Chicago—With several years now passing since the U.S. Preventive Services Task Force (USPSTF) issued its grade D recommendation discouraging PSA-based prostate cancer screening, researchers are reporting conflicting findings on its impact on clinical practice.

While a handful of studies show a significant decline in screening since the recommendation was released in 2012, two abstracts presented at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago arrived at essentially opposite conclusions. One paper, using insurance claims data, showed no significant change in screening in men who are most likely benefit from it. The second, based on self-reported data, found screening rates significantly declined in all subgroups of men, but to a lesser extent in men over age 75 years.

“I realize that the two abstracts use two different databases, but they found diametrically opposed findings on the effects of the USPSTF recommendation in older men,” said J. Brantley Thrasher, MD, professor and chair of urology at the University of Kansas Medical Center, Kansas City, and a Urology Times editorial consultant.

A number of studies presented at the AUA annual meeting in New Orleans and a recently published paper in the *Journal of Urology* suggest prostate cancer screening...
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of lidocaine on post-natal development was examined in rats by treating pregnant female rats daily subcutaneously and evidence of delayed fetal development, including a non-significant decrease in fetal weight (7%) and an

Rats were treated for 8 months with 10 or 30 mg/kg, s.c. lidocaine (60 mg/m² and 180 mg/m² on a body surface

A second study examined the effects of lidocaine on post-natal development in the rat that included assessment of

WARNINGS

EXCESSIVE DOSAGE, OR SHORT INTERVALS BETWEEN DOSES, CAN RESULT IN HIGH PLASMA LEVELS AND SERIOUS ADVERSE EFFECTS. PATIENTS SHOULD BE INSTRUCTED TO STRICTLY ADHERE TO THE RECOMMENDED DOSAGE AND ADMINISTRATION GUIDELINES AS SET FORTH IN THIS PACKAGE INSERT.

The management of serious adverse reactions may require the use of resuscitative equipment, oxygen, and other resuscitative drugs.

GLYDO should be used with extreme caution in the presence of sepsis or severely traumatized mucosa in the area of application, since under such conditions there is the potential for rapid systemic absorption.

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PRECAUTIONS

General

The safety and effectiveness of lidocaine depend on proper dosage, correct technique, adequate precautions, and readiness for emergencies. (See WARNINGS and ADVERSE REACTIONS.) The lowest dosage that results in effective anesthesia should be used to avoid high plasma levels and serious adverse effects. Repeated doses of lidocaine may cause significant increases in blood levels with each repeated dose because of slow accumulation of the drug in systemic metabolism. Tolerance to elevated blood levels varies with the status of the patient. Debilitated, elderly patients, acutely ill patients, and children should be given reduced doses commensurate with their age and physical status. Lidocaine should also be used with caution in patients with severe shock or heart block.

GLYDO should be used with caution in patients with known drug sensitivities. Patients allergic to para-amino benzoic acid derivatives (procaine, tetracaine, benzoic acid, etc.) have not shown cross sensitivity to lidocaine.

Many drugs used during the conduct of anesthesia are considered potential triggering agents for familial malignant hyperthermia. Since it is not known whether amide-type local anesthetics may trigger this reaction and since the need for supplemental general anesthesia cannot be predicted in advance, it is suggested that a standard protocol for management should be available. Early unexplained signs of tachycardia, tachypnea, lability blood pressure, and metabolic acidosis may precede temperature elevation. Successful outcome is dependent on early diagnosis, prompt discontinuation of the suspect triggering agent(s) and institution of treatment, including oxygen therapy, indicated supportive measures and dantrolene (consult dantrolene sodium intravenous package insert before using). Information for Patients

When topical anesthetics are used in the mouth, the patient should be aware that the production of topical anesthesia may impair swallowing and thus enhance the danger of aspiration. For this reason, food should not be ingested for 60 minutes following use of local anesthetic preparations in the mouth or throat area. This is particularly important in children because of their frequency of eating.

Number of the tongue or buccal mucosa may enhance the danger of unintentional biting trauma. Food and chewing gum should not be taken while the mouth or throat area is anesthetized.

Carcinogenesis—Long term studies in animals have not been performed to evaluate the carcinogenic potential of lidocaine.

Mutagenesis—The mutagenic potential of lidocaine has been assessed in the Ames Salmonella reverse mutation assay, in vitro chromosome aberration assay in human lymphocytes and in an in vivo mouse micronucleus assay. There was no indication of any mutagenic effect in these studies.

Impairment of Fertility: The effect of lidocaine on fertility was examined in the rat model. Administration of 30 mg/kg, s.c. (180 mg/m²) to the mating pair did not produce alterations in fertility or general reproductive performance of rats. There are no studies that examine the effect of lidocaine on sperm parameters. There was no evidence of altered fertility.

Use in Pregnancy

Teratogenic Effects: Pregnancy Category B

Reproduction studies for lidocaine have been performed in both rats and rabbits. There was no evidence of harm to the fetus of subcutaneous doses of up to 50 mg/kg lidocaine (300 mg/m²) on a body surface area basis in the rat model. In the rabbit model, there was no evidence of harm to the fetus at a dose of 5 mg/kg, s.c. (30 mg/m² on a body surface area basis). Treatment of rabbits with 25 mg/kg (100 mg/m²) produced evidence of maternal toxicity and evidence of delayed fetal development, including a non-significant decrease in fetal weight (7%) and an increase in minor skeletal anomalies (skull and sternal defect, reduced ossification of the phalanges). The effect of lidocaine on postnatal development was examined in rats by treating pregnant female rats daily subcutaneously at doses of 2, 10, and 50 mg/kg, (60 mg/m², 300 mg/m²) from day 15 of pregnancy and up to 2 days post partum. No signs of adverse effects were seen either in dams or in the pups up to and including the dose of 10 mg/kg (60 mg/m²). However, the number of surviving pups was reduced at 50 mg/kg (300 mg/m²); both at birth and the duration of lactation period, the effect most likely being secondary to maternal toxicity. No other effects on litter size, litter weight, abnormalities in the pups and physical developments of the pups were seen in this study.

A second study examined the effects of lidocaine on postnatal development in the rat that included assessment of the pups from weaning to sexual maturity. Rats were treated for 6 months with 10 or 30 mg/kg, s.c. lidocaine (60 mg/m² and 180 mg/m² on a body surface area basis, respectively). This time period encompassed 3 mating periods. There was no evidence of altered postnatal development in any offspring; however, both doses of lidocaine significantly reduced the average number of pups per litter surviving until weaning of offspring from the first 2 mating periods.

There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Labor and Delivery

Lidocaine is not contraindicated in labor and delivery. Should GLYDO be used concomitantly with other products containing lidocaine, the total dose contributed by all formulations must be kept in mind.

Nursing Mothers

Lidocaine is secreted in human milk. The clinical significance of this observation is unknown. Caution should be exercised when lidocaine is administered to a nursing woman.

Pediatric Use

Although, the safety and effectiveness of GLYDO in pediatric patients have not been established, a study of 19 premature neonates (gestational age <33 weeks) found no correlation between the plasma concentration of lidocaine or mononitroxylicyde and infant body weight when moderate amounts of lidocaine (i.e. 0.3 mL/ kg of lidocaine gel 20 mg/mL) were used for lubricating both intranasal and endotracheal tube. No neonate had plasma levels of lidocaine above 750 mcg/mL. Doses in children should be reduced, commensurate with age, body weight, and physical condition. (See DOSAGE AND ADMINISTRATION.)

ADVERSE REACTIONS

Adverse experiences following the administration of lidocaine are similar in nature to those observed with other amide local anesthetic agents. These adverse experiences are, in general, dose-related and may result from high plasma levels caused by excessive dosage or rapid absorption, or may result from a hypersensitivity, idiosyncrasy, or diminished tolerance on the part of the patient. Serious adverse experiences are generally systemic in nature. The following types are those most commonly reported:

There have been rare reports of endotracheal tube occlusion associated with the presence of dried jelly residue in the inner lumen of the tube. (See also WARNINGS and DOSAGE AND ADMINISTRATION.)

Central Nervous System

CNS manifestations are excitatory and/or depressant and may be characterized by lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tremors, blurred or double vision, vomiting, sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness, respiratory depression, and arrest. The excitatory manifestations may be very brief or may not occur at all, in which case the first manifestation of toxicity may be drowsiness merging into unconsciousness and respiratory arrest.

Drowsiness following the administration of lidocaine is usually an early sign of a high blood level of the drug and may occur as a consequence of rapid absorption.

Cardiovascular System

Cardiovascular manifestations are usually depressant and are characterized by bradycardia, hypotension, and cardiovascular collapse, which may lead to cardiac arrest.

Allergic

Allergic reactions are characterized by cutaneous lesions, urticaria, edema, or anaphylactoid reactions. Allergic reactions may occur as a result of sensitivity either to the local anesthetic agent or to other components in the formulation. Allergic reactions as a potential result to sensitivity of lidocaine are extremely rare and, if they occur, should be managed by conventional means. The detection of sensitivity by skin testing is of doubtful value.

OVERDOSAGE

Acute emergencies from local anesthetics are generally related to high plasma levels encountered during therapeutic use of local anesthetics. (See ADVERSE REACTIONS, WARNINGS, and PRECAUTIONS.)

Management of Local Anesthetic Emergencies

The first consideration is prevention, best accomplished by careful and constant monitoring of cardiovascular and respiratory vital signs and the patient’s state of consciousness after each local anesthetic administration. At the first sign of change, oxygen should be administered.

The first step in the management of convulsions consists of immediate attention to the maintenance of a patent airway and assisted or controlled ventilation with oxygen and a delivery system capable of permitting immediate positive airway pressure by mask. Immediately after the institution of these ventilatory measures, the adequacy of the circulation should be evaluated, keeping in mind that drugs used to treat convulsions sometimes depress the circulation when administered intravenously. Should convulsions persist despite adequate respiratory support, and if the status of the circulation permits, small increments of an ultra-short acting barbiturate (such as thiopental or thiamylal) or a benzodiazepine (such as diazepam) may be administered intravenously. The clinician should be familiar, prior to use of local anesthetics, with these anticonvulsant drugs. Supportive treatment of circulatory depression may require administration of intravenous fluids and, when appropriate, a vasopressor as directed by the clinical situation (e.g., ephedrine).

If not treated immediately, both convulsions and cardiovascular depression can result in hypoxia, acidosis, bradycardia, arrhythmias, and cardiac arrest. If cardiac arrest should occur, standard cardiopulmonary resuscitative measures should be instituted.

Dialysis is of negligible value in the treatment of acute overdosage with lidocaine.

The oral LD₅₀ of lidocaine HCl in non-fasted female rats is 459 (346 to 773) mg/kg (as the salt) and 214 (159 to 324) mg/kg (as the salt) in fasted female rats.

Mfd. for SAGENT Pharmaceuticals Schamburg, IL 60195 (USA) Mfd. by Klosterfrau Berlin GmbH Made in Germany ©2014 Sagent Pharmaceuticals, Inc. March 2014

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Please see full prescribing information for GLYDO (lidocaine HCl jelly USP, 2%).
PSA screening decline is troubling trend

I have been practicing urology for just under 2 years now and in that period have diagnosed six patients with metastatic prostate cancer at initial presentation. Anecdotally, this is not an uncommon trend. A number of urologists I spoke with at the AUA annual meeting in New Orleans recently reported seeing more prostate cancer patients with late-stage disease at presentation.

All six of my patients were some version of the same story. None of them had either a rectal exam or PSA in years. All had been told that both were useless, and most could even describe the U.S. Preventive Services Task Force (USPSTF) recommendations on PSA screening. All were shocked with the final diagnosis.

We now have credible evidence that the use of the PSA as a screening test by primary care physicians has declined since the USPSTF issued its “D” grade. At the AUA annual meeting, Dr. Wernitz et al showed a 50% decrease in the use of PSA testing by a group of primary care doctors since the USPSTF recommendations were published in 2012 (see page 1). This portends poorly for patients with prostate cancer.

This trend is incredibly important to discuss for a few reasons. First, it is confirmation that we are entering a new era (returning to a previous one?) when prostate cancer patients will walk into your office not with an elevated PSA but rather with symp-

toms. Just look at the SEER data prior to widespread PSA testing. The number of patients presenting with prostate cancer was not dramatically lower; they simply presented with significantly later stage disease.

Second, this trend stresses the importance of the urologist’s duty to educate primary care physicians that if they’re not going to check PSA, advanced prostate cancer now needs to be included in their differential in all patients who present with either obstructive voiding symptoms or back pain. Further, the decision to screen should be a shared decision between the physician and patient. If primary care doctors won’t have that discussion with patients, it is their responsibility as urologists to do it. Given the complexity of that discussion, we need a new CPT code (PSA-1?) for PSA screening counseling.

While PSA testing as a screening tool is controversial, PSA testing as a diagnostic test is not, and all primary care providers should understand the difference between screening and diagnosis when it comes to the PSA test.
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AACC LEGISLATIVE UPDATE

Obamacare survives Supreme Court challenge—again

The Affordable Care Act has survived its latest legal challenge. In a much-anticipated decision, the U.S. Supreme Court ruled in the case of King v. Burwell that tax subsidies for buying health care insurance made available through the law apply in all 50 states. After reading the decision, Dan Shaffer of the AACC discusses how the justices arrived at it and what it means to you.

READ THE UNDERPINNINGS OF THE RULING AT: urologytimes.com/ACA-ruling

BLOG

Falls are not only hazardous to your patients

In a blog earlier this year, Henry Rosevear, MD, wrote that urologists are in a wonderful position to raise awareness of patient falls and even save a life. To Dr. Rosevear’s surprise, reaction to the blog came primarily from nurses, who cautioned that health care workers are also at risk for injury when they attempt to lift a patient who’s fallen. In a follow-up blog, he discusses the risks of moving a patient and injury-prevention steps you can take.

urologytimes.com/injury-prevention

READER REACTION

Urologist takes on MOC, relinquishes certificate

After 15 years of board certification, urologist Stephen G. Weiss II, MD, says he “will no longer participate in the meaningless charade known as maintenance of certification.” Dr. Weiss, in a letter to the American Board of Urology, relinquished his certificate. He hopes his actions start a meaningful dialogue on MOC. We welcome your thoughts.

urologytimes.com/MOC-letter

@DrJohnAquino

John Aquino, MD, a Toronto urologist, is the Urology Times Twitter follower of the month! To be featured in this section, engage with us.

Our followers tweet about BAUS 2015 and more

Jonathan Glass
@jonathanmglass1
Was planning to dip toe in #SoMe water at #BAUS15. Fell in with a splash. Would encourage doubters; great urological discussions & exchange

Ben Challacombe
@benc Challacombe
#BAUS15 @BJUIjournal big take home message in prostate diagnostics: significant Ca exists outside MRI lesion. Need to biopsy whole gland.

Jake Patterson
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EXCLUSIVE VIDEO: Stacy Loeb, MD, offers perspective on recent studies examining active surveillance for low-risk prostate cancer. See www.urologytimes.com/Loeb.

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In a blog earlier this year, Henry Rosevear, MD, wrote that urologists are in a wonderful position to raise awareness of patient falls and even save a life. To Dr. Rosevear’s surprise, reaction to the blog came primarily from nurses, who cautioned that health care workers are also at risk for injury when they attempt to lift a patient who’s fallen. In a follow-up blog, he discusses the risks of moving a patient and injury-prevention steps you can take.

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Ultrasound stone repositioning facilitates passage

Technique also provides useful diagnostic information, researchers report

Mac Overmyer
UT CONTRIBUTING EDITOR

New Orleans—The first clinical trial of a novel ultrasound technology shows that it can safely reposition stones in situ to make them more amenable to natural passage and treatment.

Stone Disease

The approach can also provide useful diagnostic information in distinguishing a larger stone that would not pass from a cluster of much smaller, passable stones, according to the study’s authors.

“We have completed the first clinical trial of this technology in 15 patients and have met the goals of the study. The primary goal was to demonstrate that we could move stones within the kidney in humans. We did that in 14 of 15 patients. Secondary goals were also achieved in that it was tolerated in the clinic setting without pain, and there were no adverse events related to the procedure,” first author Jonathan Harper, MD, associate professor of urology at the University of Washington, Seattle, told Urology Times.

“By repositioning stones, we were able to facilitate stone passage in four of the six post-lithotripsy patients,” he said.

Dr. Harper described the technology developed by the Washington team as a new application of ultrasound that uses the acoustic radiation force of ultrasound waves to transcutaneously move stones within the kidney. The trial, which was presented at the AUA annual meeting in New Orleans, initially involved 13 awake, non-anesthetized patients selected without restriction of body habitus, stone size, or stone location. An additional two patients were incorporated in the study to gain more knowledge of stone repositioning by direct visualization of stone movement during ureteroscopy. This has led the group toward more optimized treatment parameters.

The majority (11) of the 15 patients were men, average age 56 (+/-11) years, and average body mass index was 29.3 kg/m² (+/-3.1). Stone sizes ranged from 1 mm to 14 mm and were located in the lower pole (24), interpolar (10), upper pole (four), and renal pelvis/ureteropelvic junction (four).

Stones were successfully relocated in all six post-lithotripsy patients, four of whom passed more than 30 fragments in the days following the procedure. One subject passed two 2-mm fragments before leaving the clinic.

An unanticipated finding

One finding that was unanticipated was that in four of the six post-lithotripsy patients, a stone that appeared to be greater than 5 mm on imaging was visually confirmed to be a composite of smaller, passable stones with repositioning.

The technology described by Dr. Harper is innovative.

“The probe we used in the trial is a standard, off-the-shelf ultrasound transducer in terms of imaging capabilities, but the ultrasonic propulsion technology is completely new and innovative. There is no published data outside our work describing this technology or its application,” said Dr. Harper, who noted that it was developed in conjunction with the University of Washington’s Applied Physics Laboratory.

“The imaging and ultrasonic propulsion are incorporated into the device for real-time feedback. The probe is used for imaging at one setting, and a different setting allows for propulsion or repositioning. The way the ultrasound is delivered is completely different than standard imaging. We have a clinical prototype, and we have had success with our first 15 patients. “Given the results of the clinical trial, there is a role for this technology in its current state, but we think we can make it better. Some of the new (probe) designs that have been developed over the past few weeks suggest it may have broader applications, whether these are moving a clump of fragments, detaching a small stone, or repositioning a larger obstructing stone,” he said.

Learning curve to technology

Moving stones using the technology is not as simple as shooting pool.

“There is a learning curve to this technology. You have to be able to use renal ultrasound and visualize the path you want to move the stone. If you are aiming into a wall, the stone is not going to go anywhere. It can take some trial and error to move the stones,” Dr. Harper said.

The finding that a larger stone was actually a collection of smaller stones or fragments turned out to be a diagnostic advantage that was unanticipated. Such findings can lead to revisions of clinical management, Dr. Harper said.

The study was funded by the National Space Biomedical Research Institute, a division of NASA, and the National Institutes of Health.

"By repositioning stones, we were able to facilitate stone passage in four of the six post-lithotripsy patients.”

JONATHAN HARPER, MD

In a video from the University of Washington’s Applied Physics Laboratory, researchers explain how ultrasound is used to visualize and reposition kidney stones so they are more likely to pass. See www.urologytimes.com/stone-repositioning.
MET found safe, efficacious in pregnant stone patients
Alpha-blocker should be included in treatment discussion, study author says

Mac Overmyer
UT CONTRIBUTING EDITOR

New Orleans—Managing stones in pregnant women can be challenging because many of the imaging technologies used to localize them, and the primary therapies to remove them or ease symptoms, may carry risks and/or side effects that might be amplified by the pregnancy. A retrospective study of 28 patients conducted by Mayo Clinic researchers suggests that medical expulsive therapy employing tamsulosin (Flomax), an alpha-1-adrenergic receptor antagonist, can benefit pregnant women with minimal risk to either mother or child, as reported at the AUA annual meeting in New Orleans.

“Our study suggests that tamsulosin as medical expulsive therapy for symptomatic stones in pregnant patients is safe and may increase stone passage rates.”

GEORGE BAILEY, MD

“Our study suggests that tamsulosin as medical expulsive therapy for symptomatic stones in pregnant patients is safe and may increase stone passage rates,” first author George Bailey, MD, a urology resident at Mayo Clinic, Rochester, MN, told Urology Times.

