Low-Fat Meal May Boost Costly Cancer Drug

Eating a low-fat meal when taking an expensive prostate cancer drug can cut the cost of the drug by three-quarters, a new study indicates. The study was presented at the 2017 Genitourinary Cancers Symposium (GUCS).

“We know this drug (Zytiga) is absorbed much more efficiently when taken with food,” said study author Dr. Russell Szmulewitz, an assistant professor of medicine at the University of Chicago. “It’s inefficient, even wasteful, to take this medicine while fasting, which is how the drug’s label says to take it,” he noted in a university news release.

But, Szmulewitz cautioned that patients shouldn’t start experimenting with drug doses on their own.

“This was a relatively small study, too small to show with confidence that the lower dose is as effective. It gives us preliminary, but far from definitive, evidence. Physicians should use their discretion, based on patient needs,” he advised.

Zytiga (abiraterone acetate) costs more than $9,000 a month and patients typically remain on the drug for 12 to 18 months, researchers said. Even patients with the best health insurance can have co-pays of $1,000 to $3,000 a month.

This study found similar outcomes between 36 advanced prostate cancer patients who took 250 milligrams of the drug with a low-fat breakfast and 36 patients who took the standard dose of 1,000 milligrams on an empty stomach.

For both groups, the time to disease progression was about 14 months.

(Continued on page 8)

Single Dose of Brachytherapy May Be an Effective Treatment for Localized Prostate Cancer

Results from a new prospective clinical trial indicate that high-dose rate (HDR) brachytherapy (BT) administered in a single 19-Gy treatment may be a safe and effective alternative to longer courses of HDR treatment for men with localized prostate cancer.

The study was reported by Krauss, et al. in the International Journal of Radiation Oncology*Biology*Physics. In contrast to low-dose rate (LDR) BT, where radioactive seed implants are placed permanently in the body and gradually deposit low levels of radiation over a period of months, HDR treatment deposits the dose in one treatment, after which the implant is removed. Typically, HDR BT is administered in four to as many as nine treatment sessions, which generally requires multiple invasive procedures to insert the implants.

Although the number of sessions can be streamlined by increasing the dose given in each session, data on the safety and tolerability of highly-escalated BT doses are still relatively new and therefore limited. In this study, researchers found that men who received a single fraction of 19-Gy HDR brachytherapy experienced similar clinical outcomes as with LDR brachytherapy, but with the convenience of a single visit.

“It is becoming apparent that patients may be treated definitively for their prostate cancer in as little as a single
**Targeted Biopsy to Detect Gleason Score Upgrading During Active Surveillance for Men with Low- Versus Intermediate-Risk Prostate Cancer**

Nassiri N, Margolis DJ, Natarajan S, et al.

*J Urol* 197: 632-639, 2017

**Purpose:** We sought to determine the rate of upgrading to Gleason score (GS) 4+3 or greater using targeted biopsy for diagnosis and monitoring in men undergoing active surveillance (AS) of prostate cancer.

**Materials and Methods:** Study subjects comprised 259 men, including 196 with GS 3+3 and 63 with GS 3+4, who were diagnosed by magnetic resonance imaging/ultrasound (MRI/US) fusion guided biopsy (from 2009 to 2015) and underwent subsequent fusion biopsy for as long as four years of AS. The primary end point was the discovery of GS 4+3 or greater prostate cancer. Follow-up biopsies included targeting of positive sites, which were tracked in an Artemis™ device. Kaplan-Meier curves were generated to determine upgrading rates, stratified by initial GS and PSA density (PSAD).

**Results:** Based on a Cox proportional hazard model, men with GS 3+4 were 4.65 times more likely to have upgrading than men with an initial GS of 3+3 at three years (P < 0.01). By the third AS year, 63% of men with GS 3+4 had been upgraded compared with 18.0% who started with GS 3+3 (P < 0.01). Of all 33 upgrades, 32 (97%) occurred at an MRI visible or a tracked site of tumor, rather than at a previously negative systematic site. Independent predictors of upgrading were GS 3+4, PSAD 0.15 ng/mL/cm³ or greater and a grade 5 lesion on MRI. The incidence rate ratio of upgrading (GS 3+4 vs. 3+3) was 4.25 per year of patient follow-up (p < 0.01).

