Fifteen Years Later: Cancer Risk Higher in 9/11 Exposed Responders/City Residents

Fifteen years have passed since the September 11, 2001 attack on the World Trade Center (WTC) in New York City (NYC), which not only killed and injured thousands of people but also exposed first responders and city residents to airborne toxins. The health impact of exposure to these hazardous substances and the long-lasting effects of the trauma are now examined in a special issue of the American Journal of Industrial Medicine. Two of the papers focus specifically on cancer risk.

One paper examined the cancer incidence in rescue/recovery workers (RRWs) as well as residents of lower Manhattan who were exposed to the dust and debris following the collapse of the WTC office towers. The authors conclude that there is some evidence of increased risk for cancer among exposed individuals and found that prostate cancer and cutaneous melanoma were significantly elevated in both populations. The other study approached the issue from a different angle and specifically examined cancer occurrence in firefighters. But instead of comparing the cancer incidence in firefighters to that in the general population, the authors used a cohort of non-WTC-exposed firefighters. This study found that the all-cancer incidence rate among the WTC-exposed firefighters was similar to that of the reference group of urban US firefighters. However, the incidence of thyroid cancer was elevated over

(Continued on page 4)

Is an Extended Prostate Biopsy Scheme Associated with an Improvement in the Accuracy Between the Biopsy Gleason Score and Radical Prostatectomy Pathology?

Prostate cancer (PCa) is the most common malignancy in elderly males in Europe and in the USA. New imaging modalities have provided useful information in the management of men with PCa. For example, the multiparametric magnetic resonance imaging (mp-MRI) of the prostate and subsequent transrectal ultrasound (TRUS) targeted biopsies of possible suspicious gland sites. It can be very helpful in special cases (for example constant increase of PSA levels, negative DRE findings and prior negative sets of prostate biopsy) to achieve the optimal therapy-option.

The incidence of PCa in Northern and Western Europe is over 200/100,000, and the rate of the newly detected PCa is continuously increasing. The PCa screening is one of the most controversial topics of the urological field. Pathological digital rectal examination (DRE) and PSA levels indicate PCa. The exact diagnosis and the decision of the further PCa-therapy depend on the histopathological verification of an adenocarcinoma in prostate biopsy (PB) samples or operative specimens. The management of men receiving a non-operative therapy (for exam-

(Continued on page 5)
Association of Survival Benefit with Docetaxel in Prostate Cancer and Total Number of Cycles Administered – A Post Hoc Analysis of the Mainsail Study


**JAMA Oncol 25 August 2016; Epub**

**Importance:** The optimal number of docetaxel (Dxl) cycles in men with metastatic castration resistant prostate cancer (mCRPC) has not been investigated yet. It is unknown whether it is beneficial for men to continue treatment upon six cycles.

**Objective:** To investigate whether the number of Dxl cycles administered to men deriving clinical benefit was an independent prognostic factor for overall survival (OS) in a post hoc analysis of the Mainsail trial.

**Design, Setting, and Patients:** The Mainsail trial was a multinational randomized phase 3 study of 1,059 men with mCRPC receiving Dxl, prednisone, and lenalidomide (DPL) or Dxl, prednisone, and a placebo (DP). Study patients were treated until progressive disease or unacceptable adverse effects occurred. Median OS was found to be inferior in the DPL arm compared with the DP arm. As a result of increased toxic effects with the DPL combination, men on DPL received fewer Dxl cycles (median, six) vs. eight in the control group. As the dose intensity was comparable in both treatment arms, we investigated whether the number of Dxl cycles administered to men deriving clinical benefit on Mainsail was an independent prognostic factor for OS. We conducted primary univariate and multivariate analyses for the intention-to-treat population. Additional sensitivity analyses were done, excluding men who stopped treatment for reasons of disease progression and those who received four or fewer cycles of Dxl for other reasons, minimizing the effect of confounding factors.