“Larger cohorts will be helpful in further defining the role of tamsulosin for pregnant stone formers, but our initial experience indicates that the option of tamsulosin medical expulsive therapy should be part of the discussion when physicians counsel symptomatic pregnant stone formers, especially when symptoms are severe enough that they are considering things like stent placement, ureteroscopy, or percutaneous nephrostomy tube,” said Dr. Bailey, who worked on the study with Amy Krambeck, MD, and colleagues.

To arrive at these conclusions, the Mayo team retrospectively identified 28 pregnant women with documented tamsulosin therapy for symptomatic urolithiasis. Of these women, 20 (71%) had urolithiasis documented by imaging and 23 (82%) had documented hydronephrosis. The median treatment period of tamsulosin was 3 days, the range, 1 to 110. Three patients (11%) were treated in their first trimester, 10 (36%) in their second, and 18 (67%) in their third trimester. Several patients had more than one course of therapy.

Dr. Bailey observed that the pattern of symptomatic stone formation in pregnant women seen in the study was somewhat typical. “Pregnant women have the same risk of stone formation as their non-pregnant peers. Most pregnant women who present with symptomatic nephrolithiasis will do so in the second or third trimester. That trend was seen in our patient population,” he said.

One of the challenges in treating stones in pregnant women is that the gold standard for imaging and localizing stones is computed tomography.

“Obviously, radiation exposure is something we try to avoid in pregnant women,” Dr. Bailey said.

“Often pregnant women with flank pain will undergo ultrasound imaging, which, unfortunately, has low sensitivity and specificity for stones. Women in our series were treated with tamsulosin, 0.4 mg/d, until the stone passed or their pain resolved.”

The median duration of in-utero exposure to the agent was 3 days, the researchers reported.

Surgery required in eight patients
Refractory renal colic requiring surgical intervention presented in eight patients (29%). This included one who required ureteral stent placement, one who required ureteroscopy without stent placement, five who required ureteroscopy with stent placement, and one who required a nephrostomy tube.

The study matched the treatment cohort 2:1 with a group of pregnant women with symptomatic urolithiasis who did not get tamsulosin and found no significant differences between

Please see EXPULSIVE THERAPY, page 10
Stone prophylaxis: Better patient adherence needed
Only 50% of 22,000-patient cohort adherent to regimen, data indicate

Cheryl Guttman Krader
UT CONTRIBUTING EDITOR

New Orleans—Numerous studies have shown poor adherence with preventive medications prescribed for patients with various chronic medical conditions, and new research shows this problem applies to patients prescribed medical prophylaxis for kidney stones.

Urologists at the University of Michigan, Ann Arbor used national pharmacy claims data from a recent 5-year period (2002-2006) to identify commercially insured adults who had one or more prescriptions filled for a thiazide, alkali citrate, or allopurinol after receiving a physician-coded diagnosis of nephrolithiasis. Medication adherence was evaluated using the validated proportion of days covered formula.

Defining adherence as >80% proportion of days covered during the first 6 months after the index kidney stone claim, only 50% of the nearly 22,000 patients included in the cohort were adherent with their regimen.

While year-by-year analyses showed a trend for adherence improving over time, the overall adherence rate was still below 55% in the last year of the study.

Logistic regression analysis was also performed to evaluate patient factors associated with adherence. Not surprisingly, the results showed that being on combination therapy or having a less generous insurance plan independently predicted lower adherence. In addition, males were significantly more likely to be adherent than females as were Midwesterners compared with patients from other parts of the country.

“To our knowledge, this is the first study examining patient adherence to medication prescribed for kidney stone prevention, and the findings are important for urologists considering that non-adherence may mitigate treatment benefit or even cause harm,” said first author Yooni Yi, MD, urology resident at the University of Michigan, who presented the research at the AUA annual meeting in New Orleans.

Patient counseling needed
Senior author John M. Hollingsworth, MD, MS, assistant professor of urology at the University of Michigan, told Urology Times, “Getting a patient to accept a prescribed regimen for kidney stone prevention and adhere to it may be difficult since a benefit of treatment is not obviously apparent to someone who is asymptomatic between stone events. Our study reinforces the need to spend time counseling patients on the importance of adherence and suggests possible targets for quality improvement in the secondary prevention of kidney stones.”

He noted that in addition to reinforcing the need for medication adherence through in-office education efforts, practitioners can suggest the use of a variety of aids, such as medication assistance programs or free mobile apps that remind patients to take their medications and keep track of their dosing schedule.

In investigating the issue of adherence to medical therapy for nephrolithiasis prevention, the study focused on medications recommended by the AUA Guideline on the Medical Management of Kidney Stones to be trialed in patients with selected metabolic abnormalities. Looking at patterns of use, the data showed that 83% of patients were prescribed a monotherapy regimen with thiazide monotherapy being most common (58% of the total population).

In examining adherence rates for the individual medications, the study identified marked variability, with adherence being best for thiazide monotherapy (42%) and lowest for alkali citrate monotherapy (~3%).

“Reasons to explain the very low adherence to citrate include the dosing frequency of a citrate supplementation regimen, its side effects, and cost. These findings highlight a potential barrier faced by providers who care for patients with hypocitraturia and low urine pH,” Dr. Hollingsworth said.

Convenience sample among limitations
The investigators noted their study has limitations. Its use of a convenience sample limits the ability to generalize the results. In addition, there is the potential for misclassification bias since it cannot be excluded that the investigated medications were prescribed for some other indication.

Importantly, while the study identified a problem with adherence, it did not investigate its consequences on clinical outcomes.

“Now we are actively investigating the impact that non-adherence has on outcome measures, including hospital admissions, emergency department visits, and stone-directed surgery among others,” Dr. Hollingsworth said.

Dr. Bailey responded to a question about the small size of the study, saying that it was not unusual.

“Practitioners are understandably hesitant to give medications without a proven safety record to pregnant women, which makes even retrospective studies difficult to conduct,” he said.

“Many investigations of medication exposure in pregnant women start with small, retrospective studies. The sample size of this study reflects those challenges and is on par with other initial single-institution investigations into medication exposure risk during pregnancy.”
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Researchers compare button, loop procedures

Bipolar vaporization: Do benefits outweigh risks?

Wayne Kuznar
UT CORRESPONDENT

New Orleans—Despite the near absence of intraoperative bleeding, bipolar vaporization of the prostate is associated with a higher rate of postoperative complications than bipolar loop resection for the treatment of lower urinary tract symptoms secondary to BPH, reported Richard Santucci, MD, and colleagues at the AUA annual meeting.

In particular, suggestions of late bleeding complications with bipolar vaporization were confirmed in a randomized clinical trial in which the two approaches were compared.

“In clinical medicine, you often get the rumor of the problem before you get proof of the problem,” said Dr. Santucci, director of the Center for Urologic Reconstruction and specialist in chief, urology, at the Detroit Medical Center.

In addition to an excess incidence of late bleeding, more irritative voiding symptoms in the early postoperative period surfaced with bipolar vaporization, which had also been the general impression all along.

“Everybody likes bipolar because it’s speedy, easy, and causes no bleeding,” said Dr. Santucci, the study’s senior author. “But you need to be aware that you may be trading a nice operation for a bad postoperative course including strictures, delayed bleeding, and increased urinary frequency. All surgeries have a cost-benefit ratio. This just better describes the cost-benefit ratio.”

Both bipolar transurethral loop resection of the prostate and bipolar button vaporization are minimally invasive surgical methods that are considered standard of care. Bipolar vaporization has become increasingly popular because it allows for concomitant vaporization and coagulation, resulting in near-zero intraoperative bleeding.

“No one knew if the benefits of bipolar vaporization—almost no bleeding and a pretty easy technique—made it better than bipolar loop, which possibly is faster and provides tissue for histopathology,” he said. “A large randomized trial had not been done, and that’s the value of the study.”

The relative safety profile of the two procedures was compared in 89 patients with BPH, who were randomized to surgery using either bipolar loop resection (44 patients) or bipolar button vaporization (45 patients). Eligible patients had a preoperative maximal flow rate (Qmax) <10 mL/sec, an International Prostate Symptom Score (IPSS) >18, and a prostate volume >40 grams. Patients were evaluated preoperatively and at 1, 3, and 9 months postoperatively by IPSS, uroflowmetry, and prostate ultrasound.

Preoperative prostate volume was 59 grams and 58 grams \((p=.52)\) in patients randomized to bipolar loop TURP and bipolar button vaporization, respectively, and IPSS was 19 and 20 \((p=.38)\), respectively.

Longer operative time with vaporization

Mean operative time was significantly longer in the vaporization group compared with the bipolar loop resection group (81 vs. 55 minutes; \(p<.001\)). Blood loss was less in patients randomized to bipolar vaporization compared with bipolar loop resection (0.8% vs. 2.0% drop in hemoglobin; \(p<.001\)). Bipolar vaporization was associated with increased rates of postoperative urinary frequency (80% vs. 50%, \(p<.001\)), hematuria

InBrief

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AUA recommendations address PSA, PCa imaging

Antimicrobial prescription, imaging for localized prostate cancer, and shared decision making for PSA screening are among the topics of the AUA’s latest Choosing Wisely recommendations.

The American Board of Internal Medicine Foundation’s Choosing Wisely campaign is designed to encourage clinicians and patients to scale back medical tests and procedures that may be unnecessary and even potentially harmful.

The AUA’s second, most recent list includes the following recommendations:

- Don’t obtain a computed tomography scan of the pelvis for asymptomatic men with low-risk clinically localized prostate cancer.
- Don’t remove synthetic vaginal mesh in asymptomatic patients.
- Offer PSA testing for detecting prostate cancer only after engaging in shared decision making.
- Don’t diagnose microhematuria solely on the results of a urine dipstick (macroscopic urinalysis).

The AUA previously issued Choosing Wisely recommendations in 2013, covering topics such as bone scans in men with low-risk prostate cancer and testosterone prescription.
Vitamin D inversely correlated with PSA in PCa patients

Effect differs in benign, cancerous prostates, cross-sectional data indicate

Cheryl Guttman Krader
UT CONTRIBUTING EDITOR

New Orleans—Serum vitamin D is inversely correlated with levels of PSA in men with prostate cancer, whereas serum vitamin D is inversely correlated with prostate volume in men without prostate cancer. Data from a cross-sectional study exploring these relationships were presented by Northwestern University researchers at the AUA annual meeting in New Orleans.

**Prostate Cancer**

The cross-sectional study was nested from a large, case-control study in which mediators of vitamin D and prostate cancer were assessed among men 40 to 79 years of age who were prospectively enrolled in academic outpatient urology clinics in Chicago.

With laboratory evidence to suggest that vitamin D could slow the growth rate of prostate cells in both benign and cancerous cell models, “the thought was that vitamin D probably will correlate with prostate size and PSA level,” said principal investigator Adam B. Murphy, MD. Instead, a differential effect of vitamin D was found in benign and cancerous prostates.

‘Very complex’ biology

“The biology is very complex,” said co-author Yaw Nyame, MD, MBA. “From a population standpoint, we are just now starting to get a glimpse as to what this hormone’s effect on the prostate really is. Very clearly, it has a different effect on cancer biology than it does benign biology.”

All men in the study had transrectal ultrasound (TRUS)-guided biopsy for an elevated serum PSA or abnormal digital rectal examination, at which time peripheral blood was collected for serum vitamin D. Prostate volume was estimated by the ellipsoid formula during TRUS. The association of prostate volume, PSA, and PSA density with serum vitamin D was assessed using three vitamin D cut points (12, 16, and 20 ng/mL).

These cut points were chosen to align with the Institute of Medicine’s definition of vitamin D deficiency based on the risk for osteoporosis.

“About 35% of the overall sample was vitamin D-deficient when defined as less than 20 ng/mL,” said Dr. Murphy, assistant professor in urology at Northwestern University Feinberg School of Medicine, Chicago. “The reason we used different cut points is that bone health doesn’t have much to do with what goes on in different tissues, so we can’t presume to know the right level.”

The final sample contained 812 men. The median age of the 509 men with positive biopsies was 62.8 years and the median age for the 303 with negative biopsies was 61.5 years (p=0.02). In the overall sample, serum vitamin D was inversely correlated with prostate volume for all the clinical cut points.

When examined according to biopsy result, the predominant association in the men with positive biopsies was an inverse correlation between serum vitamin D and PSA levels. In this group, serum PSA was 11.8 ng/mL with serum vitamin D level <12 ng/mL, and 8.7 ng/mL in men with serum vitamin D ≥12 ng/mL (p=0.005). The significant negative correlation between serum PSA and serum vitamin D remained when using 16 ng/mL serum vitamin D (p<0.0001) and 20 ng/mL (p=0.001) as cut points.

A negative correlation between serum vitamin D and PSA density also showed significance at the 16 ng/mL (p=0.03) and 20 ng/mL (p=0.03) serum vitamin D cut points.

In the men with negative prostate biopsies, an inverse correlation was observed between serum vitamin D and prostate volume, with the correlation being significant when using 20 ng/mL as the cut point. Men with serum vitamin D level <20 ng/mL had a median prostate volume of 64.5 cm³, compared with 54.3 cm³ in men with serum vitamin D ≥20 ng/mL (p=0.04).

‘Biomarker of aggressive disease’

These associations held when adjusting for known modifiers of serum PSA and prostate volume in multivariate regression models, said Dr. Nyame, a urology resident at Cleveland Clinic.

“We think that vitamin D is a biomarker of aggressive disease in cancer, so you would expect some correlation between both volume and PSA, but predominantly PSA for cancer patients,” Dr. Murphy told *Urology Times*. “It kind of helps us tease apart the relationship between PSA, volume, and vitamin D; and can you use vitamin D as a biomarker with the already established biomarkers?”

Dr. Nyame went one step further: “Vitamin D is not just a co-factor; it really has a purpose,” he said, noting that vitamin D is a hormone that exerts anti-angiogenic effects while also decreasing proliferation and increasing differentiation.

According to Dr. Murphy, the harm of excess vitamin D in cancer is concerning.

“You would expect it [serum vitamin D and PSA] to be positively correlated, but we don’t find that,” he said. “This means that vitamin D may in fact be bad for the prostate at high levels. That’s one important implication.”

**UT Table**

<table>
<thead>
<tr>
<th>Serum vitamin D level</th>
<th>Serum PSA level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;12 ng/mL</td>
<td>11.8 ng/mL</td>
</tr>
<tr>
<td>≥12 ng/mL</td>
<td>8.7 ng/mL</td>
</tr>
</tbody>
</table>

Source: Adam B. Murphy, MD, and Yaw Nyame, MD, MBA

**VAPORIZATION**

continued from page 12

with clots up to 4 weeks after surgery (20% vs. 2%; p=0.001), and postoperative urethral stricture (11% vs. 0%) compared with bipolar loop resection.

There were equivalent improvements in the bipolar vaporization and bipolar loop resection groups on the endpoints of postoperative Qmax (17 cc/s vs. 18 cc/s; p=0.22), postoperative prostate volume (32 vs. 31 grams; p=0.31), and IPSS (6 vs. S; p=0.22).

Late postoperative bleeding with bipolar vaporization may be a function of the procedure, in which a 2- to 3-mm rind of highly coagulated prostate tissue remains after the prostate is vaporized, Dr. Santucci believes.

“At 2 weeks, what may happen is that the rind of cooked tissue sloughs off, and then the fresh prostate underneath begins bleeding,” he told *Urology Times*.

The significantly increased rate of urethral stricture is “very disturbing,” he added. Although most operators would select the latest (fourth) button version of bipolar vaporization, “it could be that it’s not the right thing to do, and you should go back to version three, which is bipolar loop,” he said.
Personalized messaging: Communicating with men about their health

Six common themes describe motivations that lead men to health decisions

S. Larry Goldenberg, CM, OBC, MD  ●  Sean C. Skeldon, MD  ●  Nick Black, MA

We know that the longevity gap between men and women is much less biological than it is behavioral (Lancet 2012; 380:2144-62), but have we become so used to men dying earlier than women that it is just an accepted fact in our society? While these sex differences are well recognized and accepted (BMJ 2001; 323:1058-60; J Mens Health 2009; 6:246; BMJ 2001; 323:1061-3; Urol Clin North Am 2012; 39:37-51), attempts to effect change have proven difficult, principally because the underlying mechanisms and the ingredients of effective interventions are poorly understood (BMC Health Serv Res 2008; 8:141).

Behaviors are both challenging to influence and to change once they have been established. Traditional masculine characteristics—competitiveness, stoicism, denial, and self-reliance—are all believed to contribute to men’s reluctance to seek help (J Mens Health 2011; 8:7-15; J Adv Nurs 2005; 49:616-23). Understanding how these characteristics intersect with sociocultural, psychological, and behavioral determinants of health could inform powerful strategies for engaging men with their health. What is needed is an understanding of the implicit or underlying motivations involved in men’s health decisions and behaviors. Essentially, discerning the optimal strategy to engage men about their health can be distilled down to a messaging, communication, or marketing question (J Mens Health Gend 2004; 1:275-6). The mechanism by which to effectively communicate with men has been unexplored and undefined.

Understanding how traditional masculine characteristics intersect with sociocultural, psychological, and behavioral determinants of health could inform powerful strategies for engaging men with their health.

In this article, we describe the use of morphological market research to identify six themes or modes that shape men’s health behaviors and how those modes can be ultimately used to improve men’s health.

Morphological market research defined

Morphological market research is one of the practical applications of morphological psychology, originally advanced by Wilhelm Salber in Germany. It is an independent theoretical foundation in qualitative research based on the psychological tensions that influence human experience and behavior. Often applied in contemporary retail research, morphological market research is employed to decipher the fundamental motivating forces and unconscious processes behind everyday activities and decisions (J Advert Res 2004; 44:210-5).

Similar to other qualitative research methodologies (Qual Health Res 2007; 17:1372-80), interpretative analysis in morphological market research involves an iterative process of decontextualization and recontextualization to distill data into a set of common concepts or needs. Common conceptual themes or modes can be discerned to create a final morphological model of market and consumer motivations that could describe men’s intrinsic decision-making processes regarding their health.

The Canadian Men’s Health Foundation (www.dontchangemuch.ca) applied this methodology in a pilot study of 40 Canadian men, aged 30 to 49 years, to identify common themes involved in the motivations that shape men’s health behaviors (unpublished data). Our analyses revealed six prominent health modes or themes: learned helplessness, denial of vulnerability, suppression, controlled intervention, balanced care, and delegation (figure). Each mode can occur alone or concurrently with others, and each is influenced by factors that include gender, socioeconomics, family dynamics, cultural background, and individual personality.

Six health care modes in men identified

The six identified health care modes are defined as follows:

- **Learned helplessness** describes a health care mode where men feel unwilling or unable to look after their own health. The factors influencing this health mode are often complex and may include childhood abuse, trauma, psychological illness, and delayed gratification issues—all of which can deplete control and make proactively dealing with health a lower priority for men.

- **Denial of vulnerability** describes men’s focus on increasing their physical strength and sexual appeal. Factors influencing this health mode are societal and biological. For example, men are socially encouraged and sexually rewarded for looking younger and stronger and being financially successful, and they are penalized for showing signs of weakness and vulnerability. This can lead to a dangerous overestimation of personal capabilities.

- **Suppression or “keep on working”** is a health care mode in which men deprivitize health in order to provide for their family and become...
In men with mCRPC who progressed on ADT

The story for ZYTIGA® has significantly evolved.

Presenting...

mCRPC = metastatic castration-resistant prostate cancer; ADT = androgen-deprivation therapy.

INDICATION
ZYTIGA® (abiraterone acetate) in combination with prednisone is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (mCRPC).

IMPORTANT SAFETY INFORMATION
Contraindications—ZYTIGA® is not indicated for use in women. ZYTIGA® can cause fetal harm (Pregnancy Category X) when administered to a pregnant woman and is contraindicated in women who are or may become pregnant.

Hypertension, Hypokalemia, and Fluid Retention Due to Mineralocorticoid Excess—Use with caution in patients with a history of cardiovascular disease or with medical conditions that might be compromised by increases in blood pressure, hypokalemia, or fluid retention. ZYTIGA® may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition. Safety has not been established in patients with LVEF <50% or New York Heart Association (NYHA) Class III or IV heart failure (in Study 1) or NYHA Class II to IV heart failure (in Study 2) because these patients were excluded from these randomized clinical trials. Control hypertension and correct hypokalemia before and during treatment. Monitor blood pressure, serum potassium, and symptoms of fluid retention at least monthly.