**Conclusions:** During AS of prostate cancer, targeting of tracked tumor foci by MRI/US fusion biopsy allows for heightened detection of GS 4+3 or greater cancers. Baseline variables directly related to important upgrading that warrant increased vigilance include GS 3+4, PSAD 0.15 ng/mL/cm³ or greater and grade 5 lesions on MRI.

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**Exploring Optimal Sequence of Abiraterone and Enzalutamide in Men with Castration-Resistant Prostate Cancer: The Kyoto-Baltimore Collaboration**

**Summary:** For the Kyoto-Baltimore collaboration study, researchers combined data from two institutions to evaluate and compare the efficacy of sequential treatment with abiraterone (ABI) followed by enzalutamide (ENZA) or vice versa in men with castration-resistant prostate cancer (CRPC). They observed that the ABI-to-ENZA sequence may have more favorable efficacy in terms of combined PSA progression-free survival (PSA-PFS) than the ENZA-to-ABI sequence, but found no differences in overall survival (OS), which may be due to higher PSA response rates and longer PSA-PFS to second-line ENZA compared to ABI (ENZA retains activity after ABI but not vice versa).

**Methods:** Researchers retrospectively evaluated data on 352 consecutive patients who had received both ABI and ENZA for CRPC at Kyoto University Hospital and at Johns Hopkins Sidney Kimmel Comprehensive Cancer Center. With Kaplan-Meier analysis and log-rank tests, they compared PSA-PFS and OS in men treated with sequential ABI-to-ENZA vs. ENZA-to-ABI without intervening therapies.

**Results:** In all, 163 men received ABI-to-ENZA (pre-docetaxel [DTX] chemotherapy: 116, post-DTX: 47), and 180 received ENZA-to-ABI (pre-DTX: 85, post-DTX: 104). In the first-line CRPC setting, >50% PSA response rates to ABI and ENZA were 47% and 52% respectively, and 9% and 29% in the second-line setting. In the pre-DTX population, median PSA-PFS was not significantly different between ABI (median: 194 days) and ENZA (median: 126 days) in the first-line setting (P=0.411), but researchers observed an advantage favoring ENZA (median: 91 days) compared to ABI (median: 55 days) in the second-line setting (P=0.008).

**Conclusions:** Combined PSA-PFS was significantly longer in the ABI-to-ENZA sequence (median: 455 days) than in the ENZA-to-ABI sequence (median: 296 days) (P < 0.001). There was no statistical difference in OS between the two sequences (P=0.598).

*Presented at GUICS 2017*

MDUJmc Oncology News

16 February 2017

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**Watch videos about informed decision making for managing prostate cancer at:**

www.ustoo.org/Education-Videos
Doc Moyad’s What Works & What is Worthless Column, Also Known As “No Bogus Science” Column

“Wait? Exercise is Better than the Drugs for CRF!”

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.

One of the largest reviews ever conducted comparing different treatments for cancer-related fatigue (CRF) found that exercise is better than any current drug to reduce this problem. Where is the ticker tape parade?! Who cares anymore about the Cubs World Series win after this incredible news!

CRF is a massive problem! It can lead to so many other problems or even be associated with other medical conditions and it can even delay treatment! Yet, what do patients have as an option here? I have written about American Ginseng, which may be one of the best pill options for CRF based on some great research. However, what about all those prescription drugs that have been tested, from stimulants to anti-depressants, to reduce CRF? Now, along comes this massive meta-analysis of 113 studies with over 11,500 participants (arguably the largest and most comprehensive ever done), which found that exercise and psychological interventions reduce CRF during and after cancer treatment. And, now get this…

DRUM ROLL PLEASE (cue the dramatic music also please), and now let me open the envelope, and I mean the real envelope – not the one Warren Beatty opened first at this year’s Oscar awards!) So, the winner is EXERCISE, and as the authors mentioned in the following: “In contrast, pharmaceutical interventions do not improve cancer-related fatigue to the same magnitude.” And, then the authors hit the real crescendo by stating, “Clinicians should pre-

scribe exercise and/or psychological interventions as first-line treatments for cancer-related fatigue.”

