Nonmetastatic PCa: A changing landscape
Three agents extend metastasis-free survival, address unmet need

Jeni Williams / UT Correspondent

Are new antiandrogens the gold standard for treatment of nonmetastatic castration-resistant prostate cancer (nmCRPC)? Three novel androgen receptor inhibitors provide an embarrassment of riches when it comes to treatment options for nmCRPC patients, but there are still questions to be answered—including the extent of these drugs’ clinical benefit.

The approvals of apalutamide (Erleada) in February 2018, enzalutamide (XTANDI) in July 2018, and darolutamide (Nubeqa) in July 2019 for the nmCRPC indication were the first moves away from a “watch-and-wait” approach for managing patients with nmCRPC.

Prior to the availability of these antiandrogens for nmCRPC, “It was a dealer’s choice approach of what to do, with no clear guidelines,” said Leonard G. Gomella, MD, professor and chair of urology at Thomas Jefferson University and senior director for clinical affairs at the Sidney Kimmel Cancer Center, Philadelphia.

“We didn’t really have a good option for treatment, which meant physicians waited for something bad to happen. We’d wait for patients’ PSA to shoot up; we’d image them; and the minute we saw signs of metastasis, we would begin metastatic castration-resistant prostate cancer treatment.”

One-third of patients with nmCRPC develop metastases within 2 years.

Now, phase III clinical trials including the SPARTAN study, a trial of apalutamide; PROSPER, a study of enzalutamide; and ARAMIS, a study of darolutamide, are changing the landscape for nmCRPC by presenting options for prolonging metastasis-free survival—the endpoint that formed the basis for FDA approval of these three agents for nmCRPC.

“These drugs fulfill an unmet need for treatment of nonmetastatic castration-resistant prostate cancer,” Dr. Gomella said.

The use of metastasis-free survival as a study endpoint has drawn questions. “There’s no proven clinical benefit associated with an improvement in metastasis-free survival per se,” said Philip Kan-

PIVOTAL TRIALS OF nmCRPC DRUGS

SPARTAN
Apalutamide patients had a median metastasis-free survival of 40.5 months vs. 16.2 months in placebo group (p<.001)

PROSPER
Enzalutamide patients had a median metastasis-free survival of 36.6 months vs. 14.7 months in placebo recipients (p<.001)

ARAMIS
Darolutamide patients had a median metastasis-free survival of 40.4 months vs. 18.4 months with placebo (p<.001)


Q&A
OAB/INCONTINENCE

AUA, SUFU offer guidance on incontinence after prostate treatment

Earlier in 2019, the AUA and SUFU published a joint guideline on the subject of incontinence after prostate treatment. In this interview, Jaspreet S. Sandhu, MD, a member of this guideline’s panel, explains the rationale behind the guideline and summarizes its key points.

For the full article, please turn to page 28

Jaspreet S. Sandhu, MD

Let’s Talk Men’s Health

DeMISTifying less-invasive solutions for BPH

Urologists are enjoying a leap in innovation in office-based treatment of BPH, and several more technologies are in development in the quest for the truly minimally invasive surgical therapy (MIST). Steven A. Kaplan, MD, explains why it is important to review the goals of MIST, reach consensus on the metrics by which to measure them, and hold new treatments to these metrics.

For the full article, please turn to page 22
When confronted with challenging conditions in urology, urologists often face a tough choice: take their chances with organ-sparing approaches or opt for radical surgery and potentially expose the patient to complications or sequelae.

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*Transforming local therapies in urology*

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RTGel technology is not commercially available. The safety and effectiveness of UroGen’s investigational product candidates that utilize RTGel technology have not been established.


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Sipuleucel-T significantly improves OS in African-Americans vs. Caucasians

**Cheryl Guttman Krader**
UT Contributing Editor

**CHICAGO**—Analyses of data collected in PROCEED, a large real-world registry, corroborate phase III study findings demonstrating that sipuleucel-T (Provenge) treatment for metastatic castrate-resistant prostate cancer (mCRPC) has a particular benefit for improving overall survival (OS) in African-American men.

In a PSA-matched cohort that included 438 Caucasians and 219 African-Americans, there was a statistically significant 9.5-month difference in median OS favoring African-American patients over Caucasian patients (35.3 vs. 25.8 months; hazard ratio [HR]: 0.70; p<.001). When the men were split into two groups according to median baseline PSA (≤29.48 ng/mL and >29.48 ng/mL), a significant difference in median OS favoring the African-Americans was achieved only in the subgroup with a baseline PSA ≤29.48 ng/mL, but the difference between groups increased to almost 21 months. Within the lower baseline PSA subgroup, median OS was 54.3 months for the African-American men and 33.4 months for the Caucasians (HR: 0.52, p<.001), reported first author Oliver Sartor, MD, at the American Society of Clinical Oncology annual meeting in Chicago.

“The difference in median OS in the lower PSA subgroup is quite remarkable and represents the largest known racial difference in OS in response to any therapy for mCRPC.”

OLIVER SARTOR, MD

Review of the registry enrollees identified 1,902 men who had received at least one sipuleucel-T infusion, of whom 221 were African American and 1,649 were Caucasian. Because PSA differed significantly at baseline in the two racial groups, a PSA-matched cohort was created, matching two Caucasian patients to each African-American based on having a baseline PSA ≤10%. The matched cohort included only 219 African-Americans after excluding one man who lacked baseline PSA data and another who had a very high PSA that could not be matched according to the selection criterion.

In both racial groups, the median patient age was 71 years, about two-thirds of the men had an ECOG performance status of 0, and slightly less than one-half had a Gleason sum ≥8. Median PSA at baseline was 28.7 ng/mL in the Caucasians and 32.9 ng/mL in the African-Americans. The mean number of life-prolonging anti-cancer therapies was 1.6 in both groups; the median number received was 2.0 in the Caucasians and 1.0 in the African-Americans.

**Analysis divides patients into PSA quartiles**

Another analysis of OS divided patients into PSA quartiles (≤8, 8 to ≤29.48 ng/mL, >29.48 to ≤82.4 ng/mL, and >82.4 ng/mL). A significant improvement in median OS among African-Americans compared with Caucasians was found only in the two lowest quartiles (HR: 0.49 for men with PSA ≤8 ng/mL, 0.54 for men with PSA >8 ng/mL to 29.48 ng/mL). Analyses were also performed to identify baseline variables that were predictors of OS. In univariate analysis, age, weight, race, ECOG performance status, PSA, alkaline phosphatase, hemoglobin, lactate dehydrogenase, lymph node–only metastases, prior prostatectomy, prior abiraterone (ZYTIGA)/enzalutamide (XTANDI), and prior docetaxel (Taxotere)/cabazitaxel (Jevtana) had a statistically significant association with OS.

In a Cox regression model adjusting for the significant covariates, African-American race was independently associated with improved OS and had the strongest predictive value of all associated covariates (HR: 1.67).

Dr. Sartor noted that the explanation for racial difference in OS is unknown. “It may involve differences in pathophysiology or immune responsiveness,” he said.

Dr. Sartor is a consultant to Dendreon and to other companies that market or are developing treatments for prostate cancer. For full disclosures, see bit.ly/proceeddisclosures.

**FDA ENCOURAGES INCLUSION OF MEN IN BREAST CA TRIALS**

The FDA has issued a draft guidance encouraging the inclusion of male patients in breast cancer clinical trials.

“As breast cancer in men is rare, they have typically not been included in clinical trials for breast cancer treatment,” said Richard Pazdur, MD, director of the FDA’s Oncology Center of Excellence and acting director of the Office of Hematology and Oncology Products in the FDA’s Center for Drug Evaluation and Research.

“This has led to a lack of data, so their treatment is generally based upon studies and data collected in women. While some FDA-approved treatments are gender-neutral in their indication, many therapies are only approved for women and further data may be necessary to support labeling indications for men… We hope that the recommendations in the draft guidance issued today will, when finalized, encourage drug development for the treatment of male breast cancer and ultimately, provide additional FDA-approved treatment options for patients,” Dr. Pazdur added.