Adrenocortical Insufficiency (AI)—AI was reported in patients receiving ZYTIGA® in combination with prednisone, after an interruption of daily steroids and/or with concurrent infection or stress. Use caution and monitor for symptoms and signs of AI if prednisone is stopped or withdrawn, if prednisone dose is reduced, or if the patient experiences unusual stress. Symptoms and signs of AI may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with ZYTIGA®. Perform appropriate tests, if indicated, to confirm AI. Increased dosages of corticosteroids may be used before, during, and after stressful situations.

Hepatotoxicity—Monitor liver function and modify, withhold, or discontinue ZYTIGA® dosing as recommended (see Prescribing Information for more information). Measure serum transaminases [alanine aminotransferase (ALT) and aspartate aminotransferase (AST)] and bilirubin levels prior to starting treatment with ZYTIGA®, every two weeks for the first three months of treatment, and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of AST, ALT, or bilirubin from the patient’s baseline should prompt more frequent monitoring. If at any time AST or ALT rise above five times the upper limit of normal (ULN) or the bilirubin rises above three times the ULN, interrupt ZYTIGA® treatment and closely monitor liver function.

Please see additional Important Safety Information on the next pages.

Please see brief summary of full Prescribing Information on subsequent pages.
In men with mCRPC who progressed on ADT, consider ZYTIGA® (abiraterone acetate) first.

Final analysis of the pivotal phase 3 trial.*

Every day tells a story.

IMPORTANT SAFETY INFORMATION
Increased ZYTIGA® Exposures With Food—ZYTIGA® must be taken on an empty stomach. No food should be eaten for at least two hours before the dose of ZYTIGA® is taken and for at least one hour after the dose of ZYTIGA® is taken. Abiraterone Cmax and AUC0-∞ (exposure) were increased up to 17- and 10-fold higher, respectively, when a single dose of abiraterone acetate was administered with a meal compared to a fasted state.

Adverse Reactions—The most common adverse reactions (≥10%) are fatigue, joint swelling or discomfort, edema, hot flush, diarrhea, vomiting, cough, hypertension, dyspnea, urinary tract infection, and contusion. The most common laboratory abnormalities (≥20%) are anemia, elevated alkaline phosphatase, hypertriglyceridemia, lymphopenia, hypercholesterolemia, hyperglycemia, elevated AST, hypophosphatemia, elevated ALT, and hypokalemia.

*Study Design: ZYTIGA®, in combination with prednisone, was evaluated in a phase 3, randomized, double-blind, placebo-controlled, multicenter trial in patients with mCRPC who had not received prior chemotherapy (N=1,088). Patients were using a luteinizing hormone-releasing hormone (LHRH) agonist or were previously treated with orchiectomy. In the ZYTIGA® arm, patients received ZYTIGA® 1,000 mg orally once daily + prednisone 5 mg orally twice daily. In the placebo arm, patients received placebo orally once daily + prednisone 5 mg orally twice daily. In this study, the co-primary efficacy end points were OS and radiographic progression-free survival (rPFS). Select exclusion criteria included AST and/or ALT ≥2.5X ULN, liver metastases, moderate or severe pain, opiate use for cancer pain, and visceral organ metastases.

† At a prespecified final analysis for OS, 65% (354/546) of patients treated with ZYTIGA® + prednisone compared with 71% (387/542) of patients treated with placebo + prednisone had died.
‡ Prednisone, as a single agent, is not approved for the treatment of prostate cancer.
§ rPFS was assessed with the use of sequential imaging studies and was defined by bone scan identification of 2 or more new bone lesions with confirmation (Prostate Cancer Working Group 2 [PCWG2] criteria) and/or modified Response Evaluation Criteria In Solid Tumors (RECIST) criteria for progression of soft tissue lesions. Analysis of rPFS utilized centrally reviewed radiographic assessment of progression.

II At the prespecified rPFS analysis, 150 (28%) of patients treated with ZYTIGA® + prednisone and 251 (46%) of patients treated with placebo + prednisone had radiographic progression.

Please see brief summary of full Prescribing Information on subsequent pages.
After a median 4 years (49 months) of follow-up...

ZYTIGA® (abiraterone acetate) + prednisone achieved a median overall survival (OS) of almost 3 years (34.7 months).1

- 4.4 months improvement in median OS — 34.7 months with ZYTIGA® + prednisone vs 30.3 months with placebo + prednisone (active compound)4

Co-primary end point — median OS: hazard ratio (HR)=0.81; 95% CI: 0.70, 0.93; P=0.0033.

Co-primary end point — rPFS: median not reached for ZYTIGA® + prednisone vs a median of 8.28 months for placebo + prednisone; HR=0.425; 95% CI: 0.347, 0.522; P<0.0001.91

With a median 49 months of follow-up, there were no notable changes in the safety profile of ZYTIGA® + prednisone since the previously reported interim analyses.1

In your patients with mCRPC...

CONSIDER ZYTIGA® FIRST.

Drug Interactions — Based on in vitro data, ZYTIGA® is a substrate of CYP3A4. In a drug interaction trial, co-administration of rifampin, a strong CYP3A4 inducer, decreased exposure of abiraterone by 55%. Avoid concomitant strong CYP3A4 inducers during ZYTIGA® treatment. If a strong CYP3A4 inducer must be co-administered, increase the ZYTIGA® dosing frequency only during the co-administration period (see Dosage and Administration (2.3)). In a dedicated drug interaction trial, co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of abiraterone.

ZYTIGA® is an inhibitor of the hepatic drug-metabolizing enzymes CYP2D6 and CYP2C8. Avoid co-administration with CYP2D6 substrates with a narrow therapeutic index. If alternative treatments cannot be used, exercise caution and consider a dose reduction of the CYP2D6 substrate drug. In a CYP2C8 drug interaction trial in healthy subjects, the AUC of pioglitazone, a CYP2C8 substrate, was increased by 46% when administered with a single dose of ZYTIGA®. Patients should be monitored closely for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly with ZYTIGA®.

Use in Specific Populations — Do not use ZYTIGA® in patients with baseline severe hepatic impairment (Child-Pugh Class C).

ZYTIGA® (abiraterone acetate) Tablets

Brief Summary of Prescribing Information.

INDICATIONS AND USAGE
ZYTIGA® is a CYP17 inhibitor indicated in combination with prednisone for the treatment of patients with metastatic castration-resistant prostate cancer.

CONTRAINDICATIONS
Pregnancy: ZYTIGA can cause fetal harm when administered to a pregnant woman. ZYTIGA is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for pregnancy loss [see Use in Specific Populations].

WARNINGS AND PRECAUTIONS
Hypertension, Hypokalemia and Fluid Retention Due to Mineralocorticoid Excess: ZYTIGA may cause hypertension, hypokalemia, and fluid retention as a consequence of increased mineralocorticoid levels resulting from CYP17 inhibition [see Clinical Pharmacology (12.1) in full Prescribing Information]. In the two randomized clinical trials, grade 3 to 4 hypertension occurred in 2% of patients, grade 3 to 4 hypokalemia in 4% of patients, and grade 3 to 4 edema in 1% of patients treated with ZYTIGA [see Adverse Reactions].

Co-administration of a corticosteroid suppresses adrenocorticotropic hormone (ACTH) drive, resulting in a reduction in the incidence and severity of these adverse reactions. Use caution when treating patients whose underlying medical conditions might be compromised by increases in blood pressure, hypokalemia or fluid retention, e.g., those with heart failure, recent myocardial infarction or ventricular arrhythmia. Use ZYTIGA with caution in patients with a history of fluid retention. The safety of ZYTIGA in patients with left ventricular ejection fraction <50% or New York Heart Association (NYHA) Class III or IV heart failure (in Study 1) or NYHA Class II to IV heart failure (in Study 2) was not established because these patients were excluded from these randomized clinical trials [see Clinical Studies (14) in full Prescribing Information]. Monitor patients for hypertension, hypokalemia, and fluid retention at least once a month. Control hypertension and correct hypokalemia before and during treatment with ZYTIGA.

Adrenocortical Insufficiency: Adrenal insufficiency occurred in the two randomized clinical studies in 0.5% of patients taking ZYTIGA and in 0.2% of patients taking placebo. Adrenocortical insufficiency was reported in patients receiving ZYTIGA in combination with prednisone, following interruption of daily steroids and/or with concurrent infection or stress. Use caution and monitor for symptoms and signs of adrenocortical insufficiency, particularly if patients are withdrawn from prednisone, have prednisone dose reductions, or experience unusual stress. Symptoms and signs of adrenocortical insufficiency may be masked by adverse reactions associated with mineralocorticoid excess seen in patients treated with ZYTIGA. If clinically indicated, perform appropriate tests to confirm the diagnosis of adrenocortical insufficiency. Increased dosage of corticosteroids may be indicated before, during and after stressful situations [see Warnings and Precautions].

Hepatotoxicity: In the two randomized clinical trials, grade 3 or 4 ALT or AST increases (at least 5X ULN) were reported in 4% of patients who received ZYTIGA, typically during the first 3 months after starting treatment. Patients whose baseline ALT or AST were elevated were more likely to experience liver test elevation than those beginning with normal values. Treatment discontinuation due to liver enzyme increases occurred in 1% of patients taking ZYTIGA. No deaths clearly related to ZYTIGA were reported due to hepatotoxicity events.

Measure serum transaminases (ALT and AST) and bilirubin levels prior to starting treatment with ZYTIGA, every two weeks for the first three months of treatment and monthly thereafter. In patients with baseline moderate hepatic impairment receiving a reduced ZYTIGA dose of 250 mg, measure ALT, AST, and bilirubin prior to the start of treatment, every week for the first month, every two weeks for the following two months of treatment and monthly thereafter. Promptly measure serum total bilirubin, AST, and ALT if clinical symptoms or signs suggestive of hepatotoxicity develop. Elevations of ALT, AST, or bilirubin from the patient’s baseline should prompt more frequent monitoring. If at any time AST or ALT rise above five times the ULN, or if the bilirubin rises above three times the ULN, interrupt ZYTIGA treatment and closely monitor liver function.

Re-treatment with ZYTIGA at a reduced dose level may take place only after a minimum of 4 weeks without clinical evidence of the patient's baseline liver function or AST and ALT less than or equal to 2.5X ULN and total bilirubin less than or equal to 1.5X ULN [see Dosage and Administration (2.2) in full Prescribing Information].

The safety of ZYTIGA re-treatment of patients who develop ALT greater than or equal to 20X ULN and/or bilirubin greater than or equal to 10X ULN is unknown.

Increased ZYTIGA Exposures with Food: ZYTIGA must be taken on an empty stomach. Food should be consumed at least two hours before or two hours after the dose of ZYTIGA is taken and for at least one hour after the dose of ZYTIGA is taken. Abiraterone Cmax and AUC0-∞ (exposure) were increased up to 17- and 10-fold higher, respectively, when a single dose of abiraterone acetate was administered with a meal compared to a fasted state. The safety of these increased exposures when multiple doses of abiraterone acetate are taken with food has not been assessed [see Dosage and Administration (2.1) and Clinical Pharmacology (12.3) in full Prescribing Information].

ZYTIGA® (abiraterone acetate) Tablets

ADVERSE REACTIONS
The following are discussed in more detail in other sections of the labeling:

- Hypertension, Hypokalemia, and Fluid Retention due to Mineralocorticoid Excess [see Warnings and Precautions].
- Adrenocortical Insufficiency [see Warnings and Precautions].
- Hepatotoxicity [see Warnings and Precautions].
- Increased ZYTIGA Exposures with Food [see Warnings and Precautions].

Clinical Trial Experience: Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

Two randomized placebo-controlled, multicenter clinical trials enrolled patients who had metastatic castration-resistant prostate cancer who were using a gonadotropin-releasing hormone (GnRH) agonist or were previously treated with orchectomy. In both Study 1 and Study 2 ZYTIGA was administered at a dose of 1,000 mg daily in combination with prednisone 5 mg twice daily in the active treatment arms. Placebo plus prednisone 5 mg twice daily was given to control patients.

The most common adverse drug reactions (>10%) reported in the two randomized clinical trials that occurred more commonly (>2%) in the abiraterone acetate arm were fatigue, joint swelling or discomfort, edema, hot flush, diarrhea, vomiting, cough, hypertension, dyspnea, urinary tract infection and congestion.

The most common laboratory abnormalities (>20%) reported in the two randomized clinical trials that occurred more commonly (>2%) in the abiraterone acetate arm were anemia, elevated alkaline phosphatase, hyperglycemia, hypercholesterolemia, hyperkalemia, elevated AST, hypophosphatemia, elevated ALT and hypokalemia.

Study 1: Metastatic CRPC Following Chemotherapy: Study 1 enrolled 1195 patients with metastatic CRPC who had received prior docetaxel chemotherapy. Patients were not eligible if AST and/or ALT ≥2.5X ULN in the absence of liver metastases. Patients with liver metastases were excluded if AST and/or ALT ≥5X ULN.

Table 1 shows adverse reactions on the ZYTIGA arm in Study 1 that occurred with a ≥2% absolute increase in frequency compared to placebo or were events of special interest. The median duration of treatment with ZYTIGA was 8 months.

Table 1: Adverse Reactions due to ZYTIGA in Study 1

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>Placebo with Prednisone (N=394)</th>
<th>ZYTIGA with Prednisone (N=791)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Grades</td>
<td>%</td>
<td>All Grades</td>
</tr>
<tr>
<td><strong>Musculoskeletal and connective tissue disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Joint swelling/discomfort</td>
<td>29.5</td>
<td>4.2</td>
</tr>
<tr>
<td>Muscle discomfort</td>
<td>26.2</td>
<td>3.0</td>
</tr>
<tr>
<td><strong>General disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Edema</td>
<td>26.7</td>
<td>1.9</td>
</tr>
<tr>
<td><strong>Vascular disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot flush</td>
<td>19.0</td>
<td>0.3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8.5</td>
<td>1.3</td>
</tr>
<tr>
<td><strong>Gastrointestinal disorders</strong></td>
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<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>17.6</td>
<td>0.6</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>6.1</td>
<td>0</td>
</tr>
<tr>
<td><strong>Infections and infestations</strong></td>
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<td></td>
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<tr>
<td>Urinary tract infection</td>
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<td>2.1</td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
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<td>0</td>
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<td><strong>Respiratory, thoracic and mediastinal disorders</strong></td>
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<td></td>
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<tr>
<td>Cough</td>
<td>10.6</td>
<td>0</td>
</tr>
<tr>
<td><strong>Renal and urinary disorders</strong></td>
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<td>Urinary frequency</td>
<td>7.2</td>
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<tr>
<td>Nocturia</td>
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<td>0</td>
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<tr>
<td><strong>Injury, poisoning and procedural complications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fractures</td>
<td>5.9</td>
<td>1.4</td>
</tr>
<tr>
<td><strong>Cardiac disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>7.2</td>
<td>1.1</td>
</tr>
<tr>
<td>Chest pain or chest discomfort</td>
<td>3.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>2.3</td>
<td>1.9</td>
</tr>
</tbody>
</table>

1 Adverse events graded according to CTCAE version 3.0
2 Includes terms Arthritis, Arthralgia, Joint swelling, and Joint stiffness
3 Includes terms Muscle spasms, Musculoskeletal pain, Myalgia, Musculoskeletal discomfort, and Musculoskeletal stiffness
ZYTIGA® (abiraterone acetate) Tablets

1 Includes terms Edema, Edema peripheral, Pitting edema, and Generalized edema
2 Includes all fractures with the exception of pathological fracture
3 Includes terms Arthritis, Arthralgia, Joint swelling, and Joint stiffness
4 Includes terms Edema, Edema peripheral, Pitting edema, and Generalized edema
5 Includes terms Angina pectoris, Chest pain, and Angina unstable.
6 Includes terms Cardiac failure, Cardiac failure congestive, Left ventricular dysfunction, Cardiogenic shock, Cardiomegaly, Cardiomyopathy, and Ejection fraction decreased.

Table 2 shows laboratory abnormalities of interest from Study 1. Grade 3-4 low serum phosphorus (7%) and low potassium (5%) occurred at a greater than or equal to 5% rate in the ZYTIGA arm.

Table 2: Laboratory Abnormalities of Interest in Study 1

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>Abiraterone (N=791)</th>
<th>Placebo (N=394)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades (%)</td>
<td>Grade 3-4 (%)</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>62.5</td>
<td>0.4</td>
</tr>
<tr>
<td>High AST</td>
<td>30.6</td>
<td>2.1</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>28.3</td>
<td>5.3</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>23.8</td>
<td>7.2</td>
</tr>
<tr>
<td>High ALT</td>
<td>11.1</td>
<td>1.4</td>
</tr>
<tr>
<td>High Total Bilirubin</td>
<td>6.6</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Study 2: Metastatic CRPC Prior to Chemotherapy: Study 2 enrolled 1088 patients with metastatic CRPC who had not received prior cytotoxic chemotherapy. Patients were ineligible if AST and/or ALT ≥2.5X ULN and patients were excluded if they had liver metastases.

Table 3 shows adverse reactions on the ZYTIGA arm in Study 2 that occurred with a ≥2% absolute increase in frequency compared to placebo. The median duration of treatment with ZYTIGA was 13.8 months.

Table 3: Adverse Reactions in ≥5% of Patients on the ZYTIGA Arm in Study 2

<table>
<thead>
<tr>
<th>System/Organ Class</th>
<th>Abiraterone (N=542)</th>
<th>Placebo (N=540)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>39.1</td>
<td>2.2</td>
</tr>
<tr>
<td>Edema</td>
<td>25.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>8.7</td>
<td>0.6</td>
</tr>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>30.3</td>
<td>2.0</td>
</tr>
<tr>
<td>Groin pain</td>
<td>6.6</td>
<td>0.4</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>23.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Constipation</td>
<td>21.6</td>
<td>0.9</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>11.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Vascular disorders</td>
<td>22.3</td>
<td>0.2</td>
</tr>
<tr>
<td>Hot flush</td>
<td>21.6</td>
<td>3.9</td>
</tr>
<tr>
<td>Respiratory, thoracic and mediastinal disorders</td>
<td>17.3</td>
<td>0.0</td>
</tr>
<tr>
<td>Cough</td>
<td>11.8</td>
<td>2.4</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>13.5</td>
<td>0.2</td>
</tr>
<tr>
<td>Insomnia</td>
<td>12.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Injury, poisoning and procedural complications</td>
<td>12.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Contusion</td>
<td>8.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Rash</td>
<td>8.1</td>
<td>0.0</td>
</tr>
</tbody>
</table>

1 Based on non-fasting blood draws

Cardiovascular Adverse Reactions: In the combined data for studies 1 and 2, cardiac failure occurred more commonly in patients treated with ZYTIGA compared to patients on the placebo arm (2.1% versus 0.7%). Grade 3-4 cardiac failure occurred in 1.6% of patients taking ZYTIGA and led to 5 treatment discontinuations and 2 deaths. Grade 3-4 cardiac failure occurred in 0.2% of patients taking placebo. There were no treatment discontinuations and one death due to cardiac failure in the placebo group.

In Study 1 and 2, the majority of arrhythmias were grade 1 or 2. There was one death associated with arrhythmia and one patient with sudden death in the ZYTIGA arms and no deaths in the placebo arms. There were 7 (0.5%) deaths due to cardiorespiratory arrest in the ZYTIGA arms and 3 (0.3%) deaths in the placebo arms. Myocardial ischemia or myocardial infarction led to death in 3 patients in the placebo arm and 2 deaths in the ZYTIGA arms.

Post Marketing Experience

The following additional adverse reactions have been identified during post approval use of ZYTIGA. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Respiratory, Thoracic and Mediastinal Disorders: Non-infectious pneumonitis. Musculoskeletal and Connective Tissue Disorders: myopathy, including rhabdomyolysis.

DRUG INTERACTIONS

Drugs that Inhibit or Induce CYP3A4 Enzymes: Based on in vitro data, ZYTIGA is a substrate of CYP3A4.

In a dedicated drug interaction trial, co-administration of rifampin, a strong CYP3A4 inducer, decreased exposure of abiraterone by 55%. Avoid concomitant strong CYP3A4 inducers during ZYTIGA treatment. If a strong CYP3A4 inducer must be co-administered, increase the ZYTIGA dosing frequency.

In a dedicated drug interaction trial, co-administration of ketoconazole, a strong inhibitor of CYP3A4, had no clinically meaningful effect on the pharmacokinetics of abiraterone..