Okay, I underlined and bolded that part but WHAT THE HECK!!!? Where is the ticker tape parade?! This is big time news!!! How does exercise work so well to combat CRF? Reducing stress hormones? Improving mood? Reducing anxiety? Reducing inflammation? Increasing muscle mass, which increases metabolism, which then increases energy levels? Yup! Yup! Yup! Yup! Yay! Okay, this is my belief, so I will stop using the word “yup!” Aerobic and/or resistance exercise are both synergistic and can help fight CRF. So, exercise is the real winner here folks! See you at my ticker tape parade (you know, the same one that I am holding after Michigan wins the National Championship in Football in 2019). This is the kind of amazing and life-changing research that really can change lives ASAP! Now, should YOU go tell someone else about this research? Yup!

References:

Development of a Voided Urine Assay for Detecting Prostate Cancer Noninvasively

Scientists at the Sidney Kimmel Cancer Center at Thomas Jefferson University have developed a noninvasive technique to detect the presence of prostate cancer cells in patients' urine. The pilot study, led by Mathew L. Thakur, PhD, Director, Laboratories of Radiopharmaceutical Research and Molecular Imaging and Professor of Radiology and Radiation Oncology at Thomas Jefferson University at the Sidney Kimmel Cancer Center, was published by Trabulsi, et al. in BJU International.

The research demonstrates that a test using voided urine can target VPAC receptors, which are commonly expressed on malignant prostate cancer cells. Using optical imaging technology to detect prostate cancer cells shed in voided urine, the research team identified VPAC-positive cells in 98.6% of the patients with a prostate cancer diagnosis and none (0%) of the patients presenting with benign prostatic hyperplasia. “The two most important virtues of this technology are its accuracy and simplicity,” said Dr. Thakur. Currently, the only methods for diagnosing prostate cancer involve more invasive, costly, yet less reliable procedures, including digital rectal examination, biopsy, or urine analysis that requires direct prostate stimulation. “We believe that a diagnostic test that is simple and more comfortable for the patient will encourage more frequent screening and help improve early diagnosis of prostate cancer,” added Dr. Thakur.

The technology is patent-pending and has been licensed to NuView Dx, in Park City, Utah. “We are excited about this technology, which promises to avoid millions of unnecessary biopsies, save patient morbidity, and spare millions of health-care dollars,” said Paul Crowe, Chief Executive Officer of NuView Dx. Research team member Leonard Gomella, MD, Chair, Department of Urology at Thomas Jefferson University at the Sidney Kimmel Cancer Center, concluded, “This is a highly promising biofluid assay that, once fully developed, may play an important role in the management of prostate cancer.”

The content in this post has not been reviewed by the American Society of Clinical Oncology, Inc. (ASCO®) and does not necessarily reflect the ideas and opinions of ASCO®.

The ASCO Post
24 February 2017

Check out the new Us TOO webpage on prostate cancer drugs at:
www.ustoo.org/Prostate-Cancer-Drugs
Kraus and coauthors state that there has been no real-world data—until their new study. “For patients not in a prospective study, there are no data illustrating if they follow through with their AS protocol,” they write.

Elisabeth Heath, MD, chair of genitourinary oncology at the Karmanos Cancer Institute at Wayne State University in Detroit, MI, said the new study “is indeed what occurs out in the real world,” when asked for comment. She noted a related problem is that many prostate cancer patients have more than one health concern and are often “side tracked” by going to other doctors.

“The patient needs to distinguish AS for prostate cancer as a different medical visit than the primary care visit. For the ‘professional patient,’ going to the doctor is easy, but for others, not so much,” she told Medscape Medical News.

For the study, the USC team performed a chart review of men diagnosed with nonmetastatic prostate cancer from 2008 to 2014 at Los Angeles County Hospital, a public “safety net” institution, and at the private Norris Cancer Center, also in Los Angeles. “The two share roughly the same physicians,” said Kraus. Investigators categorized patients’ AS status as far out as June 2015.

They found 116 men at the public hospital and 98 men at the private hospital managed with AS. Among the 116 men at the public hospital on AS, 53 (45.7%) were lost to follow-up, with this probability increasing for each of five consecutive years. Among the 98 men at the private hospital on AS, 23 patients (23.5%) were lost to follow-up. Again, with each passing year, the likelihood of being lost increased.