To read the draft guidance, go to bit.ly/malebreastca.
Analysis further refines delivery of new therapies for metastatic CRPC

T
he last several years have been particularly exciting in the area of metastatic castrate-resistant prostate cancer (mCRPC). A multitude of new therapies are now available as studies continue to review the sequencing of these treatments and refine the timing, best combinations, and best subpopulations for treatment. As data continue to accumulate, reviews of these large data sets help to better define the best target populations for many of these agents.

The 2019 ASCO annual meeting included a number of interesting abstracts in the area of advanced prostate cancer (see page 4). One such study was a re-review of the PROCEED trial by Sartor et al. The authors did a deeper analysis from this large phase III trial to further evaluate the findings of an overall survival (OS) benefit for African-American men with mCRPC treated with sipuleucel-T (Provenge).

The study involves a comparison of PSA-matched cohorts of 438 Caucasian men compared to 219 African-American men with mCRPC treated with sipuleucel-T. They found a statistically significant difference in median OS favoring African-Americans by 9.5 months. Further analysis revealed a much greater OS in favor of African-American men when men were split into two groups based on baseline PSA (≤29.48 and >29.48 ng/mL). African-American men with a low PSA (≤29.48) fared much better than their Caucasian counterparts by almost 21 months.

A multivariate analysis followed in an effort to identify baseline variables that were predictive of OS. A number of covariates were evaluated. African-American race was found to be independently associated with improved OS and had the strongest predictive value of all associated covariates.

This important analysis adds to a growing body of literature that helps refine our delivery of new therapies for mCRPC. Dr. Sartor stated in an interview with Urology Times that he tries to now direct African-American men with a baseline PSA <30 ng/mL toward sipuleucel-T based on the data. To take that a step further, if this analysis is confirmed by other researchers, given the cost of sipuleucel-T, should African-American men with a PSA less than 30 be preferentially offered this therapy over their comparison cohort? Given limited health care resources, should the therapy be restricted to those who will most likely benefit?

I believe that these are the types of questions that will have to be entertained as health care costs continue to skyrocket and integrated health care systems continue to consolidate. Finally, further studies will be required to evaluate an explanation for this racial disparity. Can this be explained by immunologic differences, pathophysiological differences, or possibly a statistical aberration based on sample size? While we may not currently have the answers, studies such as this one are continually needed to advance the field.
Clinical Updates

PROSTATE CANCER / Physical quality of life higher in active surveillance cohort, survey results indicate

Mental QoL similar in PCa patients opting for AS vs. definitive treatment

Jeni Williams
UT Correspondent

CHICAGO—A survey of low-risk prostate cancer patients found men who choose active surveillance over definitive treatment have similar mental health outcomes.

“This debunks the myth that active surveillance would cause undue anxiety due to untreated cancer in the body,” Christopher C. Randall, a second-year medical student at University of Arkansas for Medical Sciences in Little Rock, told Urology Times. A study by Randall and colleagues, presented at the AUA annual meeting in Chicago, sought to explore the impact of active surveillance on quality of life in men with low-risk prostate cancer.

Most men who are diagnosed with low-risk, localized prostate cancer choose immediate treatment, Randall says, including prostatectomy, radiation therapy, and hormone therapy. While these treatments are effective in treating the disease, they also cause side effects such as urinary incontinence, uncontrollable and painful bowel movements, and decreased energy. However, recent research shows the number of men who are opting for active surveillance is significantly increasing (JAMA 2019; 321:704–6).

The authors mailed surveys to 370 patients identified through the Arkansas Central Cancer Registry as having low-risk prostate cancer, following up by phone with patients who did not respond. The surveys consisted of the Veterans RAND 12-Item Health Survey and supplemental questions, including age at diagnosis, education level, the patient’s level of trust in his urologist, and the extent to which the patient was included in the treatment decision.

Then, the authors developed a multivariate regression model that adjusted for these variables to determine the impact of active surveillance on mental or physical health outcomes. Thirty-seven percent of patients responded to the survey.

“What was surprising is that just 57% of patients recalled being offered active surveillance,” said Randall, who worked on the study with Rodney Davis, MD, and colleagues. Among those who were offered active surveillance, 37% chose it as an initial management option. AS patients more likely to report better physical QoL

Patients who underwent active surveillance were 12 times more likely to report better physical quality of life than definitive-treatment patients, including general health, physical functioning (eg, moderate activities, climbing stairs), decreased role limitation (eg, limited in activities), and pain. This is likely due to the absence of treatment complications in this group.

They also scored higher on mental quality of life, but only one of the scores in this area—vitality—was statistically significant.

“The degree to which patients trusted their physician corresponded positively with their mental score,” Randall said. For example, patients who “strongly agreed” that they trusted their physician had higher average mental quality of life scores than those who did not.

Continued analysis of the results demonstrate better quality of life outcomes in low-risk prostate cancer patients electing active surveillance, Randall said.

PSMA PET/CT beneficial for PCa staging

John Schieszer
UT Correspondent

A new study suggests that prostate-specific membrane antigen positron emission tomography/computed tomography (PSMA PET/CT) may be a highly beneficial tool for initial staging of high-risk and high-intermediate-risk prostate cancer.

At the AUA annual meeting in Chicago, researchers reported that by adopting this imaging approach, it may be possible to alter treatment plans and provide more precise and appropriate interventions to avoid treatment failure. The authors found that judicious use of PSMA PET/CT can rule in or rule out lesions suspicious on conventional imaging.

“This is a huge advance. After pathology confirmation, I think the standard of care will be changed and this approach will be adopted.”

AYDIN POOLI, MD

They conducted a prospective, single-institution database study of patients undergoing PSMA PET/CT from 2016 to 2018 (NCT03368547).

The authors included men with intermediate-risk (Gleason score 7 and/or PSA 10–20 ng/mL) and high-intermediate-risk disease (Gleason score ≥8 and/or PSA ≥20 ng/mL) who underwent PSMA PET/CT within 3 months of conventional imaging (bone scan and/or abdominopelvic imaging). They analyzed the concordance of PSMA PET/CT with conventional imaging for the identification of N+ (pelvic lymph node), M1a+ (extrapelvic lymph nodes), M1b+ (bone metastases), and M1c+ (visceral metastasis) disease. They also examined the association between PSA level and concordance of conventional imaging and PSMA PET/CT.

PET/CT identifies up to 16.5% more disease

The current analysis included 182 patients (mean age, 65.5 years), and 72% had high-risk disease. Among these patients, the median PSA was 11.4.

See PSMA PET/CT page 7
Apalutamide efficacious in previously treated patients

Jeni Williams
UT Correspondent

CHICAGO—Researchers say the use of apalutamide (Erleada) in patients with high-risk, nonmetastatic castration-resistant prostate cancer improves metastasis-free survival (MFS) in patients who have previously undergone radical prostatectomy or external radiotherapy—regardless of the type of treatment they received.

A recent clinical trial showed the use of apalutamide in patients with high-risk nonmetastatic castration-resistant prostate cancer demonstrates a more than 2-year increase in MFS and a 55% reduction in time to symptomatic progression (N Engl J Med 2018; 378:1408-18).

“At the beginning of the study, we thought men who had undergone prior therapy would have better outcomes.”

BORIS A. HADASCHIK, MD

In the current study, presented at the AUA annual meeting in Chicago, researchers sought to determine whether treatment with apalutamide, a next-generation androgen receptor inhibitor, provided the same benefit and safety profile in patients who had previously undergone radical prostatectomy and/or external radiotherapy as it does in those who have not.

The authors, from multiple institutions, separated patients randomly into two groups: those who received apalutamide (240 mg once per day) and androgen deprivation therapy (ADT) and those who received a placebo and ADT. The apalutamide-plus-ADT group was about twice as large as the ADT-and-placebo group. Forty-one percent of patients in each group (334/806 apalutamide; 166/401 placebo) had undergone radical prostatectomy or external radiotherapy—regardless of the type of treatment they received.

Aldosterone: A Guide to Understanding

The use of prior therapy did not impact patients’ outcomes, researchers report.