**Main Outcome Measures:** Total number of Dxl cycles delivered as an independent factor for OS.

**Results:** Overall, all 1,059 men from the Mainsail trial were included (mean [SD] age, 68.7 [7.9] years). Treatment with eight or more Dxl cycles was associated with superior OS (hazard ratio [HR], 1.9; 95% CI, 1.7–2.2; P <0.001), irrespective of lenalidomide treatment (HR, 1.06; 95% CI, 0.92–1.22; P=0.41). In the sensitivity analysis, men receiving a greater number of Dxl cycles had superior OS; men who received more than 10 cycles had a median OS of 33.0 months compared with 26.9 months in men treated with eight to 10 cycles; and men who received five to seven cycles had a median OS of 22.8 months (P <0.001). Conclusion and Relevance: These findings suggest that continuation of Dxl chemotherapy contributes to the survival benefit. Prospective validation is warranted.

Effects of Long-term Androgen Deprivation Therapy on Cognitive Function Over 36 Months in Men with Prostate Cancer

Alibhai SMH, Timilshina N, Duff-Canning S, et al.

**Cancer 1 September 2016; Epub**

Many men with prostate cancer (PC) require long-term androgen deprivation therapy (ADT), but to our knowledge, its effects on cognitive function beyond one year are not described. Three groups of men aged ≥50 years matched by age and education were enrolled: 77 men with nonmetastatic PC treated with continuous ADT, 82 men with PC not treated with ADT (PC controls), and 82 healthy controls. A battery of 14 neuropsychological tests, examining eight cognitive domains, was given on five occasions over 36 months. Changes in cognitive scores over time were analyzed by linear mixed effects regression, the percentage of men per group with declines in ≥1/2 cognitive tests, and a global summary of cognitive change. The mean age of the study subjects was 68.9 years, with a median of 16 years of education. In mixed effects models adjusted for age and education, ADT use was not found to be associated with significant changes over time in any cognitive test compared with healthy controls. The percentage of participants declining by ≥1.5 standard deviations in ≥2 tests or ≥2 standard deviations in ≥1 tests was similar across groups. A global summary of cognitive change found no statistically significant worsening of cognitive function among ADT users compared with controls. Sensitivity analyses adjusting for duration of ADT and using multiple imputation for missing data did not materially alter the study findings. The ongoing use of ADT for up to 36 months does not appear to be associated with cognitive decline.
New research suggests that lifting lighter weights for more times/repetition (to cause muscle exhaustion) improves muscle mass and strength as much as lifting heavier weights with less repetitions, and you can also reduce your risk of serious injury with this new method. Now, you do not have any more excuses, so please get out there and lift weights!

Have you ever been in a gym and watched some dude (aka “large man”) that looks like he loves to use steroids and probably rationalizes their use by calling them “natural” (heck poison ivy is also natural folks) and whenever he tries to lift heavier weights just a few times he screams and grunts and disrupts everyone else in the gym?! This is almost as annoying as the guy that “spots” for this muscle head and yells “come on” or “give it 110%” or “you got this!”

Okay, the thought here has always been that the more weight you can lift in general for 8-12 repetitions the stronger and bigger you can get! However, maybe it is time to challenge those muscle heads that make all the noise! New research from Canada, you know the folks who brought you hockey and good beer (love those Canadians), has preliminarily demonstrated a potentially better and safer way to be weightlifting!

Two groups of men were involved in this study for three months and were assigned to either the “higher-repetition” group that lifted weights of 30-50% of their maximal strength for 20-25 repetitions per set or a “lower-repetition” group that did eight to 12 repetitions per set, but at 75-80% of their maximal strength. At the end of the study, there was NO difference in strength and lean muscle mass increases between the groups!

Oh man! This is awesome! This means weak dudes like me can use a lower weight dumbbell for example and lift it 20-25 times and get the same result as lifting a much heavier dumbbell weight about eight times while the veins in my neck and forehead are sticking out far enough to be the main character in a horror movie! This is preliminary research and we need to get more results from all age groups but the research is beginning to show that LESS WEIGHT = MORE. Now you have no excuse not to lift weights because in my opinion this can dramatically reduce your risk of injury since you are not trying to lift a really heavy weight that could pull or tear a muscle.

So, the next time you see some silly large grunting steroid-like dude at the gym lifting make sure you walk up to him and say “Dr. Moyad said lifting less more is actually as good as lifting more less!” And then while he is trying to figure out what you mean by that, please turn around and run for the nearest door before he decides to beat the heck out of you!

In fact, actually I changed my mind! Feel free NOT to use my name during this confrontation because I want to keep writing for Us TOO (aka stay alive) and I also look less attractive with a variety of broken twisted bones and a puffy bruised face!

