies that assessed the benefit of the Decipher test in men who underwent RP between 1990 and 2010. Median follow-up was 8 years. In the group of 855 patients, 60.9% were classified as low risk (<0.45), 22.6% as intermediate risk (0.45 to 0.60), and 16.5% (>0.60) as high risk.

The 10-year cumulative incidence metastases rates of the three groups were 5.5%, 15.0%, and 26.7%, respectively (P<0.001). Pooled Decipher HRs across the five studies showed that the Decipher score was significantly associated with time to metastasis with an HR of 1.52 per 0.1 unit.

After adjusting for preoperative PSA level, RP stage, Gleason score, as well as surgical margin, SVI and LNI status, the Decipher score remained significantly associated with the risk of observing metastasis. Decipher was also associated with risk of metastasis in subgroups of white men, those who received RP alone as well as those treated with RP and salvage RT, and those treated with RP and ADT.

When the investigators adjusted for post-RP adjuvant RT and/or salvage RT or ADT, the adjusted HR for men with a high-risk Decipher score decreased from 3.31 (P<0.001) to 2.77 (P=0.001), suggesting that the predictive value of the Decipher test may be affected by RP practice patterns of treatment. For black men and those of any race treated with adjuvant RT or ADT, Decipher did not reach statistical significance for predicting risk of metastasis (HR 1.43, 1.86, and 1.52, respectively).

In addition to the study’s retrospective design, limitations included bias in observing the interval to metastasis after RP. This may have directly affected the value of the adjusted HR, the authors stated.

PET CT May Show Treatment Outcome Early in Metastatic Castration Resistant Prostate Cancer

Tracer uptake on PET/CT imaging showed significant association with clinical outcomes of bone-involved metastatic castration resistant prostate cancer (mCRPC), a small clinical trial showed.

Early change in the maximum Standardized Uptake Value (SUV) of [18F, a radioactive isotope of fluoride], sodium salt (NaF) was the strongest predictor of progression-free survival (PFS), essentially doubling the hazard ratio (HR) for disease progression or death. Changes in total functional burden (SUVtotal) had a stronger correlation with PFS than did change in the number of bone lesions.

“Global imaging metrics, such as SUVtotal and SUVmean outperformed all baseline clinical markers for predicting clinical outcomes. The results held up for men treated with chemotherapy or androgen receptor pathway inhibitors (e.g., abiraterone), supporting continued development of NaF-PET/CT.

(Continued on page 5)
mCRPC. Their median age was 71, median PSA was 82.3 ng/mL, and 35% had visceral (soft tissue) metastases. Men were randomly assigned in a 2:1 fashion to initial docetaxel (n=41) or cabazitaxel (n=22) for eight-three-week cycles of chemotherapy. Men who achieved ≥30% PSA decline by the fourth cycle (12 weeks) remained on the same drug, while those who did not were switched to the other taxane. Median follow-up was 26 weeks.

PSA levels were done every three weeks, and the primary clinical endpoint was a ≥30% decline in PSA from baseline. Circulating tumor cells (CTCs) were also isolated from the (blood) of patients at baseline and during the first chemotherapy cycle. The cells were analyzed for intracellular biomarkers of treatment effect, including percentage androgen receptor nuclear localization (ARNL) and microtubule bundling.

Of the 61 patients, 33 stayed on their initial drug, 15 were switched due to poor treatment response, and 13 discontinued therapy. Of the 15 patients who switched, seven (46.7%) achieved the primary clinical endpoint. Overall, 35 patients achieved the primary clinical endpoint – 25 on or before the fourth cycle and 10 afterward.

The investigators noted several study limitations, including the short length of follow-up and the small sample size, especially the small number of patients who switched drugs. Therefore, the study was unable to definitively prove that the taxane switch was responsible for subsequent PSA responses in those switching therapy or that biomarker modulation after the switch induced those PSA responses.