Kraus said that the “disparity between real-world and prospective studies” might be explained by physician motivation in the different settings. In short, study authors have “higher incentives” to make sure their patients are following up. “In the real world, physicians don’t have those incentives,” he said.

Furthermore, the fact that the poor men had such high drop-out rates concerns the investigators. “Further study is warranted to look at this population of patients and determine whether AS should remain a recommended course of treatment for this population,” they write.

Dr. Heath suggested that common sense should guide physicians in these decisions. She offered a different set of cancer patients to illustrate the problem of losing patients to follow-up and possible solutions: “This is a problem we encounter when treating young men with testicular cancer,” she explained. In early stage testicular cancer, chemotherapy, radiation therapy, or AS are equally acceptable treatment options. “One of the issues we often consider prior to committing to a treatment option is the patient’s circumstance regarding reliability, insight into his disease, social support infrastructure, and willingness to return monthly,” she said.

Dr. Heath also said that “a key to a successful AS program is patient education, awareness, and insight. In addition, the healthcare team has to be engaged with and committed to the patient.”

GUCC 2017, abstract 197
Medscape Medical News

Single Dose of Brachytherapy (Continued from page 1)

day with a minimally invasive outpatient procedure,” said lead study author Daniel J. Krauss, MD, a radiation oncologist at Oakland University’s William Beaumont School of Medicine. “We found that patients generally can resume normal activities the following day with typical side effects.”

The study presented the results of a nonrandomized, prospective clinical trial of 58 men with low- or intermediate-risk (nonmetastatic) prostate cancer, with a median follow-up period of 2.9 years. All patients received a single 19-Gy fraction of HDR BT. The median patient age was 63 years (range 43-73), and 91% of the patients presented with stage T1 disease.

At an average of nearly three years following treatment, cancer control rates were favorable and the toxicity profile was highly favorable. Three patients experienced recurrence or progression, yielding an estimated three-year cumulative biochemical control rate of 93%.

Within the six months following HDR therapy, seven patients (12.1%) experienced grade 2 urinary side effects, most commonly frequency/urgency (6.9%). No patients experienced short-term grade 3+ urinary toxicity or grade 2+ gastrointestinal (GI) toxicity. Rates were similarly modest for long-term side effects. Six patients (10.3%) experienced chronic grade 2 urinary toxicity and one patient (1.7%) experienced grade 3 chronic GI toxicity that subsequently resolved. No patients experienced long-term grade 3+ urinary toxicity or grade 4 GI toxicity.

“This study illustrates that a potentially curative dose of radiation may be delivered safely to the prostate en-
Genomic Test Predicts Metastasis Mortality in Prostate Cancer

The genomic-based Decipher test effectively predicted metastasis and prostate cancer-specific mortality (PCSM) from diagnostic biopsy specimens for men with intermediate- and high-risk prostate cancer, according to findings presented at the 2017 Genitourinary Cancers Symposium (GUcS).

Overall, 23.4% of those classified as high-risk by the test developed metastasis. PCSM was 9.4% at five years. Also, the findings for Decipher held up regardless of the frontline therapy utilized. The next steps in the research will be to conduct a clinical trial using the test to determine when intensification of therapy is warranted, according to lead author Paul L. Nguyen, MD.

“The Decipher classifier obtained from biopsy samples was associated with distant metastases and PCSM after radical prostatectomy (RP) or radiation therapy (RT) and androgen deprivation therapy (ADT),” said Nguyen, from the Brigham and Women’s Hospital and the Dana-Farber Cancer Institute. “Further validation is ongoing in larger cohorts. Work is planned to study the test in completed randomized trials to determine predictive value.”

For the study, diagnostic biopsy samples were obtained from 175 men from Cleveland Clinic, Brigham and Women’s Hospital, and Johns Hopkins. Testing with Decipher was used on the highest-grade core from the biopsy. By National Comprehensive Cancer Network (NCCN) classification, 87% of men had intermediate- (50.9%) or high-risk (33.7%) prostate cancer. Forty-three percent of men had received frontline RP and 57% received frontline RT plus ADT. After six years of follow-up, 32 patients had developed metastases and 11 had died from prostate cancer. Of those classified as intermediate- and low-risk by Decipher, 9.3% and 5.0% developed metastasis at five years, respectively. By NCCN criteria alone, 33.1% of those with high-risk disease developed metastasis, as did 11% and 1.2% of those with intermediate- and low-risk, respectively.