Effects of Abiraterone on Drug Metabolizing Enzymes: ZYTIGA is an inhibitor of the hepatic drug-metabolizing enzymes CYP2D6 and CYP2C8. In a CYP2D6 drug-dose interaction trial, the Cmax of dextromethorphan (CYP2D6 substrate) were increased 2.8- and 2.9-fold, respectively, when dextromethorphan was given with abiraterone acetate 1,000 mg daily and prednisone 5 mg twice daily. Avoid co-administration of abiraterone acetate with substrates of CYP2D6 with a narrow therapeutic index (e.g., thioridazine). If alternative treatments cannot be used, exercise caution and consider a dose reduction of the concomitant CYP2D6 substrate drug.

In a CYP2C8 drug-drug interaction trial in healthy subjects, the AUC of pioglitazone (CYP2C8 substrate) was increased by 46% when pioglitazone was given together with a single dose of 1,000 mg abiraterone acetate. Therefore, patients should be monitored closely for signs of toxicity related to CYP2C8 substrates with a narrow therapeutic index if used concomitantly with ZYTIGA.
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USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category X [see Contraindications]: ZYTIGA can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. While there are no adequate and well-controlled studies with ZYTIGA in pregnant women and ZYTIGA is not indicated for use in women, it is important to know that maternal use of a CYP17 inhibitor could affect development of the fetus. Abiraterone acetate caused developmental toxicity in pregnant rats at exposures that were lower than in patients receiving the recommended dose. ZYTIGA is contraindicated in women who are or may become pregnant while receiving the drug. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for pregnancy loss. Advise females of reproductive potential to avoid becoming pregnant during treatment with ZYTIGA.

In an embryo-fetal developmental toxicity study in rats, abiraterone acetate caused developmental toxicity when administered at oral doses of 10, 30 or 100 mg/kg/day throughout the period of organogenesis (gestational days 6-17). Findings included embryo-fetal lethality (increased post implantation loss and resorptions and decreased number of live fetuses), fetal developmental delay (skeletal effects) and urogenital effects (bilateral ureter dilation) at doses ≥10 mg/kg/day, decreased fetal ano-genital distance at ≥30 mg/kg/day, and decreased fetal body weight at 100 mg/kg/day. Doses ≥10 mg/kg/day caused maternal toxicity. The doses tested in rats resulted in systemic exposures (AUC) approximately 0.03, 0.1 and 0.3 times, respectively, the AUC in patients.

Nursing Mothers: ZYTIGA is not indicated for use in women. It is not known if abiraterone acetate is excreted in human milk. Because many drugs are excreted in human milk, and because of the potential for serious adverse reactions in nursing infants from ZYTIGA, a decision should be made to either discontinue nursing, or discontinue the drug taking into account the importance of the drug to the mother.

Pediatric Use: Safety and effectiveness of ZYTIGA in pediatric patients have not been established.

Geriatric Use: Of the total number of patients receiving ZYTIGA in Phase 3 trials, 73% of patients were 65 years and over and 30% were 75 years and over. No overall differences in safety or effectiveness were observed between these elderly patients and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Patients with Hepatic Impairment: The pharmacokinetics of abiraterone were examined in subjects with baseline mild (N=8) or moderate (N=8) hepatic impairment (Child-Pugh Class A and B, respectively) and in 8 healthy control subjects with normal hepatic function. The systemic exposure (AUC) of abiraterone after a single oral 1,000 mg dose of ZYTIGA increased by approximately 1.1-fold and 3.8-fold in subjects with mild and moderate baseline hepatic impairment, respectively compared to subjects with normal hepatic function.

In another trial, the pharmacokinetics of abiraterone were examined in subjects with baseline severe (N=8) hepatic impairment (Child-Pugh Class C) and in 8 healthy control subjects with normal hepatic function. The systemic exposure (AUC) of abiraterone increased by approximately 7-fold and the fraction of free drug increased 2-fold in subjects with severe baseline hepatic impairment compared to subjects with normal hepatic function.

No dosage adjustment is necessary for patients with baseline mild hepatic impairment. In patients with baseline moderate hepatic impairment (Child-Pugh Class B), reduce the recommended dose of ZYTIGA to 250 mg once daily. Do not use ZYTIGA in patients with baseline severe hepatic impairment (Child-Pugh Class C). If elevations in ALT or AST >5X ULN or total bilirubin >3X ULN occur in patients with baseline moderate hepatic impairment, discontinue ZYTIGA treatment [see Dosage and Administration (2.1) and Clinical Pharmacology (12.3) in full Prescribing Information].

For patients who develop hepatotoxicity during treatment, interruption of treatment and dosage adjustment may be required [see Dosage and Administration (2.2) in full Prescribing Information, Warnings and Precautions, and Clinical Pharmacology (12.3) in full Prescribing Information].

Patients with Renal Impairment: In a dedicated renal impairment trial, the mean PK parameters were comparable between healthy subjects with normal renal function (N=8) and those with end stage renal disease (ESRD) on hemodialysis (N=8) after a single oral 1,000 mg dose of ZYTIGA. No dosage adjustment is necessary for patients with renal impairment [see Dosage and Administration (2.1) and Clinical Pharmacology (12.3) in full Prescribing Information].

OVERDOSAGE

Human experience of overdose with ZYTIGA is limited. There is no specific antidote. In the event of an overdose, stop ZYTIGA, undertake general supportive measures, including monitoring for arrhythmias and cardiac failure and assess liver function.

ZYTIGA® (abiraterone acetate) Tablets

Storage and Handling: Store at 20°C to 25°C (68°F to 77°F); excursions permitted in the range from 15°C to 30°C (59°F to 86°F) [see USP controlled room temperature]. Based on its mechanism of action, ZYTIGA may harm a developing fetus. Therefore, women who are pregnant or women who may be pregnant should not handle ZYTIGA without protection, e.g., gloves [see Use in Specific Populations].

PATIENT COUNSELING INFORMATION

See FDA-approved patient labeling (Patient Information)

- Patients should be informed that ZYTIGA and prednisone are used together and that they should not interrupt or stop either of these medications without consulting their physician.
- Patients receiving GnRH agonists should be informed that they need to maintain this treatment during the course of treatment with ZYTIGA and prednisone.
- Patients should be informed that ZYTIGA must not be taken with food and that no food should be consumed for at least two hours before the dose of ZYTIGA is taken and for at least one hour after the dose of ZYTIGA is taken. They should be informed that the tablets should be swallowed whole with water without crushing or chewing. Patients should be informed that taking ZYTIGA with food causes increased exposure and this may result in adverse reactions.
- Patients should be informed that ZYTIGA is taken once daily and prednisone is taken twice daily according to their physician’s instructions.
- Patients should be informed that in the event of a missed daily dose of ZYTIGA or prednisone, they should take their normal dose the following day. If more than one daily dose is skipped, patients should be told to inform their physician.
- Patients should be apprised of the common side effects associated with ZYTIGA, including peripheral edema, hypokalemia, hypertension, elevated liver function tests, and urinary tract infection. Direct the patient to a complete list of adverse drug reactions in PATIENT INFORMATION.
- Patients should be advised that their liver function will be monitored using blood tests.
- Patients should be informed that ZYTIGA may harm a developing fetus; thus, women who are pregnant or women who may be pregnant should not handle ZYTIGA without protection, e.g., gloves. Patients should also be informed that it is not known whether abiraterone or its metabolites are present in semen and they should use a condom if having sex with a pregnant woman. The patient should use a condom and another effective method of birth control if he is having sex with a woman of child-bearing potential. These measures are required during and for one week after treatment with ZYTIGA.
blind to their own body. Factors that influencing this mode include financial and social pressures on men to provide, the fear of stopping to deal with health, and the fear of losing their role as provider. There is also a preference to control their body and write their own health script.

**Controlled intervention** describes a health care mode where men are scared or shocked into a period of controlled health intervention. Underlying factors include facing the health consequences of personal actions or seeing the decline of someone who is closely connected. This can create a “window of change” where intervention or behavior modification is considered.

**Balanced care** describes a health care mode in which men have the soft skills, protective habits, and social support they need to deal with their health in a balanced and proactive way. The factors influencing this health mode include having healthy male role models, degree of personal conscientiousness, and access to medical and lifestyle support. There is also a social stigma, or sense of emasculation, associated with men caring about their health that can act as a barrier.

**Delegating or sharing responsibility** indicates men’s tendency to either delegate health decision-making or learn to enjoy and share health responsibility with women. Factors influencing this health mode include whether men were taught and enjoyed the soft skills associated with health care when growing up, the extent to which women assume the role of caregiver in their life, and resistance by society to changing these gender roles.

Identifying which mode, or modes, a man aligns with can be leveraged into strategic marketing or messaging opportunities (Morphological Psychology and its Potential for Derivation of Requirements from Web Applications using Examples of Customer Self Care Instruments. In: Application Management. Wiesbaden, Germany: Springer-Verlag; 2011) and allows for the possibility of customizable, targeted health (“precision”) messaging and communication that is optimized to his personal and specific needs. These findings offer the potential to improve on and expand the current framework for men’s health promotion.

**Application to patient care**

What does this have to do with everyday urology and the care of male patients?

As leaders and advocates for men’s health “beyond the penis and the prostate,” urologists have an opportunity to lead a globally expanding men’s health movement. Because so many men will see a urologist as the first portal of entry into their health care world, this presents a unique opportunity to advise them about general preventive health, personal risk factors, environmental issues, healthy lifestyle modifications, general screening issues, and proactive recognition of symptoms (www.dontchangemuch.ca).

It has been estimated that 70% of chronic diseases in aging men are preventable by modifying risk factors, including tobacco smoking, physical inactivity, poor diet, obesity, and alcohol abuse. As a profession, we are facing both the challenge and the opportunity to begin the health conversation with our male patients and their partners. The six health care modes provide an initial framework for communicating with men most effectively—in a precise, personalized manner—about improving their health.

**Conclusion**

The potential to develop a men’s health program in our urology practices is real. Building on the expertise we currently have, we can become global leaders in the field and develop a strong model of care, awareness, education, and research. We need to work with our institutions and government leaders to coordinate a system that will better understand men’s attitude toward health, invest in male-sensitive approaches to health care provision, initiate health care education early on in life for boys and young men in schools and diverse communities, and develop coordinated health and social policies based on the best available standards of care to promote men’s and boys’ health.
BPH counseling: Can you charge a level III visit?

TREATMENT-CENTERED DISCUSSION WITH PATIENT CONSIDERED ‘SEPARATELY IDENTIFIABLE’

Q A patient was seen in the office with a UTI, problems with urination, and a history of gross hematuria. The patient was treated with an antibiotic, a computed tomography scan was ordered, and a cystoscopy was scheduled. On the return visit, the patient was told that the urine culture was negative and the CT scan was normal. A cystoscopy was performed and the patient was found to have BPH with significant obstruction. The problem of BPH and the potential treatment were discussed, including the urologist’s recommendation for a laser prostatectomy. A total of 25 minutes was spent in counseling the patient. The doctor wants to charge a level III established patient visit. I’ve tried to tell her that the E&M is included in cysto, but she won’t believe me because she’s heard you say she could charge. Please help.

A Your doctor is correct. Since the discussion was on the “treatment” of the disease process and not merely a discussion of the findings of the cystoscopy, that service would be considered “separately identifiable.” The time spent was well documented and certainly should be considered “significant.” Therefore, the encounter meets the definition of the −25 modifier: “Significant, Separately Identifiable Evaluation and Management Service by the Same Physician on the Same Day of the Procedure or Other Service,” and should be charged separately.

The time spent was 25 minutes, which is closer to a level IV (30 minutes) than a level III (15 minutes), and since the times are average times and not threshold times, the appropriate charge would be:

- 52000
- 99214–25.

Q What is the procedure code for bladder hydrodistention under moderate sedation?

A There is no specific code for bladder hydrodistention under moderate (conscious) sedation. However, there are codes for the dilation of the bladder for interstitial cystitis under general or spinal anesthesia: 52260-Cystourethroscopy, with dilation of bladder for interstitial cystitis; general or conduction (spinal) anesthesia.

There’s also a code for the same procedure under local anesthesia: 52265-Cystourethroscopy, with dilation of bladder for interstitial cystitis; local anesthesia.

If the hydrodistillation was performed because the patient has interstitial cystitis, under moderate (conscious) sedation we would recommend reporting code 52265. If the procedure was performed in a hospital or ambulatory surgical center and the sedation was given by an anesthesiologist, the work would more closely mimic 52260. However, since it specifically states “general or conduction (spinal) anesthesia,” a −52 modifier would be required and processing of the claim would result in lower payment, thus our recommendation for 52260. (We are assuming the local anesthesia is used in addition to the sedation.)

If the service was provided for another disease, we would recommend 51700-Bladder irrigation, simple, lavage and/or instillation or 53899-Unlisted Procedure. None of the codes listed include moderate (conscious) sedation according to CPT guidelines. Therefore, depending upon payer rules, you may report codes 99143-99149 depending on who provided the sedation monitoring and the amount of time spent.

Q Please provide advice on the CPT codes used for the re-positioning of a ureteral stent by a radiologist.

A We would need to know the details of the procedure in order to specifically answer your question.

There is no specific CPT code for repositioning of a ureteral catheter by a radiologist. However, there are several CPT codes to be used by radiologists for inserting and/or removing ureteral catheters, depending on the specific work performed:

- 50386: Removal (via snare/capture) of internally dwelling ureteral stent via transurethral approach, without use of cystoscopy, including radiological supervision and interpretation
- 74480: Introduction of urethral catheter or stent into ureter through renal pelvis for drainage and/or injection, percutaneous, radiological supervision and interpretation.

You ask specifically for CPT codes; therefore, we assume that you were not asking for billing advice. If that assumption is wrong and you are requesting recommendations for appropriate billing, we would not be able to give that advice without knowing your specific payer billing rules and the documentation developed to support the service rendered.
Social media: Why you need to be involved

Interactive platforms can extend the physician-patient relationship outside the exam room, improve care

If we asked a group of urologists today to identify the most important impact of technology on their professional lives, the vast majority would probably name the implementation and use of the electronic health record. While physicians have struggled to incorporate information technology in their offices, social media has become more pervasive in general, and more common in health care interactions.

In this article, Nick van Terheyden, MD (aka “Dr. Nick”), explains why you need to be active on social media and how to get started. Dr. Nick is chief medical information officer at Nuance (provider of voice and language technologies for businesses and consumers) and a recognized authority on integration of social media in health care.

Majority of adults using social media
Technology is an integral part of our patients’ lives. According to Dr. Nick, 87% of adults use the Internet, including 50% over age 65; 68% of patients bring a list of questions to their physician visit; and 77% of people seeking health care begin their journey at a search engine. Many patients have formed an opinion of their health care provider before they have even met them.

According to the Pew Research Center, 74% of online adults use social media, including Facebook (71%), Twitter (23%), Instagram (26%), and LinkedIn (28%) (http://ow.ly/Ox33y). Half of all Internet users over 65 are using social media, Pew’s research showed. Yet a 2012 physician survey from Epcrates suggests that only a minority of physicians are engaging their patients in this way (http://ow.ly/Ox3X3).

What is social media? According to Dr. Nick, a working definition is “a platform for interactions where individuals can interact, create, share, obtain, and exchange information and ideas using web-based and mobile technologies to create dialogue between organizations, communities, and individuals.” The main distinguishing feature of social media is that in its most mature form, it is collaborative and group driven.

Social media is used in many industries to build a brand, and health care is no different. Consider these facts: Most people are likely to trust information posted by providers on social media; about half of all consumers say social media is a trusted source of information; and half of all consumers say social media is an important influence on purchasing decisions. Social media has become a critical component of many businesses’ marketing strategies.

Helping physicians thoughtfully treat their patients for over 25 years.

HealthTronics products and services include:
- Lithotripsy services
- Endocare® cryoablation
- Laser equipment rentals
- Microwave ablation
- Surgical nerve monitoring

Established in 1989 and headquartered in Austin, Texas, HealthTronics provides integrated urological and interventional radiology products and services, as well as physician partnership opportunities. The company brings its advanced technology and support systems to health care providers throughout the United States.
Divorce: Understand the federal tax ramifications

Transfers made ‘incident to divorce’ not subject to federal income or gift tax

Q: In the event of a divorce, does it matter which marital assets are used for an equitable division?

A: When anticipating a divorce, it’s important to understand there are often major financial consequences and some important tax issues that need to be addressed.

The general rule is that the division of property, including cash, between divorcing spouses has no immediate federal income tax or federal gift tax consequences. Section 1041(a) of the Internal Revenue Code generally mandates tax-free treatment for transfers between spouses of real estate, personal property, investments held in taxable accounts, business ownership interests, and similar assets both before the divorce and at the time the divorce becomes final. Such transfers are considered gifts between spouses. As such, no federal income tax or federal gift tax is due.

This same tax-free treatment also applies to post-divorce transfers between ex-spouses if they are made as an “incident to divorce.” Transfers incident to divorce mean those occurring within 1 year after the date the marriage is dissolved, or 6 years after that date, as long as the transfers are made pursuant to a divorce or separation agreement.

When a transfer falls under the tax-free transfer rule, the spouse (or ex-spouse) who receives the asset takes over the existing tax basis in the asset. The spouse who ends up owning appreciated assets (fair market value in excess of tax basis) must recognize taxable income or gain when those appreciated assets are sold (unless some exception applies, such as the exclusion for gain on sale of a principal residence). When one spouse ends up with 50% of the couple’s assets in the form of cash while the other person ends up with 50% in the form of appreciated assets, a future tax liability will occur once sold. For this reason, divorce property settlements should be based on “net-of-tax values” defined as the fair market value of assets reduced by any built-in tax liabilities.

Under the tax-free transfer rule, divorcing spouses can usually make tax-free transfers of investments held in taxable accounts while they are still married or when the divorce becomes final. The same is true for post-divorce transfers between the parties, provided they are made as an “incident to divorce.” Keep in mind that after a tax-free transfer is completed, the recipient spouse’s tax basis in the investment is the same as before and so is the holding period.

The individual who winds up owning appreciated investment assets will ultimately owe the built-in tax liability that comes attached to those investments. So from a net-of-tax point of view, appreciated investments are worth less than an equal amount of cash or other assets that have not appreciated.

General care is required for any post-divorce transfers of appreciated assets to an ex-spouse. Such transfers are tax free only if they are considered incident to divorce. Within 1 year after the divorce, transfers automatically pass this test. For a later transfer to be considered as an “incident to divorce,” it must be shown that the transfer is related to the cessation of the marriage. This generally means the transfer must occur within 6 years of the divorce and be required under the divorce property settlement agreement (including any post-divorce amendments to the agreement).

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The individual who winds up owning appreciated investment assets will ultimately owe the built-in tax liability that comes attached to those investments. So from a net-of-tax point of view, appreciated investments are worth less than an equal amount of cash or other assets that have not appreciated.

Special care is required for any post-divorce transfers of appreciated assets to an ex-spouse. Such transfers are tax free only if they are considered incident to divorce. Within 1 year after the divorce, transfers automatically pass this test. For a later transfer to be considered as an “incident to divorce,” it must be shown that the transfer is related to the cessation of the marriage. This generally means the transfer must occur within 6 years of the divorce and be required under the divorce property settlement agreement (including any post-divorce amendments to the agreement).

If you plan to transfer appreciated assets to your ex-spouse more than 1 year after the divorce, the divorce papers should clearly identify such transactions as being part of the property settlement. Otherwise, you could be treated as making a taxable sale or a gift to your ex-spouse. This could result in a tax bill or it could reduce your $5.34 million federal gift tax exemption for 2015 (up from $5.34 million in 2014).

In addition to the overwhelming emotional impact, divorce is a major and often complicated financial transaction. As such, it has serious tax implications and potential tax pitfalls. Planning ahead is critical to getting good tax results, as is the importance of seeking competent legal and tax advice.

Joel M. Blau, CFP, Ronald J. Paprocki, JD, CFP, CHBC

Joel M. Blau, CFP, is president and Ronald J. Paprocki, JD, CFP, CHBC, is chief executive officer of MEDIQUS Asset Advisors, Inc. in Chicago. They can be reached at 800-883-8555 or blau@mediqus.com or paprocki@mediqus.com.

Money Matters

Social media would impact their decision to seek a second opinion; social media can be an educational tool working 24/7; and 41% of consumers say they would use social media to select a physician. Dr. Nick says best practices in social media for health care providers include:

- fostering a culture of openness and listening
- training staff on how to post, tweet, and blog
- transparency
- accuracy
- creating a specific policy in your practice for social networking.

Getting started

How do you get started? According to Dr. Nick, one place to start is by “spectating”: read blogs, online forums, and reviews. See what patients and others are saying. Next, create and maintain a profile on a social media site. While many urologists may be wary of jumping into Facebook or Twitter for professional use, LinkedIn—the business version of Facebook—is a social media platform built for professionals and a great place to get your feet wet. It can be your business storefront, and allows you to link to groups, blogs, and presentations.