“MFS on conventional imaging is a bit of an artificial endpoint for prostate cancer trials. All patients are still being followed for overall survival, and updated results of the SPARTAN study will be presented at ESMO,” Dr. Hadaschik told Urology Times.

The FDA’s approval of apalutamide for treatment of nonmetastatic castration-resistant prostate cancer represents the first use of MFS as a primary endpoint to support drug approval. Apalutamide is also the first drug approved to treat nonmetastatic castration-resistant prostate cancer.

Janssen Research & Development provided funding for the study.

PSMA PET/CT

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(6.8-24.1) ng/mL. The authors found the rate of non-concordance between PSMA PET/CT and conventional imaging was 22.2% for N+, 9.7% for M1a+, 16.9% for M1b+, and 1% for M1c+ disease. Dr. Pooli said PSMA PET/CT identified between 8% and 16.3% more disease and it potentially ruled out between 1.7% and 11.5% of disease.

“Conventional imaging is picking up some stuff that is not metastasis, but suspicious lesions. That can lead to biopsy, but PSMA can actually...”

stage these,” Dr. Pooli said in an interview with Urology Times.

He said the guidelines for primary staging of prostate cancer recommend abdominopelvic cross-sectional imaging and a bone scan for high-risk and high-intermediate-risk disease and cross-sectional imaging for intermediate-risk disease with high enough suspicion for metastasis. However, Dr. Pooli said the sensitivity and specificity of those imaging techniques are relatively low.

PSMA detected metastatic pelvic lymph nodes in 51 patients compared to 32 patients receiving conventional imaging. It also detected extrapelvic lymph nodes in 16 patients compared to five receiving conventional imaging. It detected bone metastasis in 17 patients compared to 22 patients receiving conventional imaging. Dr. Pooli said in terms of pelvic lymph nodes, PSMA detected 29 patients with metastasis that were missed on conventional imaging and did not confirm suspicious lesions in 10 patients.

Dr. Pooli said this is the largest cohort of patients with PSMA PET/CT for initial staging of prostate cancer and if validated in future investigations, it could lead to improved care.

“This can be a one-stop shop for these patients,” Dr. Pooli said. “We can get a whole-body scan, which is very sensitive for prostate cancer. It could be cost-effective.”
Salvage LND may help delay recurrence

Jeni Williams
UT Correspondent

CHICAGO—A preliminary study of the use of salvage lymph node dissection in patients with nonmetastatic, castration-resistant prostate cancer indicates the potential to delay disease recurrence as well as the use of systemic therapies through this approach.

However, more research is needed to confirm the results—specifically, multicenter studies with a larger cohort, says Luca Boeri, MD, of Mayo Clinic, Rochester, MN, who presented the results at the AUA annual meeting in Chicago.

“For sure, it is like a rock in a lake, but it is worth exploring,” Dr. Boeri told Urology Times.

Nonmetastatic, castration-resistant prostate cancer is a relatively indolent disease, and there is no high-quality evidence to guide clinical decision-making. Currently, the standard of care for patients with this disease is androgen deprivation therapy (ADT). Patients who do not exhibit evidence of bone or visceral metastases are typically managed with observation or ADT.

The AUA study sought to determine whether salvage lymph node dissection could slow disease progression and postpone the use of systemic therapies in men with node-only recurrence.

Dr. Boeri, working with R. Jeffrey Karnes, MD, and colleagues at Mayo Clinic, conducted a retrospective analysis of patients with node-only recurrence who were treated with salvage lymph node dissection or systemic therapies from January 1990 through January 2016. These patients underwent a positron emission tomography/computed tomography scan and conventional imaging to detect possible metastases (detected at 11C-choline PET/CT).

Among the patients in this cohort, 23 (51%) underwent salvage lymph node dissection for lymph node-only recurrence of castration-resistant prostate cancer and 22 (48.9%) received systemic therapies (ADT or chemotherapy) for lymph node-only recurrence of castration-resistant prostate cancer.

ADT patients were treated with a different medication—either alone or in combination with the previous ADT drug used—based on the physician’s discretion. All salvage lymph node dissection procedures were performed by a single surgeon between Nov. 1, 2009 and Dec. 31, 2016.

Biochemical recurrence was defined as a PSA greater than 0.2 ng/mL with an increased trend, while radiologic recurrence was defined as a positive imaging study or biopsy-proven metastasis after salvage lymph node dissection or systemic therapies. The Kaplan-Meier method was used to assess time to biochemical recurrence, radiologic recurrence, and cancer-specific mortality. Predictors of biochemical recurrence and radiologic recurrence were assessed via Cox regression analyses. Median follow-up for the entire cohort was 49.3 months.

The results point to the potential for salvage lymph node dissection to be used as a treatment option in men with node-only recurrence of castration-resistant prostate cancer:

• Mean PSA reduction was significantly higher after salvage lymph node dissection than after ADT (62.8% vs. 17.4%).
• Time to PSA nadir was significantly lower in the salvage lymph node dissection group than the ADT group (1.6 months vs. 7.3 months).
• The 5-year cancer-specific mortality rates were 72.7% and 72.3% for salvage lymph node dissection and ADT patients, respectively.
• There was a trend toward longer time to biochemical recurrence (13.3 months vs. 6 months) and radiologic recurrence (21.1 months vs. 14.2 months) in salvage lymph node dissection patients than ADT patients.
• Median time to standard systemic therapy was longer in the salvage lymph node dissection group than that ADT group (66.1 months vs. 43.3 months).

However, one limitation of the study—in addition to the small sample size—is that the results are based on traditional imaging techniques.

“An important dilemma arises if there is room for metastasis-directed therapy for oligorecurrent castrate-resistant prostate cancer detected on advanced imaging,” Dr. Boeri said.

Data support role for salvage LND

BPH

Durability of BPH treatments varies widely

Cheryl Guttmann Krader
UT Correspondent

The long-term durability of surgical modalities for management of BPH varies significantly, findings from a retrospective study suggest.

The study, presented at the AUA annual meeting in Chicago, included 4,985 men who underwent laser vaporization of the prostate (LVP), transurethral resection of the prostate (TURP), or simple prostatectomy (SP) as surgical management for BPH at a Cleveland Clinic location between 2001 and 2016. Of those men, 419 (8.4%) underwent a subsequent endoscopic operation at least 90 days after their index surgery.

Analyses of procedures for each procedure showed that LVP was associated with the highest long-term reoperation rate (268/2,549, 10.5%) followed by TURP (148/2,304, 6.4%). The lowest rate of reoperation was observed among men who underwent SP (5/132, 2.3%).

“We believe that our findings on relative durability of the various surgical options for BPH represent information that can be useful for patient counseling.”

BRADLEY C. GILL, MD, MS

A Kaplan–Meier survival analysis showed there was a statistically significant difference among the procedures in retreatment-free survival (p<.0001). In addition, findings from a Cox proportional hazards regression analysis that adjusted for between-group differences in baseline demographic and clinical characteristics found that primary BPH surgical modality was the only variable that was independently associated with need for repeat surgery, reported Bradley C. Gill, MD, MS, associate staff, department of urology, Cleveland Clinic.

“Variability in the durability of benefit after BPH surgery is an important issue to understand in the current era where the cost of health care is under the microscope, reimbursement is changing, and the population of men presenting for management of BPH is growing because of our aging population. Clinical trials, however, generally report only short-term or intermediate-term outcomes,” Dr. Gill told Urology Times.

“Although our study has some limitations and the shared decision-making process should also factor in other considerations, we believe that our findings on relative durability of the various surgical options for BPH represent information that can be useful for patient counseling.”
Waterjet ablation shows same efficacy in small, large prostates

Cheryl Guttman Krader
UT Correspondent

Data from prospective clinical trials show that the efficacy of high-velocity waterjet ablation (AquaBlation using the AquaBeam System) for improving BPH-related signs and symptoms is the same in patients with a large-to-very large prostate as in men with a small-to-moderate size gland, said Naeem Bhojani, MD, at the AUA annual meeting in Chicago.