Reference:

Long-Term Outcome and Side Effects in Patients Receiving Low-Dose I-125 Brachytherapy: A Retrospective Analysis

Logghe P, Verlinde R, Bouttens F

International Braz J Urol 18 August 2016; Epub

To retrospectively evaluate the disease-free survival (DFS), disease-specific survival (DSS), overall survival (OS) and side effects in men who received low-dose rate (LDR) brachytherapy (BT) with I-125 stranded seeds. Between July 2003 and August 2012, 274 men with organ-confined prostate cancer were treated with permanent I-125 BT. The median follow-up, age and pretreatment prostate specific antigen (PSA) was 84 months (12-120), 67 years (50-83) and 7.8 ng/mL (1.14-38), respectively. Median Gleason score was 6 (3-9). 219 men (80%) had stage T1c, 42 patients (15.3%) had stage T2a, three (1.1%) had stage T2b and three (1.1%) had stage T2c. The median D90 was 154.3 Gy (102.7-190.2). DSS was 98.5%, OS was 93.5%. 13 men (4.7%) developed serious disease, seven patients (2.55%) had local progression. In 139 low-risk patients, the five-year biochemical freedom from failure rate (BFFF) was 85% and nine men (6.4%) developed clinical progression. In 139 low-risk group, the five-year BFFF rate was 70% and five men (7.1%) developed clinical progression.

Median nadir PSA (nPSA) in men with biochemical relapse was 1.58 ng/mL (0.21 - 10.46), median nPSA in men in remission was 0.51 ng/mL (0.01 - 8.5). Men attaining a low nPSA had a significant higher BFFF (p<0.05). Median D90 in patients with biochemical relapse was 87.2 Gy (51 - 143.1). Patients receiving a high D90 had a significant higher BFFF (p<0.05).

In a well selected patient population, LDR I-125 BT offers excellent outcomes. Reaching a low nPSA and attaining high D90 values are significant predictors for a higher DFS.
Fifteen Years Later: Cancer Risk Higher in 9/11 Exposed Individuals (Continued from page 1)

In the first of the just-published papers, a team of researchers led by Jiehui Li, MBBS, MS, New York City Department of Health and Mental Hygiene, examined cancer incidence from 2007 to 2011 among 59,358 individuals: 24,170 RRWs and 35,188 non-RRWs (local residents, area workers, and school staff/students).

Overall, they observed a statistically significant excess of incidence of total cancers among both workers engaged in rescue/recovery operations between September 11, 2001, and July 31, 2002 and non-RRW survivors. Among RRWs, 685 first primary incident cancer cases were identified during 2007 to 2011. Cancer incidence was higher for 24 cancer sites combined and significantly differed from incidence in the reference population (adjusted standardized incidence ratio [SIR], 1.11).

The incidence of prostate cancer (number of observed cases, 223; SIR, 1.43), thyroid cancer (number of observed cases, 37; SIR, 1.79), and skin melanoma (number of observed cases, 37; SIR, 1.49) was significantly increased. Of note, the SIR for lung cancer was significantly reduced during this period (number of observed cases, 42; SIR, 0.69), and 1 mesothelioma case was reported. Among the non-RRW population, 992 first primary incident cancer cases were identified (SIR, 1.08). Of the 24 cancer sites, the incidence in four was significantly elevated: prostate (number of observed cases, 196; SIR, 1.27), skin melanoma (number of observed cases, 44; SIR, 1.54), female breast (number of observed cases, 187; SIR, 1.34), and non-Hodgkin’s lymphoma (number of observed cases, 56; SIR, 1.49).

As with rescue workers, there was also a significantly reduced SIR for lung cancer (number of observed cases, 67; SIR, 0.69); one mesothelioma case was reported. Dr. Li and colleagues concluded that the excess incidence of prostate and thyroid cancers has continued among RRWs, but a small and statistically higher than expected rate was seen for melanoma in both groups and for female breast cancer and non-Hodgkin’s lymphoma among non-RRWs. They also point out that the “increased incidence in most of these cancers lacked support from internal comparisons to examine whether there was an association with magnitude of exposure.”

For example, despite a significant dose-response trend associated with melanoma among the civilian population, the absence of information on ultraviolet light exposure before and after 9/11 (a major confounder) “makes meaningful interpretation of causality between WTC exposure and the cancer difficult,” they note.