Although this study is not sufficient to change the standard of care among men with mCRPC receiving taxane therapy, it suggests that a treatment switch from one taxane to the other may be worthy of further investigation in patients who do not achieve a ≥30% PSA reduction within the first 12 weeks. Importantly, prior studies have shown that men who do not achieve a 30% PSA decline by week 12 of treatment have a poorer survival with docetaxel and cabazitaxel than those who do.

The investigators also found that analyzing CTCs for shifts in ARNL, a known effect of taxane-based drugs, could be a quick way to determine a patient’s clinical response. After one week of taxane therapy, the percentage of ARNL in men who subsequently achieved a ≥50% decline in PSA was 44%, compared with 64% in those who did not (P=0.004).

“Changes in CTC-specific ARNL observed as early as one week after therapy initiation may potentially be a more sensitive and specific biomarker of subsequent clinical response than 12-week PSA changes,” the researchers suggested. “Future prospective studies should evaluate whether switching taxane therapy early on the basis of a CTC biomarker may improve outcomes compared with switching therapy on the basis of PSA trends (or not switching therapy at all).”

Asked for his perspective, Eric Klein, MD, chairman of the Glickman Urological & Kidney Institute at the Cleveland Clinic, who was not involved with the study, said via email: “It’s certainly a new approach in prostate cancer, where switching between two chemotherapeutic agents with similar mechanisms of action has not been tried before — there are ongoing studies comparing sequencing of agents that target the androgen receptor as well, so the concept is being tested with other sorts of agents too. The strength of the study is that the switch was predicated on a defined and uniform response criterion that is clinically meaningful (failure to achieve a ≥30% PSA reduction after several doses of the initial drug).

“The study showed that some men who don’t have a good response to an initial taxane may still derive clinical benefit from switching to another,” Klein added. “But it was a small study and, as such, is not generalizable to clinical practice yet, especially given that there are multiple other FDA-approved agents for men who fail chemotherapy. The other promising observation was that CTCs seemed to be a marker of response, adding to the growing literature that supports their use in clinical decision making.”

Dr. Antonarakis’ conclusions to this study agree with Dr. Klein’s observations stating, “Nevertheless, further dedicated prospective randomized trials focusing on a taxane switch using integral biomarkers are warranted.”

**PET CT & Treatment Outcome in mCRPC**

(Continued from page 4)

imaging metrics as biomarkers for mCRPC to bone,” as reported online in the *Journal of Clinical Oncology.*

“Increasing SUV_total in the first 12 weeks of treatment was associated with progressive disease,” Robert Jeraj, MD, of the University of Wisconsin in Madison, and co-authors concluded. “Our analysis demonstrates that [18F]NaF PET/CT may be a useful tool in early follow-up of men with mCRPC and bone metastases. Additional studies are warranted to assess the therapy-specific ability of [18F]NaF PET/CT to accurately identify response to treatment.

“No established tools exist to provide reliable quantitative measures of changes in bone metastases in response to treatment for mCRPC. Historically, post-treatment PSA measures have been used to monitor patients, but PSA has no spatial context with treatment response,” the authors noted in their introduction. “In addition, [99Tc] technetium-based bone scintigraphy (bone scan) provides limited information about response assessment based on changes in lesion count during treatment. A bone scan identifies radiographic progression (formation of new lesions) but does not capture post-treatment changes in existing lesions or in overall disease burden,” the authors continued.

“[18F]NaF-PET/CT has characteristics well suited for imaging osteoblastic activity — rapid bone uptake and blood clearance. Multiple studies showed higher sensitivity and specificity compared with technetium-based bone scintigraphy or planar single-photon emission CT. Additionally, [18F] NaF-PET/CT demonstrated...”

(Continued on page 8)
Younger Men & Active Surveillance

(Continued from page 3)

1,433 individuals choosing AS beginning in 1992, with a minimum follow-up of six months from the time of initial diagnostic biopsy. Men were a median of 63 years old at baseline, were followed for a median of 49 months, and most (89%), had a Gleason score at diagnosis of at least 3+3.