He presented data from follow-up to 12 months for men treated with waterjet ablation in the Waterjet Ablation Therapy for Endoscopic Resection of prostate tissue (WATER) and WATER II studies. WATER randomized men ages 45 to 80 years with a prostate between 30 cc and 80 cc to treatment with waterjet ablation or transurethral resection of the prostate (TURP). WATER II is a single-arm study, investigating the procedure in men with a prostate between 80 cc and 150 cc.

Dr. Bhojani reported that improvements in the International Prostate Symptom Score (IPSS) and maximum urinary flow rate (Qmax) after waterjet ablation occurred soon after the procedure and were similar in the WATER and WATER II studies. Treatment of men with large-to-very-large glands (WATER II) was not associated with a significant increase in mean operative time or patient length of stay. Waterjet ablation also had an acceptable safety profile in WATER II.

“There are limited surgical options for treating men with large prostates who are bothered by lower urinary tract symptoms related to BPH. Results from WATER and WATER II show that clinical outcomes for these patients can be normalized independent of prostate size,” said Dr. Bhojani, associate professor of urology, University of Montreal.

WATER II was undertaken based on the findings of a prespecified subset analysis of data from WATER that focused on men with a prostate volume >50 cc. Results showed that compared with the overall population, differences in efficacy endpoints favoring waterjet ablation over TURP were even greater among men with larger glands, and the rate of persistent Clavien-Dindo grade 1 or 2 events was slightly lower.

The analyses comparing outcomes from men treated in WATER and WATER II included data for 116 men enrolled in WATER and 101 participants from WATER II. The two groups of men were similar in their mean age and mean body mass index. Mean prostate volume was 54 cc for men in WATER and 107 cc for the WATER II cohort, and the middle lobe represented 50% of prostate volume for men in WATER and 83% of prostate volume for men in WATER II. There were no statistically significant differences between the two groups in mean baseline IPSS, Qmax, or scores on the MSHQ-EJD or IIEF-5 (SHIM) questionnaires.

Data for procedure outcomes in WATER and WATER II showed significant differences in mean resection time (3.9 vs. 8.8 minutes) and number of passes (1.1 vs. 1.8), but not in mean operative time (32.9 vs. 37.4 minutes). In both studies, men were discharged at approximately 1.5 days after the procedure. Mean days with a catheter were significantly longer for men in WATER II compared with WATER (3.9 vs. 2 days).

At 3 months after waterjet ablation, prostate volume was reduced from baseline by a mean of 31% in WATER and 44% in WATER II. Efficacy data showed that men treated with waterjet ablation in WATER and WATER II achieved similar improvements over time in IPSS, storage, voiding, and quality of life scores. The two groups of men also had similar improvement in Qmax and similar reduction in postvoid residual urine volume. The retreatment rate at 12 months was 2.6% for the men in WATER, and no men in WATER II had been retreated.

Not unexpectedly, rates of Clavien-Dindo grade 1, 2, 3, and 4 complications were higher among men treated with waterjet ablation in WATER II. Notably in the WATER II study, the rate of de novo incontinence was low (2%), no men developed erectile dysfunction, and the rate of ejaculatory dysfunction was only 19% even in patients with gland sizes up to 150 cc.

“The fact that even in a group of men with gland sizes up to 150 cc, 81% of patients maintained an- grade ejaculation is very interesting considering that antegrade ejaculation is essentially universal- ly lost after other surgical procedures for BPH,” Dr. Bhojani told Urology Times. Dr. Bhojani is a consultant to PROCEPT BioRobotics, which provided funding for the study.

BPH TREATMENTS
continued from page 8

Having an electronic medical record system that dates back over a decade and a regional health care system capturing a large and diverse patient population provided an excellent opportunity to study the durability of BPH surgeries, said Dr. Gill.

The study population had a median follow-up of 26.5 months. For men who had a reoperation, the median interval between the primary and subsequent surgery was 19.5 months.

SP patients 72% less likely to need reoperation

The Cox proportional regression analysis found that compared to men who underwent LVP, men were 28% less likely to need a reoperation if they had TURP as their index surgery and 72% less likely if they underwent SP. Patient age, smoking history, and various comorbidities did not predict risk of reoperation.

Dr. Gill acknowledged that the findings of the research need to be interpreted with its limitations kept in mind. He noted that the technology for LVP evolved greatly over the study period, meaning that the reported reoperation rate for the procedure represents all generations of the laser.

More importantly, the regression analysis did not account for certain factors that may be associated with longevity of benefit such as prostate size or procedure duration, baseline symptom severity, and baseline flow rate or urinary function.

“On the other hand, our study did not select patients based on specific characteristics. Thus, our population represents a fairly heterogeneous group of men undergoing surgery for management of BPH, and that may improve the generalizability of its results,” Dr. Gill said.
Urethral lift efficacious in real-world setting

Cheryl Guttmann Krader
UT Contributing Editor

A study evaluating outcomes of the prostatic urethral lift (PUL [UroLift System]) in clinical practice shows that the efficacy and safety documented in the selected group of men enrolled in clinical trials is maintained across the broader spectrum of patients who present for treatment of symptomatic BPH in the real-world setting.

The findings from the retrospective chart review were published in the Journal of Endourology (2019; 33:576-84). The analyses included 1,413 consecutive patients who underwent PUL across 14 sites in the United States and Australia. Within the retrospective study cohort, 165 men were in urinary retention at the time of their procedure. The population also encompassed patients with baseline characteristics that would have excluded them from participation in the premarketing clinical trials; ie, age <50 years, prostate volume <30 cc or >80 cc, moderate symptoms (International Prostate Symptom Score [IPSS] <13), and history of prostate cancer.

Douglas Grier, MD, who is in private practice at Sound Urological Associates, Edmond, WA, is a study co-author and principal investigator. He told Urology Times, “Results from large controlled clinical trials demonstrate the safety and efficacy of PUL for improving symptoms related to BPH. To our knowledge, this is the first report evaluating outcomes with any BPH device technology within a real-world setting. Its results show PUL is a versatile tool that benefits of PUL were achieved regardless of age, prostate volume (<30 cc vs. ≥30 cc and <80 cc vs. >80 cc), site of service (clinic office, hospital, ambulatory surgery center), prior cancer treatment, diabetic status, and body mass index.

Among men who were not in urinary retention who underwent PUL at a site where placement of a urinary catheter was not standard of care, 84% required no catheter. Considering all men who were not in urinary retention who received a catheter, rates of catheter independence were 90% at 48 hours, 94% at 5 days, and 98% at 1 month. For patients who were in urinary retention at the time of PUL, 60% were catheter-free at day 5 after PUL, 88% at 1 month, and 87% at the end of the study.

The safety review found that patients who had the procedure done in a clinic office experienced fewer side effects and had a lower rate of catheter placement than groups that had the procedure done at another type of service site. A history of TURP had the patients evaluated for TURP. A single patient who did not undergo another surgical intervention had the PUL implant removed.

Dr. Grier said that a prospective study is being planned with the aim of trying to better characterize different subgroups of BPH patients to see if the benefits of PUL and the durability of its results vary depending on pretreatment factors, including age, prostate volume, presence of median lobe involvement, prior treatment for prostate cancer, history of TURP, or presence of diabetes and other comorbidities.

Separately, data reported at the AUA annual meeting in Chicago indicate that magnetic resonance imaging artifacts in men who have undergone PUL should not affect urologists’ ability to diagnose prostate cancer in these patients.

Researchers evaluated 10 men who underwent PUL. A standard multiparametric MRI protocol using a 3T scanner was performed before PUL and repeated 1-3 months after the procedure. The images generated were compared to a separate database of 225 consecutive MR-guided biopsies.

The authors found that for the men undergoing PUL, MRI artifacts were confined to the posterior transitional zone of the prostate. No artifacts were observed in the peripheral or anterior zones. “In the series of 225 consecutive MR-guided biopsies, no cancer was found in the posterior transitional zone, which is the only area that the UroLift causes artifact,” reported Peter Chin, MD, associate professor of urology at Wollongong Private Hospital, Wollongong, Australia.

Dr. Grier is a consultant to NeoTract/Teleflex, as are several of his co-authors. NeoTract/Teleflex provided funding for study discussed by Dr. Grier.