But despite these limitations, “our findings show some evidence of increased risk of cancer among WTC exposed populations, yet they need to be substantiated by additional follow-up studies as the latency period from a potential WTC exposure increases,” the authors write.

Cancer Risk Debated

More than 13,000 career firefighters employed by the FDNY and tens of thousands of other individuals were exposed to a large array of potentially harmful substances resulting from tons of dust from the collapse of the buildings, along with combustible products from the fires that burned for several months following the attacks. These substances included pulverized cement, glass fibers, asbestos, polybrominated diphenyl ethers, polycyclic aromatic hydrocarbons, polychlorinated biphenyls, and polychlorinated furans and dioxins, some of which are classified as or are probably carcinogens.

As previously reported by Medscape Medical News, several studies have already suggested, to varying degrees, an increase in cancer risk among exposed individuals. In 2011, The Lancet reported that exposed firefighters had a higher risk for cancer compared to a similar demographic mix of the male population as well as to non-exposed New York firefighters.

A paper published a year later in JAMA reported small increases in rates of prostate and thyroid cancers and multiple myeloma in rescue and recovery workers beginning six years after 9/11.

In 2014, the FDNY released its own set of numbers for both fire fighters and emergency medical services (EMS) personnel.

Higher Cancer Risk in Responders and Residents

In the second study, William Moir, MPH, from Montefiore Medical Center and the FDNY, and colleagues compared firefighters exposed to WTC toxins (n = 11,457 white male firefighters) to a cohort of non-WTC-exposed firefighters from other urban areas (San Francisco, Chicago, and Philadelphia; n = 8220 white male firefighters).

A total of 345 individuals from the FDNY cohort and 443 individuals from the referent group were diagnosed with a first primary cancer from September 11, 2001, to December 31, 2009. The researchers found no significant difference in the overall cancer rate between the WTC-exposed firefighters and the reference group (relative rate [RR], 0.96). But among firefighters aged 35 to 60 years in the exposed group, thyroid cancer was significantly elevated (RR, 3.82). There were insufficient cases in other age groups to permit determination of risk.

The rate of lung cancer was lower for the FDNY exposed group among men aged 45 to 70 years (RR, 0.55), and no significant differences were observed for other types of cancer, including colon, prostate, and hematologic cancers and melanoma.

A secondary analysis that compared early and late post-9/11 periods showed results similar to those of the primary analysis. The incidence of thyroid cancer was elevated during the entire study period, while prostate cancer incidence rose during the late period (RR, 1.38).

“However, the elevated rates may be due in part to increased detection in the FDNY cohort,” the study authors note.

“Further follow-up should be conducted with this reference population to assess the relationship between WTC-exposure and cancers with longer latency periods and aim to control for potential confounders such as smoking,” they conclude.
**Prostate Biopsy**

(Continued from page 1)

ple high intensity focused ultrasound or brachytherapy alone) depends on the PSA value and the PB Gleason Score (GS). Men who had general sextant prostate biopsy have up to a one-in-three chance to have a significant upgrading (SU) in the final pathological report. A recent clinical study has investigated whether an extended PB scheme is associated with an improvement in the accuracy between the PB GS and radical prostatectomy (RP) pathology. Over and above, it tried to identify probable preoperative variables that stratified patients likely to harbor SU. The data of the 548 men diagnosed with PCa, who underwent RP and exhibited a SU were retrospectively reviewed. The men were divided into three groups: Group-A, who underwent a six-core (lateral) PB (36%), Group-B who underwent a 12-core (lateral-medial) PB (28.9%) and Group-C (34.9%) who underwent an 18-core (lateral-mediolateral-medial) PB.

To control interpretational bias of pathologists, all PB cores were analyzed by a highly experienced single pathologist. A multivariate analysis was conducted (PSA level, clinical T-Stage, volume of the prostate gland and duration from PB to RP). The conclusion of the study is that an extended prostate biopsy scheme is associated with a significant improvement in the accuracy between the PB GS and RP pathology. Prostate volume >35 mL in men who undergo a six- or 12-core prostate biopsy is the only preoperative variable that stratifies patients likely to harbor SU.