The use of Decipher improved the overall c-index for metastasis compared with risk levels alone. The five-year post-biopsy c-index was 0.74 for Decipher alone and 0.75 for Decipher and NCCN combined compared with 0.66 with NCCN risk classification only. “[Decipher] adds to what we already know and enhances our ability to decide which patients are going to develop metastases,” said Nguyen.

By univariate and multivariate analysis, the only statistically-significant variable for predicting metastases was Decipher (univariate HR, 1.5; 95% confidence interval [CI], 1.2-1.9; P<0.001 and multivariate HR, 1.4; 95% CI, 1.1-1.8; P=0.007). The investigators also assessed Gleason score, clinical stage, and frontline treatment, but none were statistically significant.

The use of Decipher also improved upon NCCN staging for PCSM. Those listed as being genomic high-risk had a PCSM of 9.4%. Those in the intermediate- and low-risk groups had a PCSM of 0%. For every 10% increase in Decipher score, risk of PCSM increased by 57% (HR, 1.57; 95% CI, 1.1-2.4; P=0.02). The low number of overall patients is 808.

Researchers May Have Found Key to Blocking Enzalutamide Resistance in Men with Prostate Cancer

Blocking the metabolic cascade that leads to resistance to enzalutamide—a synthetic non-steroidal antiandrogen currently approved for the treatment of metastatic, castration-resistant prostate cancer—may be a viable approach to restoring its efficacy in killing cancer cells, according to researchers from the Cleveland Clinic, Cleveland, OH. They may have discovered the pathway by which this chain of events is “turned on,” and reported their results online in eLife. Enzalutamide actively blocks the interaction between androgens within the tumor cells and an androgen receptor protein, which is then activated and instructs the tumor cell to proliferate. Thus, this agent renders the tumor’s androgens inactive.

But, there is a much more complex cascade of events that occurs when these androgen receptors are blocked via enzalutamide. In response, levels of 11β-hydroxysteroid dehydrogenase-2 (11βHSD2)—an enzyme—plummets, which creates a surplus of cortisol within the tumor cells. This cortisol activates its own receptor protein complex, which “fills in” for the disabled androgen receptor, instructing the tumor cells to produce more androgens.

Since blocking cortisol from its receptor is neither possible nor desirable, lead author Nima Sharifi, MD, Cleveland Clinic’s Lerner Research Institute Department of Cancer Biology, Glickman Urological & Kidney Institute, and Taussig Cancer Institute, and colleagues sought to find different pathways to the same end, and essentially disrupt the metabolic switch that occurs when androgen receptors are blocked with enzalutamide.

In human prostate cancer tumor cells grown in mice, they found that by restoring levels of 11βHSD2, and thus circumventing the ensuing production of surplus cortisol by the tumor cell, enzalutamide resistance was reversed.

“This major discovery demonstrates that tweaking the metabolism induced by cancer drugs can have major benefits to patients in prostate and possibly other cancers,” said Dr. Sharifi.

“We need more studies to determine how to safely increase 11βHSD2 in patients, but we are a step closer to finding answers and hopefully prolonging the lives of men who are in the unfortunate situation of being resistant to all current therapies,” said Dr. Sharifi, who also holds the Kendrick Family Endowed Chair for Prostate Cancer Research and was recently named a 2016 Harrington Fellow by University Hospitals’ Harrington Discovery Institute.

The research was supported by the National Cancer Institute (R01CA168899, R01CA172382, and R01CA190289), the Prostate Cancer Foundation, and the American Cancer Society. The funders had no role in the study’s design, data collection and interpretation, or the decision to submit the work for publication.

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14 February 2017

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Affected by Prostate Cancer?

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Researchers Link New Mutation to Higher Prostate Cancer Risk in Black Men

Researchers from the University of North Texas (UNT) have identified a new genetic mutation in the ALKBH7 gene associated with prostate cancer, particularly in African-American men. The findings suggest that this ALKBH7 mutation could not only be used as a biomarker to diagnose prostate cancer, but that therapies targeting this mutation may help such patients.