BLADDER CANCER / Combination treatment has potential to become standard of care, expert says

PD-L1 inhibitor plus chemo improves PFS

Lisette Hilton
UT Correspondent

Treatment combining the immunotherapy atezolizumab (Tecentriq) and platinum-based chemotherapy significantly improved progression-free survival in patients with previously untreated locally advanced or metastatic urothelial carcinoma compared to chemotherapy alone.

Adding atezolizumab, a monoclonal antibody that binds with programmed death ligand 1 (PD-L1), also appears to improve overall survival in these patients but the data are not yet mature, according to a statement from Roche on atezolizumab’s phase III IMvigor130 study.

One expert in the field called the results “exciting” when discussing the announcement with Urology Times.

IMvigor130 is a multicenter trial of 1,213 patients with metastatic urothelial carcinoma who have not received prior systemic therapy who were randomized to receive atezolizumab plus gemcitabine with either cisplatin or carboplatin; atezolizumab alone; or platinum-based chemotherapy with gemcitabine and either cisplatin or carboplatin plus placebo. Roche will...
**BLADDER CANCER / 89% complete response rate reported for carcinoma in situ patients**

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**Novel immunotherapy promising in BCG-unresponsive NMIBC**

Dave Levitan  
UT Correspondent

**CHICAGO—**The combination of an IL-15 cytokine agonist known as N-803 and bacillus Calmette-Guerin (BCG) was well tolerated and offered promising activity in patients with nonmuscle-invasive bladder cancer (NMIBC) who did not respond to BCG therapy, according to phase I and II study results.

“These are exciting preliminary results for patients with BCG-unresponsive disease. We do need further follow-up. If further follow-up confirms these findings, then this would represent a breakthrough,” Sam S. Chang, MD, MBA, professor of urologic surgery and oncology and vice-chair of urologic surgery at Vanderbilt University Medical Center in Nashville, TN, told Urology Times.

Dr. Chang presented the phase II study data at the AUA annual meeting in Chicago.

Treatment options for patients with NMIBC who have a recurrence or relapse after BCG therapy are limited. If patients fail to respond to BCG, they eventually often require cystectomy, which carries substantial morbidity and mortality risk.

N-803 is a first-in-class IgG1-Fc IL-15 cytokine agonist, its mechanism involving activation of the innate and adaptive immune systems could potentially rescue the immune response in BCG-unresponsive disease. BCG uptake into bladder cancer cells causes the cells to present antigens and to produce immune-stimulating cytokines; in unresponsive disease, BCG alone does not trigger enough of a response. N-803 mimics the trans-presentation of IL-15, which can selectively induce CD8+ T cells and natural killer cells and thus boost the immune response.

In a previous report, a phase I trial of N-803 in combination with BCG showed a similar safety profile to that of BCG alone, with adverse events that included hypertension, hematuria, and pollakiuria. All nine patients in that cohort had a durable complete response, and all nine were disease free at 24 months. During his presentation of phase II results at the AUA annual meeting, Dr. Chang noted that BCG alone typically has a response rate of 35% to 73% at 3 to 6 months.

The phase II trial was a single-arm, open-label trial combining intravesical N-803 and BCG. At the time of data cutoff, 35 patients had been enrolled in a cohort of carcinoma in situ (CIS) patients, and 18 were evaluable for response. Of those, 16 had complete responses (89%); 31 of the 35 patients remained on the treatment.

In a second cohort of 27 patients with high-grade Ta/T1 papillary NMIBC, there was a 6-month recurrence-free survival rate of 77% (10 of 13 evaluable patients). In that cohort, 23 of 27 patients remained on the treatment.

A safety analysis included all 62 patients enrolled to date; again, the adverse events appeared similar to those typically associated with BCG monotherapy. There were five serious adverse events, including two in the CIS group and three in the papillary cohort; all were determined to be unlikely to be related to the combination of N-803 and BCG.

“This combined therapy’s overall morbidity is very attractive. It does not require IV or subcutaneous injection. It does not require any other monitoring. And it follows a treatment course that urologic surgeons are quite familiar with,” Dr. Chang said.

He added that the trial is ongoing, with a target enrollment of 160 total patients. Other trials testing N-803 in other malignancies and in combination with other therapies are also ongoing.

Dr. Chang is a consultant for Altor BioScience, which funded the study.

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**PD-L1 INHIBITOR**

continued from page 10

be sharing specific trial results with the FDA and other global health authorities, the company said.

“The interim analysis is clearly exciting and the approach is valid. This opens up the opportunity for using immunotherapy in a broader group of patients—even those who can tolerate chemotherapy.”

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Badrinath Konety, MD, MBA

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“Triple-negative breast cancer. In 2017, atezolizumab failed a phase III trial in advanced bladder cancer when results didn’t show it could prolong patients’ lives. This was after phase II data showed a durable response to the drug. Dr. Konety, who is not an investigator with Roche, said the news dampened enthusiasm for atezolizumab and other PD-L1 inhibitors for advanced bladder cancer at the time. But these new phase III data are again encouraging because they show a clear synergistic benefit of immunotherapy and chemotherapy over standard of care.

“Of course, this is still the interim analysis. We don’t have a final analysis yet,” Dr. Konety said.

Atezolizumab is among several immunotherapy agents approved for advanced bladder cancer and being studied in various bladder cancer patient types.

Urologists will be involved in the use of PD-1 and PD-L1 immunotherapy medications in the context of neoadjuvant chemotherapy, before surgery, as well as for nonmuscle-invasive bladder cancer, particularly because bacillus Calmette-Guerin is in short supply, according to Dr. Konety. Positive phase III data might signal a paradigm shift for management of nonmuscle-invasive bladder cancer, he said.

Dr. Konety is a clinical trial investigator for Merck and Bristol-Myers Squibb.
BLADDER CANCER / Risk-stratified approaches could improve value of care, researcher says

Harms of ‘one-size-fits-all’ hematuria evaluation outweigh benefits

Cheryl Guttman Krader
UT Contributing Editor

A simulation study analyzing the harms, advantages, and costs associated with different guideline recommendations for initial evaluation of hematuria found that no approach diagnoses every cancer and suggest that the incremental costs and radiation-associated harms occurring with the most intensive recommendation, which advocates a one-size-fits-all approach with computed tomography scanning, may outweigh marginal benefits in terms of diagnostic yield, said Matthew E. Nielsen, MD, MS.

“The variability in recommendations and our study’s findings highlight implicit value judgments and a potentially high burden of harms not historically considered in many guidelines’ development process,” he added. “Urologists may want to consider discussing with patients the relative benefits and harms associated with different approaches and potentially consider applying risk-stratified approaches that focus the most intensive testing on the highest risk patients as a way to improve the value of care for this patient population.”

For the analysis, which was published online ahead of print in JAMA Internal Medicine (July 29, 2019), a microsimulation model was developed to assess urinary tract cancer detection rates, radiation-induced secondary cancers from CT radiation exposure, procedural complications, false-positive rates per 100,000 patients, and incremental cost per additional urinary tract cancer detected for a hypothetical 100,000-patient cohort evaluated according to the recommendations from five different guidelines.

The guidelines evaluated were (listed in order of increasing intensity) the Dutch, Canadian Urological Association, Kaiser Permanente, Hematuria Risk Index, and the AUA. The characteristics of the patient cohort were derived using data from the two largest published series of patients undergoing evaluation for hematuria and included subsets with gross hematuria as well as microscopic hematuria. All patients were assumed to be 35 years of age and older.

Diagnostic yields for bladder cancer, renal cell carcinoma (RCC), and upper-tract urothelial cancer (UTUC) were considered separately and as a function of which patients would undergo cystoscopy and imaging and with which modality. Real-world data on CT radiation doses were used to account for variations that exist in clinical practice.

Fewest cancers missed by following AUA guidelines

The results showed that the number of cancers missed with each guideline varied inversely with the intensity of their recommended evaluation. The fewest number of cancers was missed by following the AUA guidelines, which was the most intense, recommending cystoscopy and CT urography for all patients aged 35 years and older.