UroToday
23 August 2016

**High-Risk Prostate Cancer Found in Black Men Initially on Active Surveillance**

Black men with clinically localized prostate cancer (PCa) initially managed with active surveillance (AS) are more likely than non-black men to have higher-risk pathological disease at radical prostatectomy (RP), according to a new study published online in *The Journal of Urology*. Previous studies offered conflicting results because race often could not be investigated apart from complicating factors such as low income and comorbidity burden.

Robert Aboussaly, MD, MS, of University Hospitals Case Medical Center in Cleveland, and colleagues queried the national cancer database, which captures 70% of new cancer diagnoses in the United States. Of 48,473 American men with clinically low-risk PCa (clinical stage T2a or below, Gleason score (GS) 6 or below, and PSA level <10 ng/mL), 5,411 (11.2%) were black. Patients transitioned from AS and underwent RP from 2010 to 2013. The selected endpoints were pathologic upgrading to GS >6 (primary) or >7 (secondary) and/or upstaging to pathological T3, T4 or N1 disease.

Black men had 20% greater odds of upgrading at RP to GS >6 and/or upstaging. Also, black race independently predicted upstaging to GS >7 and/or upstaging. Results held up after accounting for patient age at diagnosis, comorbidity, income, urban residence, clinical stage and pathological findings. The investigators were unable to adjust for family history of PCa. They also could not analyze (Continued on page 8)

**Determining When to Stop PSA Monitoring after Radical Prostatectomy**

J Urol 30 August 2016; Article in Press

**Purpose:** We analyzed long-term follow-up data after radical prostatectomy (RP) to determine how long patients should be followed when the serum PSA level measured by an ultrasensitive (US) assay was consistently low.

**Materials and Methods:** We retrospectively reviewed clinicopathological data for 582 consecutive men who underwent open or laparoscopic RP between 1995 and 2004, excluding four men who received adjuvant therapy. We stratified men according to PSA levels at three and five years after surgery, and examined subsequent biochemical recurrence (BCR: PSA rise to >0.2 ng/mL) during a mean follow-up period of 9.7 years.

**Results:** At three years after surgery, PSA levels were measured by an US assay in 323 men who had not experienced BCR. In 187 men with undetectable PSA levels (<0.01 ng/mL), the 10- and 15-year BCR-free survival rates were 99% and 96%, respectively. At five years after surgery, PSA levels were measured in 315 men by the US assay. In 162 men with undetectable PSA levels, the 10- and 15-year BCR-free survival rates were both

(Continued on page 8)

**Role of PSA Failure**

(Continued from page 1)

The trial involved 206 men, 156 of whom died during a median follow-up of 16.6 years, including 46 (94%) of the men with moderate or severe co-morbidity and 115 (70%) of those with no or minimal co-morbidity.

Data showed that PSAF was associated with a statistically significant all-cause mortality hazard ratio (HR) of 1.6 in the subgroup of men with no or minimal co-morbidity (95% confidence interval [CI] 1.0-2.5, P=0.04). Among men with moderate or severe co-morbidity, the association between PSAF and all-cause mortality translated into a HR of 1.8, which was not statistically significant (95% CI 0.8-4.0, P=0.19).

External-beam RT plus six months of ADT is considered standard care for men with intermediate- and high-risk prostate cancer. However, the standard evolved from trials evaluating the effect of treatment on risk of PSAF, a surrogate for survival.

“Although the trial was conducted 15 to 20 years ago, the findings have considerable relevance for contemporary patient populations because of the typical clinical course of the disease,” said Andrew Stephenson, MD, of the Cleveland Clinic.

“Even in its most aggressive form, prostate cancer has a relatively protracted natural history relative to other common cancers that we diagnose and treat,” Stephenson told MedPage Today. “It’s important to consider the age, the life expectancy, and the overall health status of the patient before embarking on any treatment for prostate cancer. This includes the decision to have curative treatment for prostate cancer.”

“What this study tells me is that healthy patients should be the focus of our care and that we should perhaps scale back the treatment intensity that we apply to older men

(Continued on page 8)
Baseline Prostate-Specific Antigen Levels in Midlife Predicts Lethal Prostate Cancer


J Clin Oncol 2016;34:2705-11

**Purpose:** Prostate-specific antigen (PSA) level in midlife predicted future prostate cancer (PCa) mortality in an unscreened Swedish population. Our purpose was to determine if a baseline PSA level during midlife predicts lethal PCa in a US population with opportunistic screening.