The study, “ALKBH7 Variant Related to Prostate Cancer Exhibits Altered Substrate Binding,” recently appeared in *PLOS Computational Biology*. When the control mechanisms that detect and repair DNA damages fail, irreversible genetic mutations that can lead to cancer rise may occur. Understanding which mutations are involved in the onset and progression of each patient’s tumor could bring about better personalized anti-cancer therapies.

Alice Walker and her colleagues at UNT focused on the occurrence of cancer-related mutations in the ALKBH family of genes in prostate cancer. The nine genes in the ALKBH group code for enzymes responsible for correcting genetic mistakes that occur during DNA replication. Alterations in the levels of some of these family members are associated with different cancer types, including bladder, lung, rectal and prostate cancer.

Using the HyDn-SNP-S software program, Walker’s team examined the genetic material of a cohort (phs000207.v1.p1) of 1,172 men with prostate cancer and 1,157 controls of European descent. This approach allowed them to specifically compare the DNA sequence of ALKBH gene family members in controls vs. prostate cancer cases. They identified one genetic mutation in the ALKBH7 enzyme that was significantly associated with prostate cancer.

To further confirm this association, the authors used a second set of prostate cancer data (phs000306), which included 1,423 black men and 1,373 controls. They observed the same link between the mutation and prostate cancer in this second data set.

Importantly, the team found that black men who had the mutant version of the ALKBH7 enzyme had a 45 percent increased risk of developing prostate cancer compared to African-American men with a functioning enzyme. A careful examination by computer simulations and laboratory tests showed that the mutation led to a structural change in the enzyme that significantly decreased its ability to perform its normal DNA repair activity.

“Scanning the DNA of individuals in the target population for this mutation could help indicate those with a higher risk of developing prostate cancer before symptoms are evident,” Walker said in a press release, adding that further studies are still needed to learn the mechanisms through which this mutation leads to prostate cancer development.

Prostate Cancer News Today
28 February 2017

Blood Test Instead of Biopsy for Metastatic Prostate Cancer

There has been a lot of buzz recently about the use of “liquid biopsies” and how these blood tests that show cancer may be able to replace the need for tissue biopsies. The latest study shows that such a test could be useful in metastatic prostate cancer, where the biopsy sample would need to be taken from bone, which is painful, risky, and expensive, says an expert.

This study used the Guardant360 test and found that cell-free, circulating tumor DNA (ctDNA) was detected in most patients with metastatic castration-resistant prostate cancer (mCRPC). In addition, the test showed several genetic changes that appear to be similar to tumor tissue alterations and provide prognostic information.

In the current study, lead author Guru Sonpavde MD, an associate professor of medicine at the University of Alabama in Birmingham and colleagues investigated ctDNA profiling in men with mCRPC and its association with clinical outcomes and evolution with therapy. They analyzed cell-free ctDNA from 514 men who had undergone baseline ctDNA analysis for potentially actionable alterations using Guardant360 before beginning new systemic therapy.

In this cohort, most (94%) men had one or more ctDNA alterations, and the most common recurrent somatic mutations were in TP53 (36% of men); AR (22%); APC (10%); NF1 (9%); EGFR; CTNNB1 and ARID1A (6% each); and BRCA1, BRCA2, and PIK3CA (5% each). The most common genes with increased copy numbers were AR (30%), MYC (20%), and BRAF (18%).

Clinical outcomes and features available for 163 men showed that a higher number of ctDNA alterations was associated with shorter time to treatment failure (TTF, hazard ratio [HR], 1.1, P=0.026). AR alterations trended for shorter TTF (HR, 1.4; P=0.053) as well as for shorter survival (HR, 2.5; P=0.09).

Dr. Sonpavde noted that men receiving prior therapy had new alterations in AR compared with those who were treatment naïve (56% vs. 37%; P=0.028). Finally, serial ctDNA profiling of a subset of 63 men revealed evolution of alterations in AR, BRCA1, and BRCA2 after therapy.

“A higher number of overall gene alterations and AR alterations appeared to be associated with poor clinical outcomes,” said Dr. Sonpavde. “The ctDNA test is a valuable research tool to discover new molecular targets.”