From there, your adoption should become participatory: Join a group, vote or “like” websites or posts, tag online content, post comments on listservs or blogs, post ratings, and finally, publish your own blog or upload your own video. There is no training program—social media participants learn as they go.

Mayo Clinic offers a textbook example of social media in health care, according to Dr. Nick. The organization maintains multiple Facebook properties to connect providers, patients, and even the media. With over a million followers on Twitter, Mayo Clinic reaches a broad audience instantly; faculty and patients connect with blogs; and YouTube is used extensively for education and awareness. These are the contemporary tools of mature health care organizations used to attract, retain, and build a loyal base of patients and other stakeholders.

Bottom line: Social media is growing in health care. High deductibles and consumerism in health care are likely to drive even further adoption as patients “shop” using social media. As Dr. Nick points out, social media has the potential to extend the physician-patient relationship outside the exam room, and even improve care.

For more examples of social media in mature form, follow Dr. Nick at http://drnick.vanterheyden.com.
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ICD-10, quality initiatives present hurdles, solutions

Urologists praised the demise of the sustainable growth rate formula earlier this year, but a number of hurdles remain. In this interview, William F. Gee, MD, who began his term as AUA president in May, discusses current challenges facing the AUA and its members, possible solutions, and novel new AUA initiatives. Dr. Gee is clinical professor of surgery (urology), voluntary faculty, at the University of Kentucky College of Medicine and emeritus urologist at Commonwealth Urology, Lexington, KY.

Q: What are the challenges facing AUA members that you see as most important this year?

A: We have different layers of challenges, and I think one of the biggest challenges facing all urologists is the same one facing all physicians in United States: the change in our coding system to ICD-10. For over 20 years, we have been using ICD-9, but on Oct. 1, the change-over to ICD-10 will happen, and that will affect all practices, large and small. Physicians who are in large practices and academic practices may be more equipped to deal with this. Regardless, we have been told that if you don’t use the proper code, whether it’s for an office visit or a procedure, you may not get paid. This is of concern not only to urologists, but to all physicians.

The AUA has worked to help our members adapt to the new system by offering helpful tips and training courses. Many specialties including the AUA are opposed to switching to ICD-10, but it is going to happen, so we need to be realistic and prepare for it.

Another challenge that urologists face is the increasing demand for our services without an increasing number of urologists. The number of urologists entering the field annually has been relatively stable for the last 18 to 20 years (about 245 to 260 per year). At the same time, 10,000 Americans turn age 65 every day, and many of these individuals will be needing services from urologists in the coming years.

Q: Another challenge that a lot of urologists talk about relates to quality initiatives. Please discuss the new registry the AUA has started that hopefully will help members address these initiatives.

A: The AUA recognized several years ago that in the era of “big data,” it would be useful to establish a database to house information about outcomes. Such outcomes data will de-identify patient-specific data, come back to the practice, and re-identify it after some of the information has been extracted.

Q: As I understand it, the registry software will de-identify patient-specific data, come back to the practice, and re-identify it after some of the information has been extracted.

A: Correct, and the outcomes data will be available first to the physician whose patient it belonged to. The individual doctor will be able to compare his or her outcomes to those of other physicians in the practice, whether it’s a large urology group, a smaller group, or university system. It will then allow comparisons to physicians all over the United States. The data will look at factors that influence prognosis and quality of life, assess the effectiveness of treatments and their safety, measure the quality and cost of care, and as I mentioned, allow urologists to compare themselves with their peers. As of June 30, over 50 practices have enrolled in AQUA. Every urologist should go to the AUA website and read about how to enroll their practice with AQUA.

Q: What do you consider some of the major goals you hope to accomplish in the coming year?

A: The president of the AUA is just one individual who works with a large, very strong team comprised of AUA staff led by Executive Director Michael Sheppard, and a wonderful group of physicians who volunteer their time to the AUA Board of Directors and to the AUA’s many different committees. My goal is to help facilitate
the work of these individuals and groups and do what I can to ultimately serve the needs of the members. The AUA is here to help our members deal with their challenges and advance the specialty of urology; I hope to be able to facilitate that.

Q: We know that research is a very important part of the AUA mission. I hear there has been a huge expansion of the AUA Research Scholars Program this past year.

A: That’s correct. We want to continue to encourage young investigators in their work, which is why the research pillar of the AUA has evolved so much in the past decade. The most recent major change was the rebranding of the AUA Foundation as a philanthropic organization now called the Urology Care Foundation. A primary focus of this organization is to generate funding to support and ignite the careers of our young scientists through the AUA Research Scholars Program. These awards are designed to encourage young urologists and some PhDs to become interested in either basic science or clinical research.

This has been expanded greatly through a program that the AUA developed in partnership with the AUA sections a couple years ago. The AUA decided that, if an AUA section would donate $250,000 in funding, the AUA would do a 5:1 match of $1.25 million, which would mean an endowment total of $1.5 million per scholar.

Since the program was completed in December 2014, the number of scholars has increased from 14 to 27. In addition to section scholars, some research scholars are sponsored by industry partners, such as Astellas, and several scholarships are named after individuals who made substantial contributions. The Urology Care Foundation now has an endowment of over $40 million and, in 2015, will use approximately $1.3 million to support scholars.

Also, the AUA also has a new research chair, Dr. Aria Olumi from Harvard, who has presented a lot of good ideas. He succeeds Dr. Johannes Vieweg.

Q: You mentioned one personnel change in the Office of Research. Can you talk about other leadership changes that have occurred at the AUA recently?

A: Yes, we had a number of big changes in the past year. We have a new chair of education, Dr. Victor Nitti, of the New York University Langone Medical Center. Dr. Nitti, as many people know, has been very active in work with urinary incontinence and female urology. He succeeds Dr. Elspeth McDougall in this position.

The Board of Directors also named a new editor of The Journal of Urology, Dr. Jay Smith of Vanderbilt University Medical Center. Dr. Smith will be working to make some changes in terms of how the journal is presented online and taking into consideration the different ways of communicating with urologists.

The AUA also has a new secretary, Dr. Manoj Monga, who succeeds Dr. Gopal Badlani. Dr. Monga practices at Cleveland Clinic, where he is director of the Stevan B. Streem Center for Endourology & Stone Disease.

Q: There was also a change on the international education side, correct?

A: Yes. There is an increasing demand for our educational courses and products around the world. In fact, urologists from over 100 countries attended the 2015 AUA annual meeting. The AUA has formed relationships with a number of countries—in particular, China, Japan, India, and Brazil—and some other less-developed countries that are very hungry for our education.

For the last few years, the AUA secretary has been the point person for forming relationships with representatives from these countries, but this has become a unique portion of what the AUA does. So the AUA created a new position called the chair of Global Initiatives, and filling that position is Dr. Inderbir (“Indy”) Gill of the Keck School of Medicine of the University of Southern California. Dr. Gill is not only well known to U.S. urologists for his important contributions to endourology, but in many other countries around the world.

Q: You are known for your strong background in advocacy. This year, many AUA members will consider the elimination of SGR a big win for us. What are some of the other advocacy challenges on the horizon for AUA members?

A: Another issue that has become front and fore, not just with the AUA but with other physician organizations, is the Independent Payment Advisory Board or IPAB, which the AUA opposes. We have heard this referred to as a “death panel,” which I think is probably too strong of a phrase.

The IPAB, part of the Affordable Care Act that was passed 6 years ago, would be a board of about 15 physicians and other individuals tasked with achieving savings in the Medicare program; if Medicare spending exceeds targets, the IPAB would be triggered and would have the authority to make changes to payment rates and program rules to rein in spending. Congress has the power to overrule the IPAB, but only by a supermajority vote.

The physician community has objected to this since it was first announced. Now, a new bill, H.R. 1190, the Protecting Seniors’ Access to Medicare Act, has been introduced that would effectively block the IPAB. And the momentum seems to be moving in the right direction among our legislators. On June 23, the House approved H.R. 1190 by a vote of 244-154, with both Republicans and Democrats supporting it. I would not be surprised to see repeal of the IPAB in the next year or two.

Q: What other advocacy issues is the AUA currently working on?

A: Another important issue is reform of the U.S. Preventive Services Task Force (USPSTF). Urologists are all familiar with their decision to give the PSA test a “D” grade for prostate cancer screening, which means insurance companies have the option not to pay for it. They have made a number of other unpopular decisions.

The AUA has tried unsuccessfully to have the USPSTF at least consult with the appropriate specialty before issuing a recommendation. The task force consists basically of statisticians, people with expertise in public health, and some primary care physicians. They choose their own members.

There is a bill in Congress, the USPSTF Transparency and Accountability Act of 2015, which would create more transparency of the USPSTF and ensure that key stakeholders are involved in developing and reviewing USPSTF recommendations.

The AUA also continues to oppose any changes to the in-office ancillary services exception, which allows physicians to provide certain services, such as advanced imaging, in their offices.

Q: I understand the AUA and American Board of Urology (ABU) leadership are working together to make maintenance of certification as user-friendly as possible. Would you care to comment?

A: We are all committed to lifelong learning; that’s what makes medicine exciting and interesting to many of us. But maintenance of certification (MOC) is a real concern to many urologists, and I understand that the ABU is working to possibly make some changes in MOC. We will have to wait and see what they have to say.
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USPSTF continued from page 1

is trending downward (see, “New data show shifts in PSA screening”).

At the ASCO meeting, a study conducted by researchers at Case Western Reserve University in Cleveland analyzed private health insurance claims data (Optum Labs Data Warehouse) from 2008 to 2013 for men ages 40 to 80 years. It identified 11.6 million men who met eligibility criteria for inclusion in the study, of whom 2.9 million (25%) underwent PSA screening. Men ages 50-59 years represented the plurality (~43%), while just over 20% of the men were 40-49 years of age and just under 20% were in the 60-64 year age bracket. The analyses showed PSA screening rates fluctuated monthly throughout the study period.

However, between 2008 and 2013, there was no significant change in the rate of men undergoing PSA screening for the overall population (190.4/1,000 member-years vs. 196.4/1,000 member-years) or when stratifying men by age (40-49, 50-59, 60-64, 65-69, and 70-74, and 75-80 years), except in the oldest cohort. Among men ages 75-80 years, the PSA screening rate was almost 50% lower in 2013 than in 2008 (124.1/1,000 member-years vs. 201.5/1,000 member-years), although the decline really occurred by 2010, and the PSA screening rate was stable thereafter.

“By showing no appreciable drop in PSA screening for men who should be considered for screening, meaning those 55 to 69, but a significant drop in the advanced age group, our findings could be considered good news that we are not screening older men who are unlikely to benefit,” said Simon P. Kim, MD, MPH, assistant professor of urology at Case Western Reserve University School of Medicine.

**Significant decline in men ≥50 years**

In contrast, investigators using self-reported data on PSA screening from men ages 40 years and older who participated in the 2010 and 2013 National Health Interview Survey found screening significantly declined from 2010 to 2013 among all subgroups of men ages 50 years and older. The study was presented at the ASCO annual meeting and published online in the Journal of Clinical Oncology (June 8, 2015).

First author Michael W. Drazer, MD, noted the findings are consistent with those emerging from studies based on more limited populations, including one using data from a regional health system in Chicago. Most striking to Dr. Drazer and colleagues, however, was their finding that the absolute declines in PSA-based screening were bigger in the 50-59 and 60-74-year subgroups (33.2% to 24.8% and 51.2% to 43.6%, respectively) than in men ages 75 years and older (43.9% to 37.1%). In addition, they were disappointed by the fact that in 2013, more than one-third of men ≥75 years of age and nearly the same proportion of men age ≥65 years with a high predicted risk of 9-year mortality (defined as ≥52% calculated with an externally validated index) had PSA screening.

“Work from researchers at the University of California, San Francisco showed that the USPSTF recommendations have the strongest influence on PSA screening ordered by primary care physicians [Prostate Cancer Prostact Dis 2012; 15:189-94], and our findings are consistent with that information,” said Dr. Drazer, an internal medicine resident at the University of Chicago Medical Center, Chicago.

“Unfortunately, our findings are the opposite of what we hoped to see, which is that men who are less likely to benefit from early detection of prostate cancer because they are advanced in age and less healthy would be screened less often than younger, healthier men. In our study, 1.4 million men at high risk of dying with prostate cancer but not from it underwent PSA screening in 2013,” said Dr. Drazer, who worked on the study with Scott Eggener, MD, and Dezheing Huo, MD, PhD.

In a study published in 2012 that used the same methodology, Dr. Drazer and colleagues found no evidence that the 2008 USPSTF recommendations affected prostate cancer screening rates (JAMA 2012; 307:1692-4).

**Self-reported data a limitation**

Dr. Drazer said that their studies have limitations associated with use of patient self-reported data. However, he noted that patient recall of PSA screening has been shown to be reasonably reliable, and responses from survey participants on PSA screening were only included in the analysis if the man first correctly answered a question asking if he knew what a PSA test was.

On the other hand, Dr. Drazer mentioned there is evidence that physicians don’t discuss PSA screening with patients in a way that would support the accuracy of self-reported information.

“A man’s knowledge of his PSA screening probably depends on his having the right discussion with his physician. However, we recently published research showing that a lot of men are not having this conversation,” he said, citing a study appearing in Cancer (2014; 120:1491-8).

“Overall, it seems there needs to be a lot of improvement in patient and physician education on PSA screening.”

Discussing the strengths and limitations of the Case Western research, Dr. Kim told Urology Times that the study is novel because it provides a look at PSA screening 1 year after the 2012 USPSTF recommendations in a nationwide population of privately insured men, including a large sample of “younger” men who are most likely to benefit from screening. However, he acknowledged it is subject to the limitations of using insurance claims data. Furthermore, the analysis is based on a single private payer’s database and it cannot be assumed that its findings reflect screening rates for men in other insurance plans.

“It will be important to look again in a few years using more contemporary data and to investigate this question in other patient populations,” Dr. Kim said.

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New data show shifts in PSA screening

A recently published paper and studies presented at the 2015 AUA annual meeting suggest the rate of prostate cancer screening is falling.

- Vanderbilt University investigators reported that new diagnoses of prostate cancer in the United States declined 28% in the year following the USPSTF’s draft recommendation against routine PSA screening. The research appears online in the issue of Journal of Urology (June 15, 2015).

- A study presented at the AUA annual meeting focusing on PSA utilization by primary care providers at Oregon Health & Science University found a significant 50% decrease in PSA testing since the release of the 2012 recommendation. Also at the AUA, a survey of primary care providers from the University of Massachusetts showed 75% have changed their PSA practice patterns based on the recommendation; and a study from Henry Ford Hospital found that although African-American men were more likely to undergo PSA screening than Caucasian men, only six U.S. states had higher rates of screening in the African-American population relative to Caucasian men.

For a video report on the AUA abstracts, visit www.urologytimes.com/PSA-video.
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¹ Roehrborn, Urology Practice 2015 2-Year LIFT Study
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> In a prospective study, obesity was significantly associated with high-grade and metastatic disease in men with clinically localized prostate cancer.

> Current metformin use was associated with a significantly decreased risk of prostate cancer in a nested case-control study.

> In a meta-analysis of 18 studies, testosterone replacement therapy for symptomatic hypogonadism did not increase levels of PSA nor the risk of prostate cancer development.

> Metformin use was associated with a significant survival advantage among diabetic veterans with prostate cancer.

> Magnetic resonance fusion targeted biopsy reduces the detection of indolent disease while significantly improving the detection and risk stratification of high-grade prostate cancer.

> Positive [11c]choline positron emission tomography/computed tomography after biochemical failure predicts prostate cancer survival in hormone-naïve prostate cancer patients.

> Combining urine PCA3 and TMPRSS2:ERG tests can enhance detection of high-grade prostate cancer. When sensitivity was set to 95%, the specificity improved to 39%, avoiding 49% of unnecessary biopsies. In a validation cohort, specificity was improved to 33% while retaining high sensitivity (93%).

> Combined risk scoring based on epigenetic profiling of GSTP1, APS, RASSF1, and histopathology is strongly correlated with the detection of aggressive prostate cancer upon repeat biopsy.

> The 17-gene Genomic Prostate Score (GPS) assay may improve risk stratification for men with newly diagnosed prostate cancer who are candidates for active surveillance.

> For prostate cancer patients considering deferred treatment, the combined clinical cell cycle risk score provides significant prognostic information at disease diagnosis.

> The 4Kscore maintains good discrimination for risk of high-grade prostate cancer in a subpopulation of men with PSA ≤4.0 ng/mL, with a sensitivity of 95% and a specificity of 56%.

> Homogeneous PTEN loss is associated with decreased time to biochemical recurrence; this effect is much stronger in ERG-negative tumors than in ERG-positive tumors.

> Hybrid PET and magnetic resonance imaging may be advantageous in men with PSA <1.0 ng/mL by increasing diagnostic certainty.

> 68Ga-HBED-prostate-specific membrane antigen/PET hybrid imaging has a high sensitivity and superb specificity and accuracy for lymph node staging in intermediate- to high-risk patients with prostate cancer, and may replace current standard imaging in the future.

> Even in the context of node-positive prostate cancer, patients may have long-term survival after radical prostatectomy and extended pelvic lymph node dissection.

> In a single-institution review of 1,131 patients who qualified for active surveillance, 51% were found to have an upgraded Gleason score. Patients should be provided appropriate education and counseling about the risk associated with active surveillance.

> African-American men had similar functional outcomes after robotic prostatectomy as non-African-Americans, but African-Americans were slower to recover continence and less likely to achieve “tri- secta” status.

> Metabolic syndrome is associated with an increased risk of extraprostatic and high-grade disease on final RP pathology, and an increased need for salvage therapy. However, with more aggressive resection, similar failure-free outcomes can be achieved in well-selected patients.

> Intermittent androgen deprivation (ADT) may be a valid option for select patients with locally advanced prostate cancer or relapsing M0 prostate cancer.

> Results from the SEARCH database show an overall survival benefit for men with biochemical recurrence after radical prostatectomy if ADT is initiated before PSA reaches 10.0 ng/mL. This benefit is stronger when ADT is initiated before PSA reaches 5.0 ng/mL. The survival benefit of ADT, however, must be weighed against long-term side effects.

> Sipuleucel-T (Provenge) plus ADT show durable effects.

> Inhibition of pericyte function with an anti-platelet-derived growth factor receptor beta-blocking antibody induced deterioration of erectile function in normal mice.

> Alpha-adrenergic modulation improved erectile function after bilateral crush cavernosal nerve injury in rats.

> A vascular leakage blocker (SAC-1004) restored erectile function in a chemically induced mouse diabetes model.

> Gene expression profiling suggests distinct molecular subtypes of BPH driven by differences in androgen gene regulation.

> BPH expresses higher levels of ligand-independent Arv7 than normal prostate, which has implications for treatment with 5-alpha-reductase inhibitors.

> Whole exome sequencing identified NPS2 mutations in a family with nonobstructive azoospermia.

> A subset of infertile patients carries the G7SC polymorphism in FGAM4, an X-linked re trogene.

> Antioxidant supplementation during cryopreservation improves post-thawing sperm parameters.

> Decelularized colon represents a potential natural collagen scaffold for bladder replacement.

> Bioprinting of human urethra with stem cells can be done without the need for scaffold.

> ERG fusions are less frequent in the index tumors of African-American men compared with Caucasians.

> ERG overexpression is uncommon in anterior tumors, meaning that tumor genotype may be driven in part by its microenvironment.

> GI3 can bind and co-activate androgen receptor signaling.

> ERG transcription factor regulates the expression of the androgen biosynthetic enzyme AKR1C3.

> Loss of DAB2IP potentiates tumor cell growth and reprograms the expression of steroidogenic enzymes.

> SPOP mutation sensitizes prostate cancer cells to DNA-damaging agents such as PARP inhibitors.

> Small molecule inhibition of ERG with YK-4-279 inhibits tumor growth in patient-derived prostate cancer xenografts.

> sSD70, a KDM4 histone demethylase inhibitor, synergizes with approved medications for castration-resistant prostate cancer.

> Estrogen receptor alpha inhibits the development of bladder cancer using a carcinogen-induced tumor model.

> Vimentin and plectin play a role in the stability of invadopodia, which promotes cancer cell invasion.

> Aldo-keto reductase 1C1 expression is high in metastatic bladder cancer sublines, supporting a role in invasion.