**Materials and Methods:** We conducted a nested case-control study among men age 40 to 59 years who gave blood before random assignment in the Physicians’ Health Study, a randomized, placebo-controlled trial of aspirin and β-carotene among 22,071 US male physicians initiated in 1982 and then transitioned into a prospective cohort with 30 years of follow-up. Baseline PSA levels were available for 234 patients with PCa and 711 age-matched controls. Seventy-one participants who developed lethal PCa were re-matched to 213 controls. Conditional logistic regression was used to estimate odds ratios and the area under the receiver operating characteristic curve, with 95% CIs, of the association between baseline PSA and risk of lethal PCa.

**Results:** Median PSA among controls was 0.68, 0.88, and 0.96 ng/mL for men age 40 to 49, 50 to 54, and 55 to 59 years, respectively. Risk of lethal PCa was strongly associated with baseline PSA in midlife: odds ratios (95% CIs) comparing PSA in the > 90th percentile vs. less than or equal to median were 8.7 (1.0 to 78.2) at 40 to 49 years, 12.6 (1.4 to 110.4) at 50 to 54 years, and 6.9 (2.5 to 19.1) at 55 to 59 years. A total of 82%, 71%, and 86% of lethal cases occurred in men with PSA above the median at ages 40 to 49, 50 to 54, and 55 to 59 years, respectively.

**Conclusion:** PSA levels in midlife strongly predict future lethal PCa in a US cohort subject to opportunistic screening. Risk-stratified screening on the basis of midlife PSA should be considered in men age 45 to 59 years.

The Association between Sexual Function and Prostate Cancer Risk in US Veterans

Zapata DF, Howard LE, Frank J, et al.

Asian J Androl 30 August 2016; Epub

Sexual dysfunction and prostate cancer are common among older men. Few studies explored the association between these two illnesses. We examined whether sexual function is associated with prostate cancer risk among older men. Among 448 men undergoing prostate biopsy at the Durham Veterans Affairs Hospital, sexual function was ascertained from the Expanded Prostate Cancer Index Composite sexual assessment.

We tested the link between sexual function and prostate cancer risk adjusting for multiple demographic and clinical characteristics using logistic regression. Multinomial logistic regression was used to test the associations with risk of low-grade (Gleason ≤6) and high-grade (Gleason ≥7 or ≥4+3) disease vs. no cancer.

Of 448 men, 209 (47%) had a positive biopsy; these men (Continued on page 8)

Long-Term Consequences of Finasteride vs. Placebo in the Prostate Cancer Prevention Trial

Unger JM, Till C, Thompson IM, et al.

J Natl Cancer Inst 26 August 2016; Epub

Finasteride has been found to reduce the risk of low-grade prostate cancer but to have no impact on overall survival. The long-term adverse and beneficial consequences of finasteride have not been examined.

We linked data from the Prostate Cancer Prevention Trial and Medicare claims. Men were examined by randomized study arm (finasteride vs. placebo for seven years) for long-term consequences of the intervention, including cardiac, endocrine, and sexual dysfunction, depression, diabetes, and benign prostatic hyperplasia (BPH)-related events. To examine time to events, we used cumulative incidence and Cox regression, adjusting for covariates. All statistical tests were two-sided.

A total of 13,935 of 18,880 participants (73.8%) in the PCPT were linked to Medicare claims, with median Medicare follow-up assessment time of 16 years from trial registration. There were no differences between finasteride and placebo participants with respect to important baseline factors or of Medicare follow-up assessment time. Finasteride patients had a 10% higher risk of new claims for depression (hazard ratio [HR] 1.10, 95% confidence interval [CI] 1.01 to 1.19, P=0.04) and a 6% lower risk of procedures for BPH-related events (primarily lower urinary tract symptoms; HR 0.94, 95% CI 0.89 to 1.00, P=0.03). No other differences were found in rates of long-term consequences of intervention in the two study arms.

Finasteride use is associated with reduced need for procedures for relief of BPH-related events and a modest increase in depression. Overall, there is little need to worry about long-term non-cancer consequences of finasteride use in those who use it for treatment of symptomatic BPH, hair growth, or prevention of cancer.