Considering the three guidelines that make recommendations on using CT urography, the projected number of radiation-induced cancers was highest for the AUA guidelines, and its cost was approximately twofold greater than that of any of the other guidelines. Compared to the Hematuria Risk Index, which lies immediately below the AUA guideline in the intensity of its recommended evaluation, the AUA guideline was associated with an incremental cost of more than $1 million per urinary tract cancer detected.

Dr. Nielsen noted there has been limited evidence about the relative harms, advantages, and costs of different diagnostic approaches for evaluating patients with hematuria. Although cost-effectiveness analyses have been undertaken previously, their methods had several limitations. Specifically, the previous studies focused on patients with asymptomatic microscopic hematuria, one study’s model did not separate diagnostic yields of the different imaging modalities for RCC and UTUC, and the previous research did not account for real-world variation in CT doses.

“Studies of this nature reflect simplified representations of reality with limitations noted in the paper. However, we believe our approach provides a lens through which clinicians may consider more explicitly the tradeoffs of different approaches with the ultimate goal of optimizing these tradeoffs for the benefit of our patients,” Dr. Nielsen said.

“Studies of this nature reflect simplified representations of reality with limitations noted in the paper. However, we believe our approach provides a lens through which clinicians may consider more explicitly the tradeoffs of different approaches with the ultimate goal of optimizing these tradeoffs for the benefit of our patients,” Dr. Nielsen said.

In Brief

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STUDY: MUSHROOM CONSUMPTION MAY LOWER RISK OF DEVELOPING PROSTATE CANCER

A new study has found an inverse relationship between mushroom consumption and the development of prostate cancer among middle-aged and elderly Japanese men.

A total of 36,499 men, aged 40 to 79 years, were followed for a median of 13.2 years. During follow-up, 3.3% of participants developed prostate cancer. Compared with mushroom consumption of less than once per week, consumption once or twice per week was associated with an 8% lower risk of prostate cancer and consumption three or more times per week was associated with a 17% lower risk.

“Since information on mushroom species was not collected, it is difficult to know which specific mushroom(s) contributed to our findings. Also, the mechanism of the beneficial effects of mushrooms on prostate cancer remains uncertain,” said lead author Shu Zhang, PhD, of the Tohoku University School of Public Health in Japan. The results were published in the International Journal of Cancer (Sept. 4, 2019 [Epub ahead of print]).
Doctors discussing ‘moral injury’ need different mindset

As for burnout, burnout is the great Dr. Charles van der Horst whose parents survived Hitler’s Germany. He was a pioneer in the treatment of HIV and nearly committed suicide due to the despair of seeing so many young men die of a disease the nation refused to acknowledge. Burnout is my colleagues in Haiti delivering 1,200 babies and treating 700 HIV patients on a budget that continues to shrink. Burnout is our psychiatric colleagues treating addiction with jail time.

In response to the rising issue of burnout or moral injury, I would advise my colleagues to speak softly because, my studies show, nobody is gonna care, you’re making a lot of money, you have a lot of stuff and you’re still pretty much in control. As in, I am certain my receptionist would be happy to swap positions in life. The proper response to the physician version of moral injury is, to quote Natasha Romanoff of “The Avengers,” “cognitive recalibration.” We need to think differently.

I’ve pretty much given up on patient satisfaction because, I’m not here to make them happy, I’m not their friend I’m their advocate. Want a friend, go to the bar. I don’t answer emails because I’m not paid to answer emails, you want to talk about your findings, make an appointment.

As for Epic, I’ll do as little as I can, maybe less. And I’ll continue with my radio show, I got a new idea for a video deal I’ll bet fails. I quit the country club. My kids are in public school. My 12 year old Suburban is paid for and I’m gonna drive a Honda Civic. I don’t own a Rolex. And, I’m working and I’m happy to help. 

I have the privilege of working every day with these thoughtful, intelligent, principled, and hard-working young men and women. None are worried about a Rolex or a Porsche. Nothing could be farther from the truth. They (and all of my colleagues) are worried about how to best care for patients. And, they have to accomplish this while overcoming the structural and operational barriers that exist to fulfill this moral and ethical obligation. They don’t have the luxury of taking Fridays off, buying a MINI Cooper, or planning the next storyline for a radio or TV deal. Or, certainly, despite our struggles with EHRs, most of us are not doing “as little as possible” with Epic notes and tasks.

We are here to do everything to take the best care for our patient and their family—even answer emails, write thoughtful and complete Epic notes, and respond to in-baskets. And, importantly, we are here to befriend a suffering patient who needs compassion, empathy, and genuine interest—what used to be called “bedside manner.”

Moral injury is a serious issue that is truly national, complex, and systemic—with effects beyond physicians—including impacts on patients and with truly societal implications.
The UroLift System procedure is FDA-cleared for the treatment of symptoms due to urinary outflow obstruction secondary to BPH, including lateral and median lobe hyperplasia, in men 45 years of age or older. Results and patient experience may vary. Most common adverse events reported include hematuria, dysuria, micturition urgency, pelvic pain, and urge incontinence. Most symptoms were mild to moderate in severity and resolved within 2 to 4 weeks after the procedure. Consult the Instructions for Use (IFU) for more information.

Dr. Walter is UroLift faculty and a paid consultant for NeoTract Teleflex.

1. LIFT study showed an IPSS reduction of 47% at 1 year. Roehrborn, J Urology 2013
2. Roehrborn, J Urology 2013
3. No instances of new, sustained erectile or ejaculatory dysfunction.

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Antiandrogens may increase mortality risk in men with CVD

Patients with CVD taking abi or enza have 43% higher risk of hospitalization

Advanced prostate cancer and cardiovascular disease often coexist in older men. Over the last 5 years, new second-generation antiandrogens, namely abiraterone (ZYTIGA) and enzalutamide (XTANDI), are being used with more frequency in men with advanced prostate cancer. Patients with significant cardiovascular disease (CVD) are often excluded from clinical trials for reasons that are understandable. But in clinical practice, the excluded patients are often the ones treated with those same medications.

A new study suggests that newer antiandrogens may increase the risk of early mortality and hospitalization, especially in men with known CVD such as myocardial infarction, atrial fibrillation, congestive heart failure, stroke, or ischemic heart disease (Eur Urol Aug 2, 2019 [Epub ahead of print]).

Lu-Yao and colleagues used the Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked files (representing nearly 31% of the U.S. population) to identify men with prostate cancer who had received chemotherapy and abiraterone or enzalutamide. A total of 3,876 patients were eligible for the study, including 2,845 treated with abiraterone and 1,031 treated with enzalutamide. The main goal of the analysis was to determine the mortality rate within 6 months after starting therapy with these two antiandrogens. They also wished to determine the risk of hospitalization after the initiation of antiandrogen therapy.

Interestingly, 67% of the eligible patients had one or more documented CVD before receiving abiraterone or enzalutamide. In the post-chemotherapy group of patients being treated with abiraterone, 24% died within 6 months, compared with 17% in the pivotal trial that led to its approval. Among patients being treated with enzalutamide, 28% died within 6 months, compared with 12% in the pivotal trial. In the group without chemotherapy, 18% of patients died within 6 months of starting abiraterone and 17% died within 6 months of starting enzalutamide.

In the post-chemotherapy cohort receiving either abiraterone or enzalutamide, there was no significant difference in hospitalization rates between the two drugs. However, those with one or two CVDs had a 43% increased risk of hospitalization compared to those with no CVDs.

The subjects of this study had also received androgen deprivation therapy, which is associated with developing CVDs.

Higher hospitalization rate in abi patients with no chemo

In the group without chemotherapy, abiraterone was associated with a higher rate of hospitalization than enzalutamide among patients with one or more CVDs. In this group, hospitalization rate was higher with abiraterone use even in the patients with no history of CVD.