> Long noncoding RNAs have been implicated in bladder cancer proliferation, invasion, and maintenance of self-renewal in bladder cancer stem-like cells.
Adipose tissue-derived factors can promote bladder cancer migration.

Exosomes from bladder cancer cells can induce epithelial-mesenchymal transition in recipient urothelial cells.

Targeted sequencing demonstrated that bladder tumors following radical nephroureterectomy are true recurrences as opposed to de novo tumors.

Novel targets identified from high throughput screening include an androgen receptor antagonist, mTORC1/2 inhibitor, and an FGFR inhibitor.

Pooling DNA from multiple tumor regions accurately profiles a renal tumor’s genetic landscape.

Loss of DNA 5-hydroxymethylcytosine in clear cell renal cell carcinoma (RCC) has a potential role in the hypermethylation phenotype.

Aggressive chromophobe RCC showed enrichment for TP53 mutation in 70% and PTEN loss in 45%.

PI3kteta Inhibitor TGX221 selectively inhibits clear cell RCC with VHL and SETD2 mutations.

Overexpression of Mps1 in ccRCC confers tumor selectivity of heat shock protein 90 inhibitors.

Infection/Inflammation

Presented by Majid Mirzazadeh, MD,
Wake Forest University Health Sciences, Winston-Salem, NC

PP1alpha gene therapy could be a novel treatment of overactive bladder/hypersensitive bladder disorders and interstitial cystitis (IC)/bladder pain syndrome (BPS).

A randomized controlled trial demonstrates that subcutaneous tanezumab is a promising therapy for female patients with IC/BPS.

A single intravesical injection of botulinum toxin A (Botox) is effective to reduce bladder pain symptoms in patients with IC/BPS.

Preliminary results from a 15-patient study indicate that a single intravesical instillation of 2.00 U of botulinum toxin A premixed with 40 mL of reverse-thermal gelation hydrogel has efficacy for weeks in the treatment of painful bladder syndrome/IC.

Late-onset hypogonadism was significantly correlated with the presence and severity of prostatitis-like symptoms.

Testosterone replacement therapy (TRT) can improve clinical symptoms, quality of life, and psychological status in hypogonadal patients affected by chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS).

Installation of fecal microbiome of IC patients into rats induced bladder pain behavior. Specific taxa may modulate IC symptoms and represent novel biomarkers for diagnosis.

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rate of complications and infection-related hospitalizations, without an increase in irritating symptoms.
> A correlation exists between the duration of catheter use and fibrinogen deposition, which may explain why prolonged catheterization leads to more UTIs than CIC.

> In a retrospective cohort study of 44,292 men with prostate cancer, active surveillance (AS) was frequently applied and the rate seemed to increase over time, from 26.4% in 2002 to 36.0% in 2010. About 62% of men on AS eventually moved on to definitive treatment.

> Future diagnostic/therapeutic approaches for neurogenic bladder may involve the manipulation of the microbiome.

> Actinobaculum may contribute to lower urinary tract symptoms.

> Transcutaneous near-infrared spectroscopy system optical monitoring of an absolute measure of bladder wall oxygenation may offer a means of screening for diagnosis of UTI.

> A biosensor array consisting of 16 sensors, each capable of detecting specific bacterial 16S rRNA, reduces the time of pathogen identification and minimum inhibitory concentration from 2 or 3 days to 6 hours.

> Factors associated with a higher risk of recurrent infections after surgical stone extraction included African-American race, males with type 2 diabetes, and hypertension. Patients undergoing percutaneous nephrolithotomy were more likely to be rendered infection free compared to shock wave lithotripsy.

> Concentrated cranberry supplementation reduces colony counts and prolongs the time to symptomatic UTI in patients with neurogenic bladder dysfunction who are dependent on self-catheterization.

> Current smokers remain at increased risk of readmission following radical cystectomy.

> Among 47 cases of stent and urine culture in patients with neurogenic bladder dysfunction, the couple desires to have, obstructive interval from the time since vasectomy, costs involved with vasectomy reversal of intracytoplasmic sperm injection (ICSI), long-term safety of ICSI, concerns of the couple, and their religious beliefs.

> The reported risk of aggressive and potentially lethal prostate cancer in men who undergo vasectomy is modest, and there is no plausible biologic link.

> Men with azospermia have a greater risk of cancer compared with men with sperm in ejaculate.

> Men with ≥2 abnormal semen parameters have a greater risk of mortality compared with men with ≤1 abnormal semen parameter.

> Up to 40% of men with normal semen parameters can display significantly elevated levels of sperm aneuploidy.

> The evidence for medical therapy for idiopathic male infertility remains empiric. Controlled trials with clearly defined outcomes are needed before medical therapy can be used routinely for the management of male infertility.

> Enolcumine citrate does not significantly affect sperm density, whereas gel-induced TRT decreases sperm density.

> LPCN 1021, a novel oral TRT, maintains testosterone levels in the eugonadal range, with a mean C_{10} of 447 ng/dL and mean C_{100} of 1.128 ng/dL. Some 85% of hypogonadal men required one titration or fewer.

> Testosterone studies have numerous obstacles (ie, the number of levels drawn, time at which they are drawn, laboratories with different normal ranges, assay variability) that must be considered when analyzing and interpreting results.

> The appropriate indications for TRT are primary hypogonadism and secondary hypogonadism. Myocardial infarction and stroke are now on the label as possible risks of TRT.

> A study of 217 men shows that TRT appears to be safe, with no excess of thrombotic events, for the treatment of hypogonadism in elderly men.

> There is a need for sexual and reproductive health education, specifically for minority young males.

Only 0.2% of ultrasound procedures performed for pain identified a non-palpable malignant scrotal mass. A cost-benefit analysis is necessary to determine whether scrotal ultrasound should be performed in the management of scrotal pain.

The odds of sperm banking increased threefold in men who received counseling.

Male fertility insurance coverage is disproportionately excluded from state laws.

Factors that should be considered when a patient presents with obstructive azoospermia following vasectomy are the female’s age, number of children the couple desires to have, obstructive interval from the time since vasectomy, costs involved with vasectomy reversal of intracytoplasmic sperm injection (ICSI), long-term safety of ICSI, concerns of the couple, and their religious beliefs.

The reported risk of aggressive and potentially lethal prostate cancer in men who undergo vasectomy is modest, and there is no plausible biologic link.

Men with azospermia have a greater risk of cancer compared with men with sperm in ejaculate.

Men with ≥2 abnormal semen parameters have a greater risk of mortality compared with men with ≤1 abnormal semen parameter.

Up to 40% of men with normal semen parameters can display significantly elevated levels of sperm aneuploidy.

The evidence for medical therapy for idiopathic male infertility remains empiric. Controlled trials with clearly defined outcomes are needed before medical therapy can be used routinely for the management of male infertility.

Enolcumine citrate does not significantly affect sperm density, whereas gel-induced TRT decreases sperm density.

LPCN 1021, a novel oral TRT, maintains testosterone levels in the eugonadal range, with a mean C_{10} of 447 ng/dL and mean C_{100} of 1.128 ng/dL. Some 85% of hypogonadal men required one titration or fewer.

Testosterone studies have numerous obstacles (ie, the number of levels drawn, time at which they are drawn, laboratories with different normal ranges, assay variability) that must be considered when analyzing and interpreting results.

The appropriate indications for TRT are primary hypogonadism and secondary hypogonadism. Myocardial infarction and stroke are now on the label as possible risks of TRT.

A study of 217 men shows that TRT appears to be safe, with no excess of thrombotic events, for the treatment of hypogonadism in elderly men.

There is a need for sexual and reproductive health education, specifically for minority young males.

In a retrospective cohort study of 44,292 men with prostate cancer, active surveillance (AS) was frequently applied and the rate seemed to increase over time, from 26.4% in 2002 to 36.0% in 2010. About 62% of men on AS eventually moved on to definitive treatment.

Future diagnostic/therapeutic approaches for neurogenic bladder may involve the manipulation of the microbiome.

Actinobaculum may contribute to lower urinary tract symptoms.

Transcutaneous near-infrared spectroscopy system optical monitoring of an absolute measure of bladder wall oxygenation may offer a means of screening for diagnosis of UTI.

A biosensor array consisting of 16 sensors, each capable of detecting specific bacterial 16S rRNA, reduces the time of pathogen identification and minimum inhibitory concentration from 2 or 3 days to 6 hours.

Factors associated with a higher risk of recurrent infections after surgical stone extraction included African-American race, males with type 2 diabetes, and hypertension. Patients undergoing percutaneous nephrolithotomy were more likely to be rendered infection free compared to shock wave lithotripsy.

Concentrated cranberry supplementation reduces colony counts and prolongs the time to symptomatic UTI in patients with neurogenic bladder dysfunction who are dependent on self-catheterization.

Current smokers remain at increased risk of readmission following radical cystectomy.

Among 47 cases of stent and urine culture in patients with neurogenic bladder dysfunction, the couple desires to have, obstructive interval from the time since vasectomy, costs involved with vasectomy reversal of intracytoplasmic sperm injection (ICSI), long-term safety of ICSI, concerns of the couple, and their religious beliefs.

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> Low estimated glomerular filtration rate in living kidney donors without other major comorbidities did not have a significant impact on health-related quality of life.
> PSA screening to determine kidney transplant candidacy did not affect overall survival of patients who received kidney transplants, but their survival was significantly reduced by a diagnosis of prostate cancer.
> A review of 17 published series supports the safety of radical prostatectomy in renal transplant recipients as they had similar morbidity compared to the general population of men with prostate cancer.
> Analyses based on data from four major European centers found that renal transplant recipients with nonmuscle-invasive bladder cancer could be safely treated with either mitomycin-C or bacillus Calmette-Guérin. Cancer recurrence rates were similar in the treated patients compared to those who had no treatment, raising the question of whether the recurrence rate was affected by a change after bladder cancer diagnosis to mTOR inhibitor treatment for immunosuppression.
> A review of current evidence suggests renal transplant using kidneys after excision of renal cell carcinoma is safe and feasible in selected patients with end-stage renal disease.
> The risk of prostate cancer in men receiving immunosuppression after solid organ transplantation was significantly increased (29- to 34-fold, depending on ethnicity), but only after 10 years, probably due to the effect of prostate cancer screening prior to transplant.

A survey of transplant surgeons revealed variations in practice patterns for PSA screening and prostate cancer treatment, suggesting a need for developing universal guidelines.

> The United Network of Organ Sharing seems to have attenuated racial disparity in kidney transplantation, but rates of live donations in the United States are still low in African-Americans.
> A meta-analysis showed antiplatelet agents may reduce allograft thrombosis after kidney transplantation, although antiplatelet use alone did not reduce thrombosis risk and was associated with increased bleeding rates.
> Non-simultaneous extended altruistic donor chains were an effective tool for increasing the efficiency of kidney paired donation.
> A systematic PubMed review found that compared with endourologic management, an open approach for treating distal ureteric stricture after renal transplantation had a higher success rate (85% vs. 58%) and fewer complications. The authors also developed a decision-tree diagram to guide management decisions.
> Surgeon experience based on procedural volume correlates with risk of complications after renal transplant, regardless of surgeon specialty.
> Pre-implantation biopsies of kidneys from deceased donors may help to reduce kidney discard rates.
> Reduction of immunosuppression during Clostridium difficile-infectious diarrhea did not increase the risk of graft rejection in kidney transplant recipients.
> Among cytomegalovirus (CMV) seropositive patients who underwent kidney transplantation without CMV prophylaxis, pre-transplant low IgG titer against CMV, being on a potent immunosuppressive protocol, and a high MPA level at 1 month post-transplant were risk factors for developing high-grade CMV reactivation.
> Heat shock protein 90 could be a new biomarker for acute rejection after kidney transplant.
> Vitrification of metanephros showed promise as a technique for biobanking kidney tissue.
> A study investigating the mechanism of allograft rejection after partial lymphocyte depletin suggested a role for strategies that can control T cell proliferation and differentiation during lymphopenia.
> Risk of dyslipidemia after renal transplantation may be influenced by the glucoconorticoid receptor Bcl I G allele.
> Renal vascularization is helpful in preserving renal function in patients with renal artery stenosis due to Takayasu’s aortoarteritis and appears to minimize the need for antihypertensive medications.
> Low-dose intravenous heparin improved kidney-pancreas transplant outcomes by reducing pancreas graft thrombosis and did not increase bleeding risk.
> Routine ureteral stenting in kidney transplantation did not decrease the rate of ureteral complications.
> Resecting the inferior vena cava (IVC) without grafting in patients with advanced urologic malignancies was associated with a 23% rate of deep venous thrombosis and a 36% rate of lower extremity edema, but mitigated complications associated with IVC graft replacement.
> Urologic complications after pediatric kidney transplant occur more often in children who are younger and who have a urologic etiology for end-stage renal disease. Voiding cystourethrogram does not need to be done routinely postoperatively, but can be performed in patients who develop a UTI.

Penile, Testis, and Urethral Cancer
Presented by Makarand Khochikar, MD

Siddhi Vinayak Ganapati Cancer Hospital, Miraj, India

> Management of bulky inguinal lymph node masses in patients with penile cancer remains controversial, but neoadjuvant chemotherapy can be chosen in carefully selected patients.
> Inguinal extranodal extension or having ≥2 inguinal tumor-positive lymph nodes predicted pelvic tumor positivity in penile cancer patients without evidence of pelvic involvement; the 5-year disease-specific survival rate for patients with pelvic involvement treated with surgery alone was only 17%.
> An analysis of Surveillance, Epidemiology, and End Results data found local tumor excision for treatment of early-stage penile squamous cell carcinoma is increasing and was associated with a 4-year penile cancer-specific mortality rate of 9.8%.
> There has been excessive use of imaging in men with low-risk penile cancer.
> Pelvic extranodal extension in penile cancer patients is associated with a worse outcome, but adjuvant chemotherapy may provide a slight survival benefit for these men.
> In vivo optical biopsy using confocal laser endomicroscopy predicted histology, especially carcinoma in situ, in penile cancer patients who subsequently underwent penectomy.
> Among patients with various genitourinary malignancies, those with bladder cancer had the highest suicide rate within the first 5 years after diagnosis and the rate was highest among prostate cancer patients at 15 years after diagnosis. Increasing age, aggressive disease, and Caucasian race were risk factors for suicide.
> Urethra-preserving surgery was shown to be a feasible technique for managing distal urethral carcinoma and carcinoma in situ; there was a positive marginal rate of 33% after primary excision despite frozen sections.
> Among patients with locally advanced primary urethral cancer, use of neoadjuvant chemotherapy/chemoradiotherapy was associated with better survival than surgery followed by adjuvant chemotherapy.
> A history of testicular cancer was associated with an increased risk of intermediate/high-risk prostate cancer.
> Abnormal pituitary-Leydig cell function was present prior to orchectomy in 72% of patients with testicular germ cell cancer; pituitary-Leydig axis dysfunction was most common in patients with non-seminomatous germ cell tumors (NSGCT) or stage III disease.
> In the United States, retroperitoneal lymph node dissection (RPLND) in patients with testicular cancer is being performed more in academic centers than in community or comprehensive cancer centers.
> Rates of RPLND for stage 1 NSGCT decreased significantly between 1998 and 2011 from 23% to 12.9%, while use of primary chemotherapy increased from 20.7% to 32.5%.

Trauma/Reconstruction/Diversion
Presented by Robert C. Kovell, MD, Wake Forest Baptist Medical Center, Winston-Salem, NC

> Practice patterns for the treatment of urethral stricture are changing, with the shift favoring urethroplasty versus endoscopic treatment.
> A review of 91 men treated for anterior urethral strictures found 84% underwent direct vision internal urethrotomy/dilatation without previous imaging, 90% were treated without being counseled about urethroplasty, and 70% had multiple dilations without being informed of urethroplasty.
> Use of a non-transacting anterior urethroplasty technique in patients with short, proximal bulbar strictures
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had a low incidence of side effects and a 97% success rate based on no evidence of stricture recurrence.

> Stricture resolution rates were similar comparing transected and non-transected bulbar urethroplasty for bulbar urethral strictures.

> Cavernosal arterial blood flow was not predictive of the success of pelvic fracture urethral injury repair, but there was a trend for an association between low flow (<25 cc/sec) and increased rate of bulbar necrosis.

> A noninvasive protocol to monitor for stricture recurrence after urethral reconstruction that combines patient-reported outcome measures and uroflowmetry data had a 92% sensitivity and 63% specificity; its use would have allowed nearly 60% of men to avoid unnecessary cystoscopy.

> Experience matters when it comes to success rates of male urethral reconstruction—surgeons reach proficiency (>90% success rates) after performing about 100 urethroplasty cases.

> In a study including data from four centers of excellence, a 91.5% overall success rate was achieved in men who underwent reconstruction of rectourethral fistulas after prostate cancer treatment.

> Initial results are promising for robotic buccal mucosa graft urethroplasty as an approach for managing difficult urethral strictures.

> Readmission rates after treatment of grade 3 and grade 4 renal injuries may be higher than appreciated (18% and 24%, respectively), but these patients can usually be managed conservatively.

> Understanding the epidemiology of concomitant colorectal and genitourinary injuries in armed service personnel is being looked at to guide strategies for injury prevention, initial surgery, and subsequent reconstructive surgery.

> Robotic radical cystectomy with intra-corporal urinary diversion was technically feasible and associated with about the same level of complications as open diversion.

> Researchers reported success with technology to print 3-D organ structures.

Sexual Function/Dysfunction

Presented by Landon Trost, MD,
Mayo Clinic, Rochester, MN

> Results of ultrasound-guided evaluation of erectile dysfunction depend on the anatomic placement of the probe on the penis.

> Vascular risk factors do not predict hemodynamic outcomes.

> Failure to achieve full stretched penile length predicts veno-occlusive dysfunction.

> Use of audiovisual stimulation did not affect total erectile rigidity or number of intracavernosal injections required for treatment.

> De novo Peyronie’s disease occurred in

17.4% of 276 men following radical prostatectomy, suggesting a need to address the issue during preoperative counseling.

> Percutaneous stent revascularization of the internal pudendal artery is safe and appears promising.

> Analysis of eight studies of extracorporeal shock wave lithotripsy for ED showed safety and clinically significant, durable improvement overall and across the individual trials.

> Low-dose extracorporeal shock wave therapy improves erectile function in diabetic rats, and the effect is enhanced with the addition of sildenafil citrate (Viagra). Separately, researchers found that low-intensity pulsed ultrasound improved erections and restored endothelium and smooth muscle in diabetic rats.

> Cultures of clinically non-infected implanted penile prostheses (IPPs) showed a threefold higher rate of positive cultures in uncoated versus coated devices.

> A subcoronal incision for IPPs showed a 75% satisfaction rate and 3% infection rate at 90 days in >100 procedures.

> Cardiac and pudendal arteries exhibited similar remodeling and calcium content, failing to support the hypothesis that ED precedes cardiovascular disease because of smaller arterial circumference.

> Pericytes function as a cellular regenerator, suggesting a potential new target for ED therapy.

> Pioglitazone (Actos) enhanced survival of pelvic ganglion in a preclinical model of pelvic nerve crush, suggesting a possible role in neuroprotection.

> A study of timing of surgical repair for penile fracture showed that surgery initiated more than 8 hours after ER admission was associated with worse erectile function at 1 and 3 months.

> Treatment of Peyronie’s disease was associated with a decrease in the rate of partners’ sexual dysfunction from 75% before treatment to 33.3% afterward.

Female Urology/Incontinence/Urodynamics

Presented by Ganmal M. Gholieni, MD,
University of California, Irvine

> A retrospective review of 46,648 patients with overactive bladder (OAB) showed that only 34% of women and 19% of men received anticholinergic therapy, and diagnostic testing was performed infrequently.

> Among patients receiving botulinum toxin (Botox) injections, asymptomatic bacteriuria significantly increased the risk of urinary tract infection, but not urosepsis or hospitalization.

> Decreasing the number of botulinum toxin injection sites from 20 to 10 did not reduce efficacy.

> A 4-year follow-up study of patients with neurogenic bladder showed consistent maintenance of improvement from year to year after treatment with onabotulinum toxin.

> Onabotulinum toxin and abobotulinum toxin (Dystport) for neurogenic bladder led to similar outcomes.

> A study of 103 patients with idiopathic OAB showed that 30% of patients required clean intermittent catheterization after treatment with onabotulinum toxin, suggesting a need for standardized definitions and better defined risk factors for patient counseling.

> A 3-year follow-up study of 272 patients treated with sacral neuromodulation (InterStim) showed improvement in depression, pain, and sexual function, and a device-related adverse event rate of 44%.