Significant baseline differences in the younger age group included lower PSA values, lower Gleason scores, and lower Cancer of the Prostate Risk Assessment (CAPRA) scores.

AS has been shown to safely mitigate overtreatment of low-risk prostate cancer in this era of PSA screening, and as noted recently in MedPage Today, it is increasingly, though inconsistently, used.

In the absence of standardized surveillance protocols, the younger cohort in this study received more surveillance biopsies than those over 60 in the same interval (median of three versus two; P<0.01), and similar numbers of PSA tests (median of 10 vs. nine; P=0.27).

“From this perspective, the lower risks of progression, despite greater scrutiny (i.e., an approximately 30% lower risk of upgrading over time), should be informative to counsel younger men with low-risk prostate cancer who are considering initial management with surveillance,” the authors suggested.

Given the higher baseline sexual and urinary function younger patients have at the time of diagnosis, they stand to lose the most by immediate treatment – yet age remains an empirical driver of treatment decisions, thereby “favoring early treatment in younger individuals.”

Indeed, older patients in the study were more likely to receive radiation therapy than younger patients (38% vs. 21%) and were less likely than their younger counterparts to receive RP (58% vs. 78%; P=0.01 for both), although these differences were not significantly associated with age after (statistical) adjustment.

“Increasing the thoughtful application of AS in patients with low-risk prostate cancer has the potential for benefits to healthcare systems as a whole, including improved health-related quality of life, reductions in treatment burden, and reduced costs,” Mark Garzotto, MD, of the Veterans Administration Portland Health Care System in Oregon, wrote in an accompanying editorial.

Reiterating the authors’ acknowledgement that age only “marginally” improved the performance of multifactor risk models, Garzotto suggested that younger age may be better used to predict individual patient risk.

“Evaluation should consider current health status, known risk factors for progression, and age,” Garzotto noted. “It is important for clinicians to understand and explain to a younger patient that he concurrently has both the most to gain and the most to lose.”

Leapman and colleagues wrote that, “although there is no consensus on the optimal screening approach, a growing body of literature supports obtaining an initial baseline screening at a young age — as young as 45 — and basing subsequent screens on this initial result.”

Garzotto said that limitations to the study included the fact that a lower rate of cancer progression was seen in one in four patients referred externally (HR ratio, 0.754; 95% CI, 0.60 to 0.95). “More information is needed to determine if they represent a random sample of the population or a selected group with more favorable underlying risk features.”

Other limitations included the increased proportion of younger than older patients who had lower-risk disease profiles and an initial diagnosis outside the authors’ institution, and that the median follow-up duration after prostatectomy of 41 months may have underestimated the rates of recurrence.

MedPageToday, 16 June 2017

Post-RP Radiotherapy Benefits Selected Men with Elevated PSA

Postoperative radiotherapy (RT) for men who have persistently elevated PSA levels following radical prostatectomy (RP) for prostate cancer is associated with improved survival among those with adverse pathologic characteristics, according to a new study. In addition, persistently elevated PSA after RP is not always associated with a poor prognosis.

Giorgio Gandaglia, MD, of IRCCS Ospedale San Raffaele and Vita-Salute San Raffaele University in Milan, Italy, and colleagues studied 496 men who underwent RP and lymph node dissection at two referral centers from 1994 to 2014 and had persistently elevated PSA (0.1 to 2 ng/mL at six to eight weeks after RP). There were 251 men who received postoperative RT and 245 who did not.

The median follow-up for survivors was 110 months, the investigators reported in a paper published online ahead of print in European Urology. “In all, 49/496 (9.9%) men died from prostate cancer. The 10-year cancer-specific mortality (CSM)-specific mortality was 88%. Receipt of postoperative RT was associated with a survival benefit only among patients with a CSM risk of 30% or higher. Patients with a CSM risk less than 30% did not benefit from postoperative RT, and should be initially managed expectantly,” according to the researchers.

Among the 245 men who did not receive postoperative RT, those in pathologic grade 4 or higher had a nearly sevenfold higher risk of CSM than those in pathologic grade 3 and lower.