As stated by the authors, the worse outcomes (cardiovascular toxicity and/or mortality) following the use of abiraterone have been reported by previously published meta-analyses. In the STAMPEDE trial, the addition of abiraterone was associated with improved cancer-free-survival but no real improvement in overall survival, likely due to increased cardiovascular mortality. It appears that abiraterone is associated with worse outcomes even if there is no documented chemotherapy or CVDs. However, without direct comparison, we cannot suggest that one drug is superior to the other. Other antiandrogens such as apalutamide (Erleada) and darolutamide (Nubeqa) have been approved recently and the use of antiandrogens has been moving “upfront,” eg, before chemotherapy and without metastases. This will likely result in increased use of drugs in this class, making the issue of adverse outcomes even more relevant.

The usual limitations of a retrospective analysis apply to this study as well. The data do not allow for a comparison with an appropriate control group that did not receive abiraterone or enzalutamide, or direct comparison. However, the Medicare-linked SEER data represent a broad cross-section of the population that is afflicted with prostate cancer and CVDs, which makes the information presented here quite pertinent for most clinicians.

The phenomenon of worse outcomes in the real-world setting after the initial approval of a drug or device has been well documented. Clinicians often loosen the criteria beyond what was allowed in the clinical trials, exposing the patients to a host of drug-drug or drug-disease interactions.

The subjects of this study had also received androgen deprivation therapy, which is associated with developing CVDs. Is it possible that these subjects were primed, through previous use of ADT, for worse outcomes following the addition of abiraterone and enzalutamide? The unique contribution of these second-generation antiandrogens to cardiovascular mortality is not entirely clear.

Several professional organizations are offering workshops geared towards incorporating these and other oral anti-cancer agents into the practice of urology. Hopefully, the educational activities will sufficiently emphasize a more careful selection of patients for these drugs. There is clear impetus for a multidisciplinary program to monitor the treatment and adverse outcomes of newer antiandrogens which, at present, may be out of the comfort zone of many urologists.
SEXUAL DYSFUNCTION

Penile prosthesis offers durability, natural feel
Boston Scientific recently launched the Tactra Malleable Penile Prosthesis in the U.S. for the treatment of erectile dysfunction. Approved by the FDA earlier this year, the prosthesis utilizes natural-feeling dual-layer silicone and includes a Nitinol core to optimize comfort, rigidity, and durability for effective penetration and concealment, the company says. The implant is manually lifted up for intercourse and manually pushed down when not in use. New design features of the Tactra Penile Prosthesis allow physicians to provide patients unable to take oral medications or who are ineligible/uninterested in an inflatable penile prosthesis with a device to help restore their sexual function with excellent rigidity and dependable concealment in a device that is easy to use and natural to the touch, according to Boston Scientific.

For more information, visit www.bostonscientific.com.

Enteric-coated formulation of cystinuria Tx approved
Retrophin, Inc. recently announced the FDA approval of 100-mg and 300-mg tablets of tiopronin (THIOLA EC), a new enteric-coated formulation of tiopronin (THIOLA) to be used for the treatment of cystinuria. The recommended initial dosage of tiopronin in adult patients is 800 mg per day, and in clinical studies the average dose of tiopronin was approximately 1,000 mg, or 10 pills per day, according to the company. The original formulation of THIOLA 100 mg is recommended to be administered at least one hour before or two hours after meals. THIOLA EC 100-mg and 300-mg tablets are recommended to be administered with or without food. THIOLA EC tablets were approved through the 505(b)(2) regulatory pathway, which allows the FDA to reference previous findings of safety and efficacy for an already-approved product, combined with reviewing findings from further studies of the product.

For more information, visit www.retrophin.com.

FDA approves new combination antibacterial for UTI
The FDA has approved imipenem, cilastatin, and relebactam (RECARBrio) for injection, 1.25 grams, a new combination antibacterial. The treatment is indicated in patients 18 years of age and older who have limited or no alternative treatment options for the treatment of complicated urinary tract infections, including pyelonephritis, caused by limited or no alternative treatment options for the treatment of complicated urinary tract infections, including pyelonephritis, caused by the following susceptible Gram-negative microorganisms: Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella pneumoniae, and Pseudomonas aeruginosa.

For more information, visit www.merck.com.

Urologist-hosted podcast focuses on men's health
“`The Original Guide to Men’s Health” is a podcast hosted by urologist Richard S. Pelman, MD. It consists of 25- to 60-minute episodes that serve as a gateway and resource for men of all ages to learn what they should know about their biology and health, how and when to access the health care system, and what they can do to achieve and manage good physical, mental, and reproductive health. Notable episodes include “Testosterone—Myths, Facts, and Everything in-Between;” “BPH—Three Letters that Impact Every Guy;” and “Understanding and Navigating the Health Insurance System.”

For more information, visit bit.ly/menshealthpod.

KIDNEY STONES

Hyperoxaluria agent shows substantial treatment effect
Allena Pharmaceuticals, Inc. recently announced interim data from Study 206, its phase II basket clinical trial of reloxaliase, an orally administered, recombinant oxalate-degrading enzyme. Study 206 includes adult and pediatric patients suffering from the progression of primary hyperoxaluria or enteric hyperoxaluria with advanced chronic kidney disease. Consistent with Allena’s prior clinical experience, enteric hyperoxaluria patients treated with reloxaliase in Study 206 demonstrated a substantial treatment effect. This includes enteric hyperoxaluria patients with advanced chronic kidney disease, a patient population not previously treated with reloxaliase, who showed reductions in urine oxalate and plasma oxalate. Treatment with reloxaliase was well tolerated in all patient populations, with no reported treatment-related serious adverse events, according to Allena.

Clinical registry launched for ED treatment
Urologist Judson Brandleis, MD, is launching the world’s largest clinical registry focusing on GAINSWave for erectile optimization. The Shock Wave Erectile Enhancement Trial (SWEET) Clinical Registry will utilize 50 top GAINSWave providers, led by Dr. Brandleis. GAINSWave is a marketing organization that educates consumers and raises public awareness for low-intensity shock wave therapy for erectile dysfunction. The primary goal of the SWEET Registry is to evaluate the efficacy of shock wave therapy across a wide group of participants, treating physicians, and shock wave protocols. Other targets of interest include identifying optimal treatment plans, identifying factors that predict superior outcomes, and quantifying long-term efficacy. AFFIRM Science, producer of the Nitric Oxide Boosting supplement, AFFIRM, and Premature Ejaculation supplement, PreLONG, is funding the initial stages of this prospective observational research study on shock wave therapy for erectile dysfunction.

Positive phase III data announced for PARP inhibitor
AstraZeneca and MSD Inc. announced positive results from the phase III PROfound trial of the PARP inhibitor olaparib (Lynparza) in men with metastatic castration-resistant prostate cancer (mCRPC) who have a homologous recombination repair gene mutation (HRKrm) and have progressed on prior treatment with new hormonal anticancer treatments (eg, enzalutamide [XTANDI] and abiraterone [ZYTIGA]). Study results showed a statistically significant and clinically meaningful improvement in the primary endpoint of radiographic progression-free survival with olaparib versus enzalutamide or abiraterone in men with mCRPC selected for BRCA1/2 or ATM gene mutations, a subpopulation of HRR gene mutations. The safety and tolerability profile of olaparib was generally consistent with previous trials. AstraZeneca and Merck said they plan to present full data from the trial at a forthcoming medical meeting.

Supplemental NDA submitted for prostate Ca treatment
The FDA has accepted for review the filing of a supplemental new drug application for enzalutamide (XTANDI) to add an indication for the treatment of men with metastatic hormone-sensitive prostate cancer, according to Astellas Pharma Inc. and Pfizer Inc. The application has also been granted priority review. Enzalutamide is currently indicated in the U.S. for the treatment of patients with castration-resistant prostate cancer. The submission is based on results from the phase III ARCHES trial presented at the Genitourinary Cancers Symposium and published in The Journal of Clinical Oncology (July 22, 2019 [Epub ahead of print]). Additionally, the submission is supported by data from ENZAMET, an Astellas-supported, investigator-sponsored phase III research study led by the Australian and New Zealand Urogenital and Prostate Cancer Trials Group and sponsored by the University of Sydney. Results from ENZAMET were presented at the American Society of Clinical Oncology annual meeting and simultaneously published in The New England Journal of Medicine (2019; 381:121-31). Both trials met their primary endpoint. The FDA has set a Prescription Drug User Fee Act date in the fourth quarter of 2019.
We have entered a renaissance in the care for patients with benign prostatic hyperplasia (BPH)-related lower urinary tract symptoms (LUTS). After 6 decades with our bread-and-butter monopolar transurethral resection of the prostate (TURP) or open prostatectomy, the early ‘90s ushered in pharmaceutical solutions that quickly dominated in uptake. The mid-‘90s and beyond saw the advent of laser fibers and vaporization electrodes for tissue removal, various heat sources for office-based tissue necrosis, and metal urethral stents to mechanically open the prostate, all with the goal of rendering interventional treatment less invasive. While lasers and bipolar electrodes have clearly converted most TURP procedures, the purportedly less invasive and tissue necrotic technologies (radiofrequency, microwave, interstitial laser, high-frequency ultrasound) have all but come and gone.