Enzalutamide as a Fourth- or Fifth-Line Treatment Option for Metastatic Castration-Resistant Prostate Cancer


Oncology 20 August 2016; Epub

To evaluate the efficacy of enzalutamide (Enz) as a fourth- or fifth-line treatment in men with metastasized castration-resistant prostate cancer (mCRPC), by analyzing a retrospective cohort of heavily pretreated patients.

We evaluated toxicity, overall survival (OS), progression-free survival (PFS) and time to PSA progression data from 47 CRPC patients treated with fourth- or fifth-line Enz.

All men were treated with docetaxel and abiraterone acetate and 42 (89%) with cabazitaxel. The median age of the men was 69 years (IQR, 63-73.5), 79% had bone metastases, 55% had lymph node metastases, and 17% had visceral metastases. The median duration of Enz treatment was 12.0 weeks (IQR, 8.3-20.4), and 11 men (23%) responded to Enz (maximum PSA decline (Continued on page 8)
P1, “Is an Extended…” How many biopsy cores are needed to assess the true pathologic grade of prostate cancer? That question was addressed in a European study. Men were stratified according to biopsies with six, 12, or 18 cores. Authors found that men having a six-core biopsy had a greater risk of having significant upgrading compared to the 12- or 18-core group. Does this mean that 18 cores are needed to avoid undergrading? The answer is not necessarily. Six core biopsies are no longer performed because they were insufficient in previous studies. This study was not prospective so other factors may have been important that could not be analyzed in this retrospective analysis. For now, 12 cores remains the minimum number that should be used. A well-done study is needed to determine if 18-core biopsies are truly necessary.

The Bottom Line: Although this study suggests that six cores is more likely to result in tumor undergrading, most doctors are routinely using at least a 12-core regimen to evaluate men undergoing a prostate biopsy and the need for 18 cores is unclear.

P2, “Association of…” Does the number of cycles of docetaxel have an impact on the long-term androgen deprivation therapy (ADT) is a decline in cognitive function. In an interesting study, Alibhai et al. prospectively evaluated cognitive function in three groups of men receiving ADT for 36 months. In contrast to uncontrolled trials, this study found no difference in cognitive decline for men on long-term ADT vs. prostate cancer patients not receiving ADT or to a control group of men without prostate cancer. This is a very important finding because some men may have been reluctant to go on ADT when it is appropriate to do so out of fear of a decline in cognitive function.

The Bottom Line: In a well-designed prospective study, up to 36 months of ADT did not worsen cognitive function beyond that expected in an aging population.

P3, “High-risk Prostate…” As more men diagnosed with prostate cancer consider active surveillance (AS), one may question if the same selection criteria should apply for African American men as Caucasians. A general concept is that African-Americans have a greater risk of dying from prostate cancer. Does that mean that AS is not a good idea for them? Results of a study by Abousaly, et al. found that, of those men on AS who underwent definitive treatment, African-Americans were more likely to have worse pathologic features at the time of surgery. This information must be interpreted carefully, because it is unknown from this study the details of the PSA levels or biopsy findings. Nevertheless, it does mean more work is needed to determine if different and possibly stricter selection criteria should be used for African-American men.

The Bottom Line: African-American men may have a greater chance of worse pathology following AS but a prospective study is needed to confirm this finding.

P4, “Baseline PSA…” Would it be helpful if a single PSA test obtained at midlife could determine if a man might be harmed by prostate cancer? Preston and coworkers compared PSA levels in men from the Physicians Health Study that died from prostate cancer with men without prostate cancer. They found that most prostate cancer deaths occurred in men whose baseline PSA was above the median level of the control group. This raises several questions: (1) would serial PSA testing in at-risk men lead to a marked reduction in cancer death; (2) should a man undergo a biopsy when he is found to have a PSA above the median for his age group; (3) what proportion of men in a large screening population fall into that group; (4) how many men will not have lethal prostate cancer; and (5) would the benefits of this selective screening approach outweigh the harms?

The Bottom Line: Having a baseline PSA in midlife may help identify men with a long-term risk of prostate cancer mortality but this does not prove the merits of this alternative screening approach.