Pathologic grade and stage independently predicted CSM. In multivariable analysis, a pathologic grade group of 4 or higher was associated with a significant 2.7-fold higher risk of CSM compared with a pathologic grade group of 3 or less. A pathologic tumor stage of pT3b/4 vs. pT2-pT3a was associated with a significant 2.3-fold higher risk of CSM.

The association between CSM-free survival and post-RP PSA differed by the baseline risk of CSM, as defined by pathologic characteristics. The effect of rising PSA was evident only in men with a CSM risk ≥10%. “Increasing PSA levels should be considered as predictor of mortality exclusively in men with worse pathologic characteristics,” the study concluded.

Renal and Urology News 20 June 2017
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, “Negative Confirmatory…”
One of the negative aspects of active surveillance (AS) is the current recommendation that men undergo repeat prostate biopsies as part of their follow-up management. Even with some form of anesthesia, patients find the biopsies unpleasant. The study by Berglund et al. adds additional data to other reports that suggest a negative confirmatory biopsy means that a man has lower risk of progression and may need less aggressive follow-up. They found that half the men had a negative second biopsy and their risk at five years was lower than older men with a negative biopsy. Follow-up is less than six years; longer follow-up that shows the same benefit could lead to eventual changes in AS protocols. These studies do raise a curious question. If these findings are correct, looking at men who had saturation biopsies may be worthwhile. What are the results of those men the first time it was done? If men in the current studies entered AS with three or fewer positive cores out of a 12-core biopsy, theoretically having the same number of positive cores out of a 24-core saturation biopsy should give the same result. If that were true, one could consider doing 24 cores initially and avoiding a confirmatory biopsy.

The Bottom Line: A negative confirmatory biopsy in men on AS may allow less intense surveillance, but longer follow-up is needed to be sure.

P1, “Poor Responders…”
Currently, two taxanes are in use for men with metastatic castration-resistant prostate cancer (mCRPC), docetaxel and cabazitaxel. Docetaxel is primarily used first, in part because it is generically available and has a more favorable side effect profile. Unfortunately, the response rate with either drug is not 100%; the question is when and if the first drug should be switched to the second drug. The study by Antonarakis et al. provides preliminary data on one approach to answer this question. Results showed that about 50% of men who did not have at least a 30% decline in PSA initially in 12 weeks did respond after being switched to the other taxane.

The authors acknowledge study limitations, including a non-randomized design and a small sample size. Comparing survival between men randomized to a full course of primary therapy and men switched to the second drug is required to answer this question. Perhaps that study is worth doing.

The Bottom Line: Switching taxanes after 12 weeks if the PSA does not decline by 30% may help some patients, but more data are needed.

P1, “Significance of…”
A survey report involving over 1,100 men from North Carolina found some potentially useful information for counseling patients about their treatment options for local disease. The report found that African-American men were more concerned about how the treatment would affect their daily activities and about the costs of treatment. One wonders how their cost concerns are related to their health insurance. Are they more concerned because they would have more out of pocket costs? Another factor that needs to be evaluated is the adequacy of baseline sexual function. The study did not report on the factors that could have influenced the survey results.

The Bottom Line: African-American men in North Carolina appear to have different concerns than Caucasians about the consequences of local therapy. Whether those concerns are the same in other states and whether it relates to differences in sexual function need to be determined. These findings could influence how doctors counsel their patients.

P3, “Some Younger Men…”
As the years of follow-up accumulate for men on AS, clinicians are looking more closely at the effect of including younger men. Leapman et al. reported on over 1,400 men under age 60 and found they were less likely to have upgrading at five years than men over 60. This does not yet prove that AS is clearly safe for younger men, as the follow-up is too short. Furthermore, it is not enough proof that a less-intensive protocol is appropriate for them.

The Bottom Line: The Decipher test to predict metastases after radical prostatectomy is required to answer this question. Results showed that 16% of men could benefit from the test, a relatively low value. In fact, the test was only 5% more accurate than conventional methods. Given these values, one might question the utility of this test for this group of patients. More data are needed to further determine who should undergo this test, but the current data are not very supportive.