> A retrospective review of sacral neuromodulation cases showed that most procedures that began as bilateral implant cases ended with unilateral leads.

> A single functional electrode in a timed lead predicted clinical success in patients treated with sacral nerve stimulation.

> Age does not adversely affect outcomes after sacral nerve stimulation.

> A 10-year review of 100 patients with cerebral palsy and neurogenic voiding dysfunction suggested that a non-operative approach should be performed in the absence of compelling indications.

> Following an FDA announcement about complication risks with surgical mesh for pelvic organ prolapse and stress incontinence, use of mesh decreased progressively and use of bulking agents and pubovaginal slings increased.

> A review of 6,900 pelvic organ prolapse repairs showed that use of mesh was associated with higher rates of blood transfusion and surgical site infection.

> A study of 60,000 community-based patients with stress urinary incontinence treated with mesh showed revision rates of 1.2% at 1 year and 2.5% at 10 years.

> A randomized study of open versus laparoscopic sacral colpopexy for prolapse showed similar outcomes but less morbidity and blood loss and shorter recovery with laparoscopic procedures. However, asymptomatic anterior wall prolapse occurred more than twice as often with laparoscopic procedures.

BPH/LUTS

Presented by Richard K. Lee, MD,
Weill Cornell Medical College, New York

> Older age and obesity are associated with suppression of 5-alpha-reductase 2 (5AR2) gene expression and increased methylation of the 5AR2 gene promoter, suggesting a mechanism of resistance to treatment with 5AR inhibitors.

> Molecular profiling of tissue specimens identified “androgen up” and “androgen down” subtypes, sug-
In case you missed this must-read promotional supplement published with the May 2015 issue of *Urology Times*—

**SURGICAL TREATMENT OF BENIGN PROSTATIC HYPERPLASIA:**
What Defines a Gold Standard?

**The Panel Consisted Of:**
- Claus Roehrborn, MD
  Moderator
- Mahmood Hai, MD
- Ricardo Gonzalez, MD
- Kevin McVary, MD
- Alexander Bachmann, MD
- Kevin C. Zorn, MD

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gesting a mechanism for lack of response to 5-ARI therapy.

> Bladder outlet obstruction (BOO) associated with detrusor overactivity and BPH without overactivity have different mRNA transcriptomes and gene expression profiles.

> Body mass index and metabolic syndrome were associated with prostate growth in a population-based study of 1,108 men.

> Analysis of data from the Prostate Cancer Prevention Trial showed that statin use was associated with a 41% increase in the risk of BPH.

> Men with a waist circumference >102 cm had an increased likelihood of incomplete recovery of lower urinary tract function and storage as assessed by the International Prostate Symptom Score (IPSS).

> Older men with BPH had improved hematogenesis and bone mineral density when treated with dutasteride (Avodart).

> Combination therapy with an alpha-blocker and tadalafil (Cialis) proved more effective for BPH than an alpha-blocker alone.

> Three-year results with prostatic urethral lift (UroLift) treatment for BPH showed a 43% improvement in AUAsymptom Score compared with baseline, preserved sexual function, and a 9% retreatment rate.

> A randomized, sham-controlled trial of water vapor treatment for BPH showed greater than 50% reduction in IPSS and 4.9 ml/sec improvement in urinary flow rate.

> A small clinical trial of image-guided, robot-assisted water jet ablation of the prostate showed an improvement in mean IPSS from 23 to 8.9 and increase in peak urinary flow from 8.6 to 21.7 ml/sec at 6 months.

> Six-year follow-up results for 500 patients with BPH treated with a thulium laser showed durable outcomes in all age groups and baseline prostate volumes.

> A study of male urethral sling revision by means of imbricating sutures showed that seven of 16 patients had a decline in sexual function with a subsequent plateau.

> “Crowdsourced” reviews of laparoscopic/robotic surgical videos posted on the Internet compared favorably with assessments by faculty physicians.

> Studies of head-worn 3-D cameras to improve outcomes with endoscopic and laparoscopic procedures received positive reviews in trials involving bedside surgical assistants.

> A randomized trial to compare concomitant bladder neck sling and robotic prostatectomy alone showed higher rates of continence at 1 months and 1 year, although the difference did not achieve statistical significance.

> Studies of agents to preserve sexual potency after robotic prostatectomy yielded favorable results with hyaluronic acid-carboxymethyl cellulose and dehydrated human amniotic membrane allograft, although the number of patients treated remains small and duration of follow-up is brief.

> A 319-patient study of expanded-indication robotic partial nephrectomy (T1b, ≥4 cm) had goals of negative surgical margins, absence of perioperative complications, and a warm ischemia time of <25 minutes. All three goals were met in 43.6% of cases.

> Another study of expanded-indication robotic partial nephrectomy (23 tumors in a single kidney) showed no change in the creatinine/glomerular filtration rate (GFR) ratio across 54 patients with chronic kidney disease I-III. Among patients with preoperative GFR <60 mL/min, mean creatinine level increased by 12% and estimated GFR decreased by 10%.

> A study of conversion from laparoscopic to open nephrectomy showed an overall conversion rate of 4.7% in 9,592 procedures. Factors associated with conversion were bleeding, difficult dissection, failure to progress, and tumor size.

> A review of 1,838 robotic partial nephrectomies showed an intraoperative complication rate of 2.1%, postoperative complication rate of 15.2%, transfusion rate of 2.7%, embolization in 0.2%, fistula in 0.7%, and postoperative acute renal failure in 0.05%.

Outcomes Analysis

Presented by Karim Chamie, MD, MSHS,
UCLA, Los Angeles

> All transurethral resections of bladder tumors are not the same. Patients with larger tumors had longer lengths of stay, longer OR times, increased risk of transfusions, increased risk of complications, and a 1.9% risk of mortality versus patients with smaller tumors.

> Robotic prostatectomy can decrease the risk of grade I and grade II complications in obese patients, but it had no impact on grade III, IV, and V complications.

> Two-thirds of patients with a 10-year life expectancy were treated aggressively for small renal masses. In patients who had a less than a 5-year life expectancy, one-third were aggressively treated.

> The compliance rate for selective medical therapy among kidney stone patients is about 55%. Patients were most likely to be compliant with thiazides and allopurinol and less likely to be compliant with citrates.

> In men screened for prostate cancer, use of herbal supplements declined significantly from 2003 to 2012. One exception was multivitamin utilization, which showed no difference.

> Patients on active surveillance for low-risk prostate cancer who had a family history of prostate cancer or increased risk of urinary symptoms were more likely to have anxiety.

> In a study of the appropriateness of imaging for prostate cancer, patients who were treated at a VA were less likely to receive inappropriate imaging for low-risk prostate cancer than their fee-for-service Medicare peers. For patients with high-risk prostate cancer, there was no difference in utilization of appropriate imaging.

> A change in CMS policy that increased reimbursement for office-based bladder cancer procedures by 600% led to a 600% increase in utilization of these procedures. Although CMS anticipated that increased office-based utilization would be associated with lower utilization of hospital-based procedures, there had been no reciprocal decrease.

> Using a Markov model to determine whether MRI-guided prostate biopsies are more cost effective than a standard 12-core biopsy, researchers found that MRI-guided biopsy was cost effective at 10, 15, and 20 years.

> An examination of side effect profiles after localized prostate cancer found that 59% were treated with radical prostatectomy, 24% with radiation, and 17% were managed with active surveillance. Patients receiving radiation had a slight decline in bowel dysfunction and a decrease in sexual function. Those who had RP had an initial decline in incontinence with a small rebound after 12 months, and they had a decline in sexual function with a subsequent plateau.

> In patients undergoing radical cystectomy, the enhanced recovery after surgery (ERAS) protocol showed no differences in 90-day minor or major mortality, number of complications, readmission or ER visits, but patients had a 12% lower risk of GI complications and a 9% lower risk of wound complications.

> Researchers developed a composite measure—notable outcomes and trackable events after surgery (NOTES)—defining an uncomplicated post-prostatectomy course: no rectal injuries, blood loss <400 cc, length of stay of ≤2 days, drain placement of ≤2 days, catheter placement of ≤16 days, no readmissions, and no mortalities. Twenty percent of patients had at least one deviation from this protocol; most common causes were blood loss, length of stay, and prolonged drains.
Researchers examining the impact of readmissions to secondary hospitals after major urologic cancer surgery found that 10% of patients get readmitted, most often to the primary hospital but 29% of the time to an outside facility. Those admitted to an outside facility are at 7 times higher odds of dying compared to the primary hospital. High-volume centers were more likely to have readmissions to secondary hospitals, which is associated with increased mortality.

Utilization of androgen deprivation therapy for localized prostate cancer decreased from 4% in 2004 to 2.5% in 2009.

In patients with stage 1 seminoma, there has been a significant decrease in the use of radiation therapy over time, a significant increase in observation, and an increase in use of chemotherapy.

Kidney Cancer
Presented by Gennady Bratslavsky, MD.
State University of New York, Syracuse

Delivery of sorafenib (Nexavar) using PLGA and HMC-coated liposomes shows promise in the treatment of renal cell carcinoma (RCC).

An antibody-independent platform shows potential for detecting circulating tumor cells in metastatic RCC patients.

Expression profiles from a panel of 7 miRNA can be used to stratify patients with clear cell RCC.

Interleukin-6 receptor antibody enhances the effect of tyrosine-kinase inhibitors.

Inhibition of carbonic anhydrase 9 confers radiation sensitivity to RCC.

Clusterin inhibition potentially enhances the anti-tumor activity of temsirolimus (Torisel).

Overexpression of Mps1 in ccRCC confers tumor selectivity on heat shock protein-90 inhibitors.

A non-diagnostic renal mass biopsy does not imply absence of malignancy.

In a man aged 55 to 75 years with a T1a small renal mass, a pre-operative biopsy resulted in average savings of $5,447 per patient and a 0.19 quality-adjusted life year increase compared with empirc treatment.

Average body mass index predicts total and fatal RCC. However, another group found improved cancer-specific survival in obese patients.

The use of hemostatic agents during open and laparoscopic partial nephrectomy does not reduce perioperative blood transfusion rate.

The debate over partial versus radical nephrectomy continues. One group reported no improvement in overall survival with partial compared with radical nephrectomy. However, another study found that partial nephrectomy patients were less likely to experience chronic kidney disease (CKD) stage ≥3 and/or end-stage renal disease as well as improved overall survival.

Despite being younger and healthier, donor nephrectomy patients had a much greater decrease in glomerular filtration rate than a cohort of partial nephrectomy patients, including partial nephrectomy patients with warm ischemia time >30 minutes.

A comparison of renal surgery patients with surgical CKD, preexisting CKD, or normal perioperative renal function found that surgical CKD appears to be a distinct subtype of CKD.

Robotic multiport partial nephrectomy is a reasonable surgical approach for multifocal renal tumors, even in patients with impaired renal function preoperatively.

There is an increased rate of utilization of partial nephrectomy for T2 tumors.

A survey of endourologists and urologic oncologists—Please see TAKE-HOMES, on page 34.

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TAKE-HOMES

Presented by Amar Singh, MD.
University of Tennessee, Chattanooga

In the search for markers in urothelial carcinoma, a microRNA panel in urinary cell pellets showed promising results in urothelial carcinoma detection. A 10-biomarker panel showed not only the ability to screen but also differentiate between urothelial and squamous cell carcinoma of the bladder. Blood-based markers—CEA, CA 19-9, and CA 125—may have a role in urothelial cancers.

Robotic cystectomy has become more popular, and is safe in the elderly population. A robotic versus open series showed survival was similar, but the robotic group had more extranodal and peritoneal disease.

A meta-analysis of factors predicting intravesical recurrence in upper tract urothelial cancer (UTUC) identified positive cytology, ureteral location, stage, necrosis, multifocality, extravesical cuff removal, laparoscopic approach, and positive surgical margins.

The role of a nomogram in predicting UTUC recurrence at 12, 24, and 36 months was further validated; recurrences were seen in 29% of patients.

Decreased urinary pH (<5.5) may be a risk for bladder recurrence, and perioperative blood transfusion is also an independent risk factor for worse survival in UTUC patients.

Basic science papers showed that differences in DNA methylation helped predict metastatic potential and aggressiveness of urothelial carcinoma; neutrophil-to-lymphocyte ratio appears to be an important prognostic marker in urothelial carcinoma; and ACE inhibitors may have a role in prevention of bladder cancer.

Having a bladder cancer pathology review at a tertiary center by an experience GU pathologist is important, as it led to change in pathology in 27% of cases and a change in treatment recommendations in 16%.

Bladder Cancer

Incidental bladder wall thickening on CT was correlated with an overall cancer rate of 4.3%. Focal thickening was correlated with cancer in 15% of cases and diffuse imaging in only 4%.

In nonmuscle-invasive bladder cancer, an embolus resection using both electrocautery and laser showed acceptable safety and efficacy.

Bacillus Calmette–Guérin (BCG) was shown in several papers to be still the mainstay of effective intravesical therapy.

BCG following a second transurethral resection for even a negative pathology may decrease bladder cancer recurrence.

Compliance with maintenance BCG remains poor. Surprisingly, most cases of discontinuation (60%) are due to low-grade toxicity.

The role of docetaxel (Taxotere) in BCG-refractory disease remains promising.

In patients with high-grade nonmuscle-invasive disease, mitomycin C plus BCG and BCG alone showed similar recurrence and survival.

Despite BCG being the standard of care for carcinoma in situ, its delivery is extremely low. Examination of a SEER-Medicare database of nearly 3,800 patients in the pre-BCG shortage era found that only 10% of patients who were eligible for BCG received it, and 85% received no adjuvant treatment. The BCG group had superior overall survival and delayed time to cystectomy.

In muscle-invasive bladder cancer, a comparison of radical cystectomy versus bladder-sparing treatment including a chemoradiation protocol showed that cystectomy was associated with improved survival when the disease was organ confined, but if the disease was more advanced, there was no difference between the two treatments in overall survival or outcome.

The interval time between diagnosis and radical cystectomy for muscle-invasive disease does not impact outcomes in patients on neoadjuvant chemotherapy.

Neoadjuvant chemo does not increase surgical complexity or perioperative complications and is not associated with renal function decline.

In the neoadjuvant chemo setting, dose-dense methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) is becoming more popular, as it may help decrease toxicity and decrease time to radical cystectomy in very high-risk patients.

Deep vein thrombosis (DVT) remains a concern in radical cystectomy patients. In those receiving neoadjuvant chemo, 33% may have occult DVT that may be undiagnosed. Changing DVT prophylaxis from the inpatient-only setting to extended-duration enoxaparin or lovenox may decrease thromboembolic events.

Prooperative antacid use, acute postoperative renal failure, and large antibiotic usage were identified as risk factors for developing Clostridium difficile after cystectomy, which is a complication in up to 10% to 15% of patients in this population.

Long-term survival in patients undergoing radical cystectomy is independent of pathologist and lymph node count if surgeons adhere to a pelvic lymph node dissection template.

Wound dehiscence in radical cystectomy is predicted by wound infection, smoking, increased operative time, and body mass index.

Allogenic blood transfusion is related to increased perioperative infection rates.

Broader antimicrobial coverage and adding antifungal may help decrease wound infection rates.

Uncontrolled diabetes and obesity remain risk factors for post-cystectomy complications, reoperations, and mortality.

Readmission after cystectomy remains a major challenge, with the highest rates between day 4 and 5 post-discharge. An approach using phone calls to detect patients at risk of readmission helped minimize it. Neobladder has the highest readmission rates; 50% of complications occur post-discharge; and 25% of readmissions happen even when enhanced recovery after surgery (ERAS) protocols are followed, UTI being the most common reason.

Performance status, nutrition, absence of sarcopenia, and absence of obesity predict better outcome in patients following cystectomy.

Robotic cystectomy has become more popular, and is safe in the elderly population. A robotic versus open series showed survival was similar, but the robotic group had more extranodal and peritoneal disease.

A meta-analysis of factors predicting intravesical recurrence in upper tract urothelial cancer (UTUC) identified positive cytology, ureteral location, stage, necrosis, multifocality, extravesical cuff removal, laparoscopic approach, and positive surgical margins.

The role of a nomogram in predicting UTUC recurrence at 12, 24, and 36 months was further validated; recurrences were seen in 29% of patients.

Decreased urinary pH (<5.5) may be a risk for bladder recurrence, and perioperative blood transfusion is also an independent risk factor for worse survival in UTUC patients.

Basic science papers showed that differences in DNA methylation helped predict metastatic potential and aggressiveness of urothelial carcinoma; neutrophil-to-lymphocyte ratio appears to be an important prognostic marker in urothelial carcinoma; and ACE inhibitors may have a role in prevention of bladder cancer.
Some of these just make sense. I don’t know all of the labeling changes, but most stuff like that makes sense. Don’t take it if it isn’t prescribed by a physician. Don’t take it unless you have low testosterone, things like that—I think that makes perfect sense.

I think most people think that way, but I do know that testosterone clinics have opened up, which is why a lot of this is happening. All of a sudden, we have more headaches in getting approval for testosterone replacement from a lot of insurance companies.

My son lives in Houston, right next to a testosterone clinic where men can just walk in, complain about something, and get shots. I think it’s just been overprescribed for people who don’t really need it.

I still feel that any symptomatic hypogonadism regardless of cause should be treated and especially if associated with metabolic syndrome. These changes could lead to patients who are currently on treatment to have to stop treatment if insurance companies change policy of coverage.”

Alan Strumeyer, MD
Millburn, NJ

The FDA is being very cautious, which as the protector of public health, it’s got to be. A good practice is to prescribe testosterone to men with hypogonadism who have low testosterone and symptoms. Patients who have cardiovascular disease, low testosterone, and symptoms should be treated with testosterone because in my opinion, the risk of having low testosterone exceeds the risk of treatment, because cardiovascular risk from treating low testosterone is probably nonexistent.

There is a gradual decline in testosterone level with increasing age, but I’m not aware of any studies that define what a normal testosterone level is in relationship to age. If any patient has low testosterone and clear symptoms of low testosterone, they should be treated. The idea of saying, ‘Don’t prescribe testosterone for conditions related to aging’ is meaningless because there are no standards for normal testosterone by age.

Clinics that prescribe testosterone indiscriminately are bad practice, but people in the testosterone treatment business to make a buck aren’t going to pay a whole lot of attention to these warnings. They will face increased risk for malpractice action when there are complications from inappropriate overtreatment with testosterone. It might put some brakes on that sort of practice.”

Ira Sharlip, MD
San Francisco

Testosterone replacement therapy provides so many benefits for the aging male, such as maintaining muscle mass, maintaining bone density, and even maintaining short-term memory and higher mental function. It keeps men functioning, not only physically, but mentally and emotionally in the workplace, as our changing American economy is requiring Americans to continue working longer in their lifespan. We need to know more, and the way to get the information is not to react like the medical regulatory ostrich.

Shot clinics have destroyed the public and administrative perspective of good medical treatment of low testosterone with symptoms in men with a variety of conditions. It gives a tawdry appearance, much like the shot clinics did for ED.

When practitioners treating low testosterone and ED provide best-practice policies, and practitioners follow the best-practice policy statements, that’s a softer form of regulation that is more self-regulation. Leave it to the legal system to punish those who practice outside of established standards.”

Jeffrey Buch, MD
Frisco, TX

Dr. Strumeyer
Dr. Sharlip
Dr. Buch
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EOE/AA
House votes to repeal Medicare pay panel
White House threatens veto of measure, however

Washington—The Independent Payment Review Board (IPAB), created by the Affordable Care Act as a way to keep Medicare spending under control, appears to be headed out of existence, much to the pleasure of much of the provider community—including urologists.

“It would put significant health care decisions in the hands of a group of unelected, unaccountable individuals with little or no clinical expertise or the oversight required to protect access to care for America’s seniors,” the Alliance said in a statement posted on its website.

The IPAB, designed to be a 15-member independent body that would recommend cuts to the Medicare budget if program spending exceeds a target growth rate, has not even had members nominated by the president.

Medical groups, including the AUA and the American Medical Association (AMA), have been advocating repeal of the IPAB since the ACA was enacted, contending that the board would have unfettered power to slash Medicare payments without input from organized medicine.

“Significant health care decisions must not be made by a group of unelected, unaccountable individuals with little or no clinical expertise or the oversight required to protect access to care for America’s seniors.”