New AR alterations appeared frequently following therapy,” he noted. “These data suggest that developing salvage therapy agents targeting AR alterations holds promise.

“Noninvasive alternatives to traditional tumor biopsy are needed,” he said. “Repeated analysis of tumor tissue from men with metastatic prostate cancer is difficult due to the need for bone biopsies in most cases,” he said.

“This is one of the largest clinically-annotated data sets looking at ctDNA in metastatic prostate cancer,” commented Sumanta Pal, MD, a medical oncologist at the City of Hope Cancer Center in Los Angeles, CA, and an expert from the American Society of Clinical Oncology who was not involved in the study. “It showed that ctDNA offers a simple and effective way to look at tumor composition, so clinicians can use that to personalize therapy,” he said.

*Presented at the 2017 Annual GUCS, Abstract 149*

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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, “Low-Fat Meal May...”
An interesting report by Russell Szmulewitz, et al. was presented at ASCO. The authors were part of a multi-institutional study involving 72 men with progressive disease who were randomized to receive the standard dose of abiraterone on an empty stomach or one-quarter of the standard dose along with a low-fat meal at breakfast. The rationale is that the drug is absorbed better with food in the stomach and the implications are significant given the high monthly price of the drug. The authors found that the PSA progression rate was similar at 14 months regardless of the dose and food intake and they suggest that patients work with their doctors to consider using the lower dose. More work is needed from a larger study and with a better end point than PSA progression, but clearly this is a study that should be done urgently because of the potential cost savings that could occur.

The Bottom Line: More work is needed to prove that a lower dose of abiraterone taken on a low-fat meal could save significant amounts of money for patients.

P1, “Single Dose of...” One of my goals in writing this column is to evaluate the way doctors evaluate the findings from clinical studies they conduct. Too often conclusions are over-inflated. Such is the case in the report by Krauss and co-workers who evaluated 58 men with stage T1 disease treated using a single session of HDR. This is a quote from the author: “It is becoming apparent that patients may be treated definitively for their prostate cancer as little as a single day with a minimally invasive outpatient procedure.” Unfortunately, their data does not yet come close to justifying this statement. Several problems are evident. First, they treated only 58 men in a non-randomized study, which by itself precludes any way of assessing the outcomes relative to other more established treatments. Second, they included men with low-risk disease with 71% having a Gleason score less than 7. How many of those were at risk from their disease is unclear, but showing good outcomes in men who do not need treatment does not justify a therapy. Third, they have a median follow-up of only 2.9 years, which is far too short to predict long-term outcomes, and lastly they used biochemical recurrence, which is not a good enough outcome to know what would happen to survival over 10-15 years.

The Bottom Line: The authors presented VERY preliminary data using a single session of HDR but this study will never be able to determine if this approach is as good as radical prostatectomy, external radiation or low-dose brachytherapy.

P1, “In Sunny LA, Prostate...” Among the concerns voiced by many clinicians regarding AS of low-risk prostate cancer is that the patient may neglect to continue with careful follow-up, placing him at risk of having a cancer that progresses and eventually harms him. Krauss and co-workers bring that concern to light in their report. At five years, 58% of men in a public hospital and 32% at a private hospital were lost to follow-up. The question is why? Did they misunderstand the information they received when starting AS? Did other health issues cause them to focus on a more pressing health problem? Without further study we cannot determine the answers, nor develop a program to change these numbers. One helpful solution would be for the urological community to develop a more standardized program that makes efforts to ensure that patient education is consistent and periodic contacts with patients occurs. Clearly what happens in an academic program is not the same as what happens in the community.

The Bottom Line: Patients on AS at non-academic centers may be more at risk to being lost to follow-up and programs need to be developed to lower that risk.

P2, Targeted Biopsy to...” As more men accept AS for a low- or intermediate-risk cancer, the challenge is to carefully identify the men who should get definitive treatment. Although expensive, monitoring with MRI fusion biopsy may be an effective way to identify men that are at added risk. The report by Nassiri, et al. provides supporting data for that approach. Using the test, authors were able to detect Gleason 4+3 or higher disease in 18% of men with initial Gleason 3+3 cancer vs. 63% of men with Gleason 3+4 by three years after diagnosis. This clearly demonstrates that AS in men with Gleason 7 cancer have a high risk of progression and ultimately only a small percentage of them will be able to remain on AS. For Gleason 6 disease, however, one has to determine whether the same, relatively small number of men progressing is worth the added costs of doing MRI vs. standard random biopsies. For this group, the added benefit may be extremely low. Nevertheless, the authors make a strong point for using MRI in the intermediate-risk group.