The Bottom Line: The Decipher test after radical prostatectomy does not yet add enough information beyond conventional methods to warrant routine use after radical prostatectomy, as was the conclusion in the editorial comment.

Screening Benefits & View of Side Effects

(Continued from page 2)

berger, assistant professor at UMIT who coordinated the study. While AS reduced overtreatment, the study showed gains in life expectancy were offset by delayed treatment and additional tissue sampling, illustrating the delicate balance of screening.

“The study highlights the problem of overdiagnosis and illustrates the dependency of screening benefits on individual risk factors and preferences,” said Dr. Wolfgang Horninger, dean of the urology department at Austria’s Medical University of Innsbruck, which collaborated with UMIT. “Thus, it contributes to the improvement of patient counseling and supports an individual use of screening examinations, which all of us consider important issues.”

Medical News Today
5 July 2017
PET & CT (Continued from page 5)

potential for quantitative evaluation of bone disease, including quantitative accuracy and ability to monitor functional changes during treatment,” Jeraj and colleagues noted.

Continuing the assessment of [18F]NaF-PET/CT, investigators studied 56 men with mCRPC with bone metastases, 16 treated with chemotherapy and 40 with androgen receptor-targeted agents. The patients had [18F]NaF-PET/CT imaging at baseline and after three cycles of therapy (midway through planned treatment).

At data collection, 40 of 46 evaluable patients had progressive disease, three died, and three did not progress and remained in follow-up. The authors reported that 30 patients had radiographic progression. The patients had a median baseline SUV_{max} of 75.5 g/mL (range 28.8 to 225.3 g/mL) and median baseline lesion count of 34 by [18F]NaF-PET/CT.

The median time from start of treatment to disease progression was 7.6 months and did not differ significantly between treatment groups. Baseline SUV_{max}, SUV_{mean}, and lesion count had significant correlations with PFS (P=0.008 to P=0.002). Mid-treatment SUV_{total} had the strongest association with PFS in a univariate analysis (HR 1.97, 95% confidence interval (CI) 1.44-2.71, P<0.001). By multivariable analysis SUV_{mean} (HR 3.40, 95% CI 2.02-5.73, P<0.001) and number of lesions (HR 2.90, 95% CI 1.86-4.53, P<0.001) had the strongest associations.

In the subgroup of patients who received androgen receptor-targeted therapy, mid-treatment SUV_{total} had the strongest association with PFS and lesion count. *MedPageToday* 30 June 2017

Dr. Berglund and colleagues found that among 242 men with three or more biopsies, a negative confirmatory biopsy was associated with 72% lower odds of overall reclassification (European Urology (Vol. 66, pp. 337-342, 2014), did not differentiate between grade- and volume-related reclassification.

Dr. Berglund’s team also cited a study by K. Clint Cary, MD, and colleagues, which found that among 242 men with three or more biopsies, a negative confirmatory biopsy was associated with 72% lower odds of overall reclassification (European Urology (Vol. 66, pp. 337-342, 2014), did not differentiate between grade- and volume-related reclassification.

Dr. Berglund and colleagues acknowledged some study limitations. The study was observational and, as such, subject to selection bias “and imbalance in unquantified variables.” In addition, the limited median follow-up time of 55.8 months may not fully capture the natural history of slow-progressing prostate cancer. Third, it remains to be determined how the endpoints of grade and volume reclassification will ultimately reflect overall or cancer-specific survival. *Renal and Urology News* 26 June 2017

Treatment-related Factors in Black and White Men

(Continued from page 1)

Black men were significantly more concerned about recovery time (81% vs 50%, respectively). There were significant racial differences when it came to costs, as well; 66% of black men rated cost as very important vs. 32% of white men.

Presented at the 2017 Annual ASCO meeting, Abstract 6517

Oncology Nurse Advisor
19 June 2017

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