ALLIANCE OF SPECIALTY MEDICINE

Fast Facts
Repeal of the Independent Payment Advisory Board:

- was part of a measure passed by the House of Representatives on June 23
- would cost an estimated $7.1 billion between fiscal year 2016 and 2025
- is a much-sought-after goal of medical groups such as the AUA and AMA

The IPAB was part of a measure passed by the House of Representatives on June 23, would cost an estimated $7.1 billion between fiscal year 2016 and 2025, and is a much-sought-after goal of medical groups such as the AUA and AMA.

The IPAB was scheduled for June 15, but that was delayed as Democrats, many of whom agree that the board should be scrapped, objected to the Republican plan to cover the cost of repeal by reducing funding for prevention and public health.

Then came a threat from the White House that President Obama would veto both IPAB repeal and the plan to eliminate the medical device tax, which is also unpopular within the health care industry—should the Senate go along with the House’s action.

The repeal of the device tax “would take away a funding source for financial assistance that is working to improve coverage and affordability and would increase the federal deficit by $24 billion over 10 years,” the White House said in a statement. The plan to ditch the tax—also approved by the House in mid-June—does not include a plan to cover that cost, unlike the IPAB repeal initiative.

The Congressional Budget Office (CBO) estimated that the IPAB repeal cost would be $7.1 billion between fiscal years 2016 and 2025.

The House IPAB repeal vote was originally scheduled for June 15 but was delayed as Democrats, many of whom agree that the board should be scrapped, objected to the Republican plan to cover the cost of repeal by reducing funding for prevention and public health.

When the Ways and means Committee voted 31-8 to repeal the IPAB, the AMA praised the action.

“IPAB is a flawed policy and the AMA has been advocating for the repeal of it since the ACA was passed,” said AMA President Robert Wah, MD. “It would put significant health payment and policy decisions in the hands of an independent body of individuals with far too little accountability.”

Is repeal necessary?
Some health care experts have pointed out that even if Congress fails to repeal IPAB, the issue is moot because the Republican-controlled Senate is not likely to confirm nominations to the board, even if qualified, willing nominees could be found.

Moreover, under the ACA, the IPAB would not be required to act unless Medicare missed its spending target. CBO projects that Medicare growth rates will remain beneath those targets until at least 2022.

However, opponents of the IPAB argue that the only way to make sure it never springs to life in a new Congress with a different political makeup is to drive a nail in its coffin now.

All of this is part of the GOP effort on Capitol Hill to knock off parts or all of the ACA and put Democratic supporters in a vulnerable position with the electorate, which Republicans view as generally “anti-Obamacare.” House Republicans have voted more than 50 times to take such action, all to no avail.

Feedback Send your comments to
Bob Gatty c/o Urology Times, at UT@advanstar.com

UT Washington

Bob Gatty, a former congressional aide, covers news from Washington for Urology Times.
**TODAY SHOW HEALTH**

Men remember first car, but not last doctor’s appointment

**MANY MEN** can’t remember the last time they visited the doctor. They’re more likely to remember their first car.

Orlando Health commissioned a survey and asked 1,000 men, ages 18 to 65 years, which they remember best: the make and model of their first car, the month/year of their last checkup, the name of their senior prom date, their eighth grade teacher’s name, and the time that they were born.

Researchers found that 81% of men remembered the make and model of their first car, while only 54% remembered the last time they visited their physician.

Urologists Sijo Parekattil, MD, and Jamin Brahmbhatt, MD, in community practice in Clermont, FL, conducted the survey as part of the Tesla Drive for Men’s Health, a 6,008-mile cross-country drive from June 15-20 to raise awareness about men’s health issues.

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**THE WALL STREET JOURNAL**

**BCG shortage frustrates patients, docs**

A **GLOBAL SHORTAGE** of the bladder cancer drug bacillus Calmette–Guérin (TheraCys, TICE BCG) is frustrating doctors and patients who are relying on it.

Two of the few makers of the drug have had manufacturing problems, including a mold infestation at a Toronto factory owned by Sanofi SA and production delays from Merck and Co.

Patients who need BCG have had to call hospitals and travel hundreds of miles to find the drug, the Wall Street Journal reported. Some have gone without, while others have found less effective alternatives.

“There are patients who aren’t getting optimal therapy right now,” said Edward M. Messing, MD, of the University of Rochester Medical Center, Rochester, NY.

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**HEALTHDAY NEWS**

**CV autonomic neuropathy linked with erectile dysfunction, LUTS**

**CARDIOVASCULAR** autonomic neuropathy is associated with erectile dysfunction and/or lower urinary tract symptoms in men with type 1 diabetes, according to a recent study.

First author Rodica Pop-Busui, MD, PhD, of the University of Michigan, Ann Arbor and colleagues obtained data for 635 men in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) with type 1 diabetes.

Compared to men without ED or LUTS, those with the conditions had significantly lower respiratory rate variation and Valsalva ratio at DCCT closeout and EDIC year 16/17. The odds of ED and LUTS were increased 2.65-fold among participants with cardiovascular neuropathy.

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**Severe acne observed with transgender patients taking testosterone**

**PEOPLE WHO ARE TRANSITIONING** from female to male and taking testosterone may experience severe acne as a side effect of treatment, according to an online report in JAMA Dermatology (May 20, 2015).

Researchers from Ramón y Cajal Hospital in Madrid, Spain describe the cases of two transgender men. The first patient experienced severe acne that left scarring on his face and chest. The second patient had never had significant acne in the past, but had it on his face and buttocks, along with seborrhea. Skin problems started 6 months after beginning testosterone therapy.

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**NEWS ODDITIES**

**Syndrome leads to arousal without desire**

A **DISORDER** called restless genital syndrome (RGS) is known to give feelings of persistent genital arousal that occur without sexual desire.

RGS can occur with symptoms of throbbing, tingling, or sensitivity in the genitals but with zero sexual thought, according to a report in Men’s Health.

“The guy we encountered said he was always on the verge of orgasm, but he wasn’t turned on,” said Tobias Köhler, MD, MPH, a urologist at Southern Illinois University School of Medicine, Springfield, who published a paper on a case of RGS online in Case Reports in Urology (Feb. 12, 2015).

RGS occurs in about 1% of women and so far is diagnosed in only a handful of men. Until experts can study potential patients, it’s hard for doctors to pinpoint what actually causes RGS. For now, physicians think it might be caused by a sensory abnormality of genital nerves.

Although there doesn’t appear to be any negative health effect associated with RGS, the disorder can pose a psychological burden.

One treatment option may be antidepressants, as they have an unintended side effect of lowering libido and helped in one patient’s case. Other drugs that have helped patients include neurologic agents.
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Initial U.S. Approval: 2012

BRIEF SUMMARY OF PRESCRIBING INFORMATION

The following is a brief summary. Please see the package insert for full prescribing information.

INDICATIONS AND USAGE

XTANDI is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

CONTRAINdications

Pregnancy XTANDI can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. XTANDI is not indicated for use in women. XTANDI is contraindicated in women who are or may become pregnant. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for pregnancy loss [see Use in Specific Populations (8.1)].

WARNINGS AND PRECAUTIONS

Seizure In Study 1, which enrolled patients who previously received docetaxel, 7 of 800 (0.9%) patients treated with XTANDI experienced a seizure and no patients treated with placebo experienced a seizure. Seizure occurred from 31 to 603 days after initiation of XTANDI. In Study 2, 1 of 871 (0.1%) chemotherapy-naïve patients treated with XTANDI and 1 of 844 (0.1%) patients treated with placebo experienced a seizure. Patients experiencing seizure were permanently discontinued from therapy and all seizure events resolved. There is no clinical trial experience re-administering XTANDI to patients who experienced seizure. Limited safety data are available in patients with predisposing factors for seizure because these patients were generally excluded from clinical trials. These exclusion criteria included a history of seizure, underlying brain injury with loss of consciousness, transient ischemic attack within the past 12 months, cerebral vascular accident, brain metastasis, and brain arteriovenous malformation. Study 1 excluded the use of concomitant medications that may lower the seizure threshold, whereas Study 2 permitted the use of these medications. Because of the risk of seizure associated with XTANDI use, patients should be advised of the risk of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

ADVERSE REACTIONS

Clinical Trial Experience Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Two randomized clinical trials enrolled patients with metastatic prostate cancer that has progressed on androgen deprivation therapy (GnrH therapy or bilateral orchectomy), a disease setting that is also defined as metastatic CRPC. In both studies, patients received XTANDI 160 mg orally once daily in the active treatment arm or placebo in the control arm. All patients continued androgen deprivation therapy. Patients were allowed, but not required, to take glucocorticoids.

The most common adverse reactions (≥ 10%) that occurred more commonly (≥ 2% over placebo) in the XTANDI-treated patients from the two randomized clinical trials were asthenia/fatigue, back pain, decreased appetite, constipation, arthralgia, diarrhea, hot flush, upper respiratory tract infection, peripheral edema, dyspnea, musculoskeletal pain, weight decreased, headache, hypertension, and dizziness/vomiting.

Study 1: Metastatic Castration-Resistant Prostate Cancer Following Chemotherapy Study 1 enrolled 1199 patients with metastatic CRPC who had previously received docetaxel. The median duration of treatment was 8.3 months with XTANDI and 3.0 months with placebo. During the trial, 48% of patients on the XTANDI arm and 46% of patients on the placebo arm received glucocorticoids.

Grade 3 and higher adverse reactions were reported among 47% of XTANDI-treated patients and 53% of placebo-treated patients. Dis discontinuations due to adverse events were reported for 16% of XTANDI-treated patients and 18% of placebo-treated patients. The most common adverse reaction leading to treatment discontinuation was seizure, which occurred in 0.9% of the XTANDI-treated patients compared to none (0%) of the placebo-treated patients. Table 1 shows adverse reactions reported in Study 1 that occurred at a ≥ 2% higher frequency in the XTANDI arm compared to the placebo arm.

Table 1. Adverse Reactions in Study 1

<table>
<thead>
<tr>
<th>Event</th>
<th>XTANDI</th>
<th>Placebo</th>
<th>Grade 1-4 (%)</th>
<th>Grade 3-4 (%)</th>
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</thead>
<tbody>
<tr>
<td>General Disorders</td>
<td></td>
<td></td>
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<tr>
<td>Asthenic Conditions</td>
<td>50.6</td>
<td>9.0</td>
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<td>Peripheral Edema</td>
<td>15.4</td>
<td>1.0</td>
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<tr>
<td>Musculoskeletal And Connective Tissue Disorders</td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Back Pain</td>
<td>26.4</td>
<td>5.3</td>
<td>24.3</td>
<td>4.0</td>
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<tr>
<td>Arthralgia</td>
<td>20.5</td>
<td>2.5</td>
<td>17.3</td>
<td>1.8</td>
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<tr>
<td>Musculoskeletal Pain</td>
<td>15.0</td>
<td>1.3</td>
<td>11.5</td>
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<tr>
<td>Muscular Weakness</td>
<td>9.8</td>
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<tr>
<td>Musculoskeletal Stiffness</td>
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<tr>
<td>Gastrointestinal Disorders</td>
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<tr>
<td>Diarrhea</td>
<td>21.8</td>
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<tr>
<td>Vascular Disorders</td>
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<tr>
<td>Hot Flush</td>
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<tr>
<td>Hypertension</td>
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<tr>
<td>Nervous System Disorders</td>
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<td>Headache</td>
<td>12.1</td>
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<td>Dizziness</td>
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<td>Spinal Cord Compression And Curva Equina Syndrome</td>
<td>7.4</td>
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<tr>
<td>Paresthesia</td>
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<td>Mental Impairment Disorders</td>
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<tr>
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<td>Infections And Infestations</td>
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<td>Upper Respiratory Tract Infection</td>
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<td>Lower Respiratory Tract And Lung Infection</td>
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<td>Psychiatric Disorders</td>
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<td>Insomnia</td>
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<td>0.5</td>
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<td>Anxiety</td>
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<td>4.0</td>
<td>0.0</td>
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<td>Renal And Urinary Disorders</td>
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<td></td>
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<tr>
<td>Hematuria</td>
<td>6.9</td>
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<td>Pollakiuria</td>
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<tr>
<td>Injury, Poisoning And Procedural Complications</td>
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<tr>
<td>Fall</td>
<td>4.6</td>
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<tr>
<td>Non-pathologic Fractures</td>
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<td>0.3</td>
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<td>Skin And Subcutaneous Tissue Disorders</td>
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<tr>
<td>Pruritus</td>
<td>3.5</td>
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<td>1.3</td>
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Table 2. Adverse Reactions in Study 2

<table>
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<th>XTANDI</th>
<th>Placebo</th>
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<th>Grade 3-4 (%)</th>
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</table>
enzalutamide by 1.3-fold in healthy volunteers [see Clinical Pharmacology (12.3)].

The effects of CYP3A4 inducers on the pharmacokinetics of enzalutamide have not been evaluated in vivo. Co-administration of XTANDI with strong CYP3A4 inducers (e.g., carbamazepine, phenytoin, rifabutin, rifampin, rifapentine) may decrease the plasma exposure of XTANDI and should be avoided if possible. Selection of a concomitant medication with no or minimal CYP3A4 induction potential is recommended. Moderate CYP3A4 inducers (e.g., bosentan, efavirenz, etravirine, modafinil, naltrexone) and St. John's Wort may also reduce the plasma exposure of XTANDI and should be avoided if possible [see Clinical Pharmacology (12.3)].

Effect of XTANDI on Drug Metabolizing Enzymes

Enzalutamide is a strong CYP3A4 inducer and a moderate CYP2C9 and CYP2C19 inducer in humans. At steady state, XTANDI reduced the plasma exposure to midazolam (CYP3A4 substrate), warfarin (CYP2C9 substrate), and omeprazole (CYP2C19 substrate). Concomitant use of XTANDI with narrow therapeutic index drugs that are metabolized by CYP3A4 (e.g., alfentanil, cyclosporine, diltiazem, ergotamine, fentanyl, ponazol, quinidine, sertraline, and tacrolimus), CYP2C9 (e.g., phenytoin, warfarin) and CYP2C19 (e.g., S-mephentoin) should be avoided, as enzalutamide may decrease their exposure. If co-administration with warfarin cannot be avoided, conduct additional INR monitoring [see Clinical Pharmacology (12.3)].

USE IN SPECIFIC POPULATIONS

Pregnancy - Pregnancy Category X [see Contraindications (4)].

Risk Summary

XTANDI can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. While there are no human data on the use of XTANDI in pregnancy and XTANDI is not indicated for use in women, it is important to know that maternal use of XTANDI and other androgen receptor inhibitor could affect development of the fetus. Enzalutamide caused embryofetal toxicity in mice at exposures that were lower than in patients receiving the recommended dose. XTANDI is contraindicated in women who are or may become pregnant while receiving the drug. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, apprise the patient of the potential hazard to the fetus and the potential risk for pregnancy loss. Advise females of reproductive potential to avoid becoming pregnant during treatment with XTANDI.

Animal Data

In an embryo-fetal developmental toxicity study in mice, enzalutamide caused developmental toxicity when administered to females by oral gavage at 10 or 30 mg/kg/day throughout the period of organogenesis (gestational days 6-15). Findings included embryo-fetal lethality (increased post-implantation loss and resorptions) and decreased anogenital distance at ≥ 10 mg/kg/day and cleft palate and absent palate bone at 30 mg/kg/day. Doses of 30 mg/kg/day caused maternal toxicity. The doses tested in mice (1, 10 and 30 mg/kg/day) resulted in systemic exposures (AUC) approximately 0.4, 0.4 and 1.1 times, respectively, the exposures in patients. Enzalutamide did not cause developmental toxicity in rabbits when administered at oral doses of 10 or 30 mg/kg/day (approximately 10 times the human exposure based on AUC).

Manufactured by: Cataltal Pharma Solutions, LLC, St. Petersburg, FL 33716

Manufactured for and Distributed by: Astellas Pharma US, Inc., Northbrook, IL 60062

Manufactured by: Astellas Pharma US, Inc., Northbrook, IL 60062

Medivation, Inc., San Francisco, CA 94105

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Rx Only

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Important Safety Information

Contraindications  XTANDI (enzalutamide) capsules can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. XTANDI is not indicated for use in women. XTANDI is contraindicated in women who are or may become pregnant.

Warnings and Precautions In Study 1, conducted in patients with metastatic castration-resistant prostate cancer (CRPC) who previously received docetaxel, seizure occurred in 0.9% of patients who were treated with XTANDI and 0% treated with placebo. In Study 2, conducted in patients with chemotherapy-naïve metastatic CRPC, seizure occurred in 0.1% of patients who were treated with XTANDI and 0.1% treated with placebo. Patients experiencing a seizure were permanently discontinued from therapy and all seizure events resolved. There is no clinical trial experience re-administering XTANDI to patients who experienced a seizure, and limited clinical trial experience in patients with predisposing factors for seizure. Study 1 excluded the use of concomitant medications that may lower threshold, whereas Study 2 permitted the use of these medications. Because of the risk of seizure associated with XTANDI use, patients should be advised of the risk of engaging in any activity during which sudden loss of consciousness could cause serious harm to themselves or others. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

Adverse Reactions The most common adverse reactions (≥ 10%) reported from the two combined clinical trials that occurred more commonly (≥ 2% over placebo) in the XTANDI-treated patients were asthenia/fatigue, back pain, decreased appetite, constipation, arthralgia, diarrhea, hot flush, upper respiratory tract infection, peripheral edema, dyspnea, musculoskeletal pain, weight decreased, headache, hypertension, and dizziness/vertigo.

Other Adverse Reactions include:
- Laboratory Abnormalities: In the two studies, Grade 1-4 neutropenia occurred in 15% of patients treated with XTANDI (1% Grade 3-4) and in 6% of patients treated with placebo (0.5% Grade 3-4). The incidence of Grade 1-4 thrombocytopenia was 6% of patients treated with XTANDI (0.3% Grade 3-4) and 5% of patients on placebo (0.5% Grade 3-4). Grade 1-4 elevations in ALT occurred in 10% of patients treated with XTANDI (0.2% Grade 3-4) and 16% of patients treated with placebo (0.2% Grade 3-4).
- Grade 1-4 elevations in bilirubin occurred in 3% of patients treated with XTANDI (0.1% Grade 3-4) and 2% of patients treated with placebo (no Grade 3-4).
- Infections: In Study 1, 1% of XTANDI versus 0.3% of placebo patients and in Study 2, 1 patient in each treatment group (0.1%) had an infection resulting in death.
- Falls: In the two studies, falls including fall-related injuries occurred in 9% of XTANDI patients vs 4% treated with placebo. Falls were not associated with loss of consciousness or seizure. Fall-related injuries were more severe in XTANDI patients and included non-pathologic fractures, joint injuries, and hematomas.
- Hypertension: In the two studies, hypertension was reported in 11% of patients receiving XTANDI and 4% of patients receiving placebo. No patients experienced hypertensive crisis. Medical history of hypertension was balanced between arms. Hypertension led to study discontinuation in < 1% of XTANDI or placebo treated patients.

Drug Interactions
- Effect of Other Drugs on XTANDI - Administration of strong CYP2C8 inhibitors can increase the plasma exposure to XTANDI. Co-administration of XTANDI with strong CYP2C8 inhibitors should be avoided if possible. If co-administration of XTANDI cannot be avoided, reduce the dose of XTANDI. Co-administration of XTANDI with strong or moderate CYP3A4 and CYP2C8 inhibitors may alter the plasma exposure of XTANDI and should be avoided if possible.
- Effect of XTANDI on Other Drugs - XTANDI is a strong CYP3A4 inducer and a moderate CYP2C9 and CYP2C19 inducer in humans. Avoid CYP3A4, CYP2C9 and CYP2C19 substrates with a narrow therapeutic index, as XTANDI may decrease the plasma exposures of these drugs. If XTANDI is co-administered with warfarin (CYP2C9 substrate), conduct additional INR monitoring.

Please see adjacent pages for Brief Summary of Full Prescribing Information.
XTANDI (enzalutamide) capsules is indicated for the treatment of patients with metastatic castration-resistant prostate cancer (CRPC).

Select Safety Information

XTANDI can cause fetal harm when administered to a pregnant woman based on its mechanism of action and findings in animals. XTANDI is not indicated for use in women. XTANDI is contraindicated in women who are or may become pregnant.

Seizure occurred in 0.9% of patients receiving XTANDI who previously received docetaxel and in 0.1% of patients who were chemotherapy-naive. Patients should be advised of the risk of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others. Permanently discontinue XTANDI in patients who develop a seizure during treatment.


Please see inside page for additional Important Safety Information.
Please see adjacent pages for Brief Summary of Full Prescribing Information.