The Bottom Line: MRI fusion biopsies may be worth doing in men with Gleason 3+4 disease on AS.

P2, “Exploring Optimal...” Men with castrate resistant prostate cancer (CRPC) are fortunate to have two non-chemotherapy treatments available, abiraterone and enzalutamide. Since these drugs were approved for clinical use, clinicians have debated the merits of starting with either drug and then switching to the second one after disease progression occurs. A new non-randomized study evaluated men treated with either approach and found that initial abiraterone therapy had a better PSA progression-free result compared to starting with enzalutamide; however, they did not detect any difference in overall survival. Unfortunately, the fact that the study is not randomized precludes any definitive conclusions about which one should be started first. Only a randomized study can make that assessment. So, for now that means that starting either drug first is reasonable, but hopefully a randomized study will be performed.

The Bottom Line: Until a randomized study is conducted, patients with CRPC can receive either abiraterone or enzalutamide as their first-line approach.

P3, “Development of a...” (Continued on page 8)
The Bottom Line (Continued from page 7)

Imagine the possibility of reliably diagnosing prostate cancer without doing a biopsy! That may be possible given the data from Thakur, et al. that measured vasoactive intestinal peptide receptor (VPAC) in urine of men with prostate cancer or BPH. They found that the test detected almost 99% of the cancers and was negative in the men with BPH. These are exciting data, especially considering the very high detection rate and low false positive rate. It could greatly reduce the cost of diagnosing the disease and lower the morbidity that occurs from a conventional biopsy procedure. One can expect that as soon as the test is commercially approved, extensive investigation will occur into using it as a screening test in place of PSA.

The Bottom Line: A potentially new test for diagnosing prostate cancer could eliminate the need for a biopsy.

P5, “Genomic Test...” It is known that curative therapies for localized disease are not always curative; some men still develop metastases and die. Clinical predictors including PSA, tumor stage, etc., can provide some probabilities of possible disease progression although they are not 100% accurate. A relatively new test called Decipher may add to predictive accuracy, but it remains somewhat imprecise. The most important question, for which there is not yet good information, is whether using the test to institute therapy will result in improved survival, and at what cost? A recent study by Nguyen, et al. compared Decipher results with NCCN criteria and found Decipher provided greater accuracy. Now we must wait to see if the test can guide earlier therapy in men with a high risk of disease progression. But until that is done, the value of the test is unclear.

The Bottom Line: More data are needed to demonstrate whether using the Decipher test can help improve clinical management by identifying whether high-risk patients benefit from earlier therapy.

Genomic Test (Decipher) Predicts Metastasis (Continued from page 5)

mortality prevented a multivariate analysis of survival. However, “by univariate analysis, Decipher was the only factor associated with PCSM,” said Nguyen.

The Decipher test utilizes the expression levels of 22 RNA biomarkers. The test has been explored on samples from over 2,000 prostate cancer patients in clinical studies following RP. In these studies, 60% of men classified as intermediate- and high-risk were reclassified as low-risk. Of those reclassified, 98.5% had not developed metastasis after five years of assessment post-RP. The c-index for Decipher across these trials remained around 0.75.

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Low-fat Meal Boosts Drug (Continued from page 1)

“Our results warrant consideration by doctors who care for prostate cancer patients, as well as payers,” according to Szmulewitz.

He said the findings suggest that advanced prostate cancer patients who have difficulty affording the drug could, with close monitoring by their doctor, consider taking a smaller dose with a low-fat breakfast. That could lead to a per-patient savings of up to $7,500 each month.

“If we could reduce the cost of medication for this stage of the disease by a few thousand dollars each month simply by having patients take it with food, that would be significant,” Szmulewitz said.

The researchers noted that taking the drug with a high-fat meal increased absorption of the drug even more. However, levels of the drug rose more unpredictably than with low-fat meals.

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