P5, “The Association…” Does sexual function correlate with risk of prostate cancer? Zapata et al. assessed this possibility using a validated questionnaire with men undergoing a prostate biopsy. They found that higher sexual function correlated with a lower risk of prostate cancer and high-grade disease. But, does this mean that a man with a suspicious PSA level and normal sexual function should not undergo biopsy? The answer is no. We cannot determine if any cause and effect relationship exists between sexual function and prostate cancer in this study. As the authors suggest, more data are needed.

The Bottom Line: A possible association between prostate cancer risk and sexual function has been suggested, but the implications or significance of this finding are unclear at this time.

P6, “Long-term…” Preventing prostate cancer was a long-term goal of the PCPT trial using finasteride. Unfortunately, the results were controversial because, although it lowered the risk of prostate cancer, it may have increased the risk of a more dangerous cancer. As a result, the FDA did not grant approval of the drug for prostate cancer prevention. A new study by Unger and coworkers looked at 74% of the men in that trial to determine if other non-cancer health conse-
Role of PSA Failure *(Continued from page 5)*

who have limited life expectancy because of co-morbid medical conditions."

"This raises the question as to whether time to PSAF, an endpoint that often occurs many years before metastasis and death from prostate cancer, is a clinically relevant endpoint only in men who have no or minimal comorbidity," the authors noted. "This is a clinically relevant question because multiple contemporary randomized controlled trials have recently demonstrated significant improvements in relapse-free survival, predominantly driven by PSAF-free survival but no significant difference in overall survival."

"In principle, fewer competing risks for mortality should provide more opportunity for PSA failure to translate into an increased risk of all-cause mortality," the authors added.

MedPage Today 12 September 2016

Sexual Function & US Veterans *(Continued from page 6)*

were less likely to be white (43% vs 55%, P=0.013), had higher PSA (6.0 vs 5.4 ng/mL, P<0.001), but with lower mean sexual function score (47 vs. 54, P=0.007). There was no difference in age, BMI, pack years smoked, history of heart disease and/or diabetes. After adjusting for baseline differences, sexual function was linked with a decreased risk of overall prostate cancer risk (OR: 0.91 per 10-point change in sexual function, P=0.004) and high-grade disease whether defined as Gleason ≥7 (OR: 0.86, P=0.001) or ≥4+3 (OR: 0.85, P=0.009). Sexual function was unrelated to low-grade prostate cancer (OR: 0.94, P=0.13). Thus, among men undergoing prostate biopsy, higher sexual function was associated with a decreased risk of overall and high-grade prostate cancer. Confirmatory studies are needed.

Enzalutamide *(Continued from page 6)*

cline ≥50%). In general, Enz was well tolerated, with the most frequently reported adverse events being fatigue and nausea. The median OS was 40.1 weeks (95% CI, 25.4-61.4), the median PFS was 12.1 weeks (9.9-14.0) and the median time to PSA progression was 15.7 weeks (14.0-28.7).

Analysis of this retrospective cohort suggests that Enz is well tolerated and has a 23% response rate in heavily pretreated CRPC patients, which is comparable with third-line treatment outcomes.

The Bottom Line *(Continued from page 7)*

quences developed from finasteride use. Results showed a higher risk of depression and a lower risk of needing treatment for lower urinary tract symptoms. Depression was not prospectively tested and no other major health problems were reported.

The Bottom Line: Long-term finasteride (seven years) may reduce the need to treat lower urinary tract symptoms, but its effect on causing depression cannot be determined from this analysis.

AS in Black Men *(Continued from page 5)*

lyze long-term oncologic outcomes, which is a limitation.

Black men with clinically low-risk PCa "are more likely to harbor higher-risk disease, which may lead to adverse outcomes," Dr. Aboussaly and colleagues concluded. "By itself, this finding does not preclude AS; however, race should be considered as men weigh the risks and benefits of AS versus treatment."

* Renal and Urology News 30 August 2016

PSA Monitoring *(Continued from page 5)*

100%. In this group, the PSA level at last follow-up was <0.01 ng/mL in 132 patients, 0.01-0.03 ng/mL in 27 patients, and 0.06 ng/mL, 0.07 ng/mL, and 0.11 ng/mL in one patient each.

Conclusions: This long-term review indicates that if patients have continuously undetectable PSA levels by an ultrasensitive assay for five years, PSA monitoring can be stopped with an extremely low risk of subsequent BCR.

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