Now, 20 years later, we are enjoying another leap in innovation in office-based treatment of BPH. Tens of thousands of patients have been treated with steam injection, a new form of tissue ablation better known as Rezum, and with a new mechanical solution, the prostatic urethral lift (PUL, [UroLift]). Due to their growing uptake, several more technologies are in development in the quest for the truly minimally invasive surgical therapy (MIST). (Other technologies such as Aquablation and plasmakinetic and laser TURPs are not included in this article as they are hospital-based procedures.)

With such a resurgence in activity and with such rich history, it would behoove us as a specialty to review what the goals of MIST are, reach consensus on the appropriate metrics by which to measure them, and hold each new treatment to these metrics.

Why MISTS play important role
If the sole clinical goal in treating BPH was effectively eliminating bladder outlet obstruction, R&D would have concluded decades ago with the description of the suprapubic prostatectomy. No other treatment option has since been shown to more effectively unobstruct a prostate.

However, decades of highly dynamic medical technology and technique developments have occurred, as they have focused primarily on reducing morbidity associated with reducing obstruction. In 1926, Stern and McCarthy performed the first “minimally invasive alternative” to open surgery, transurethral resection of the prostate using the first direct-vision resectoscope. Now, 93 years later, nearly every manuscript published on BPH still asserts that TURP is the “gold standard.” Interestingly and ironically, our patients often do not agree.

Of the 12.4 million men in the U.S. with moderate to severe BPH, less than 2% choose TURP as their treatment of choice and only an additional 1% choose any of the interventional alternatives to TURP. While TURP may be the gold standard for reducing bladder outlet obstruction, to our patients and ideally to us, TURP is clearly not the gold standard for net health outcome—the balance of efficacy, morbidity, and patient experience. To better serve the majority of our patients needing treatment for BPH-related LUTS, we must pay close attention to the reasons men avoid TURP and measure alternative treatment options carefully in their ability to avoid these issues.

By sheer uptake it would appear that the BPH “gold standard” to our patients is chronic medication, as approximately 77% of our patients fill prescriptions for a selective alpha-blocker and/or 5-alpha-reductase inhibitor. Numerous large-scale studies, however, have shown that pharmaceuticals have only a modest effect on LUTS and can be associated with unwanted side effects, such as erectile and ejaculatory dysfunction, loss of libido, weakness, fatigue, blurred vision, dizziness, and nasal congestion.

Also important, after 20 years since the launch of finasteride and tamsulosin, are the increasing reports of potential long-term effects such as depression, self-harm, complications in cataract surgery, and possibly increased propensity for stroke or dementia (JAMA Intern Med 2017;177:683-91; CLIP 2016; 188:255-60). For these reasons, population studies show that over 60% of our patients are not compliant in taking BPH medication (Eur Urol 2015; 68:418-25). It would
MIST FOR BPH
continued from page 22

appear that medications are less of a gold standard to our patients than a hopeful means to avoid surgery. With millions of men noncompliant or discontinuing medications yet clearly not electing surgery, a very significant number of our patients are seeking an alternative, MIST.

What must MIST do to succeed?
The truly minimally invasive interventional answer to BPH would be a treatment option that most of our clearly dissatisfied patients will actually choose and thus improve their lives and avoid further bladder damage. It should be a procedure that we can reliably perform with predictable results, adequate effective reduction of bladder outlet obstruction, and acceptable durability.

But these are already true of our surgical options. MIST, to address those avoiding surgery, must have additional attributes. The MIST score sheet includes:

- offers acceptable relief from LUTS: Symptoms and quality of life improve; generally durable for 5+ years
- is not associated with serious harms of surgery: transfusion, stress or total urinary incontinence, stricture and bladder neck contracture, erectile dysfunction, ejaculatory dysfunction
- can be delivered in the office setting (tolerable under local anesthesia)
- allows for rapid recovery and symptom relief (no postoperative catheter and return to work and full preoperative activity within days).

What are the appropriate MIST metrics?
Historically, the urology community has focused on validated instruments to measure efficacy, namely the AUA Symptom Index (AUA-SI), aka International Prostate Symptom Score, along with the single LUTS-specific quality of life question. We have determined the minimal clinically important difference, the smallest change in AUA-SI that a patient perceives, is about 3 points (J Urol 1995; 154:1770–4). Objectively, we measure peak flow rate (Qmax) and postvoid residual (PVR), but neither reliably correlates with symptom improvement post treatment.

Since the focus of MIST is to not only deliver on efficacy but also greatly reduce morbidity and render a more attractive overall patient experience, it is important that we focus on consistent measures and reporting of adverse effects to understand how BPH options differ. Adverse effects must be chronicled as reported event rates. Since their incidence is ideally low, it is particularly important to report the low percentages. For more prevalent adverse effects, it is also beneficial to report validated instrument means.

### Table 2: OUTCOMES TREATING LUTS

<table>
<thead>
<tr>
<th>Measure</th>
<th>UroLift</th>
<th>Rezum</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AUA-SI Improvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efficacy (6 months)¹-³</td>
<td>10.9-13.0</td>
<td>12.2</td>
</tr>
<tr>
<td>Effectiveness (3-6 months)⁸⁻¹⁰</td>
<td>10.2-13.2</td>
<td>10.1-11.6</td>
</tr>
<tr>
<td><strong>QoL improvement</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efficacy (6 months)¹-³</td>
<td>2.4-2.8</td>
<td>2.3</td>
</tr>
<tr>
<td>Effectiveness (3-6 months)⁸⁻⁹</td>
<td>2.0-2.2</td>
<td>2.0</td>
</tr>
<tr>
<td><strong>Surgical retreatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efficacy³⁵</td>
<td>13.6% @ 4 and 5 years</td>
<td>4.4% @ 4 years</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>9% missing</td>
<td>19% missing</td>
</tr>
</tbody>
</table>


**Sexual dysfunction**
Because sexual dysfunction and BPH are independent predictors of each other, it is also important that studies conduct a substantive baseline evaluation before treatment. Results have varied greatly across BPH studies, showing that TURP hurt, helped, or had no effect on erectile function. The LIFT study of PUL was the first to report sexual dysfunction in a new light: de novo, sustained dysfunction. This was defined as dysfunction occurring within 3 months of treatment (and thus assignable to the treatment) and sustained at 12 months, ruling out transient events. For PUL these rates for ED and EjD were in fact 0%, which indeed sets a gold standard on sexual function preservation. Interestingly, when PUL was randomized to TURP, TURP also showed 0% de novo, sustained ED, but TURP did show 40% anejaculation (Eur Urol 2015; 68:643-52). Perhaps the lower-than-expected ejaculatory dysfunction was due to rigorous baseline data or perhaps the stringent criteria for de novo, sustained dysfunction.

**Catheterization**
Patients are also concerned with the need for postoperative catheterization. Historically, MISTs have overpromised and underdelivered on this criterion. Catheters were commonly placed and remained for days or even weeks following treatment with tissue necrotic technologies. It is important in clinical studies to test the need for catheter by conducting void trials. It is also important to accurately report the percent of patients requiring a catheter and the duration in terms of both means and ranges. Retention rates and catheter rates can be conflated and must both be reported.

One could propose “catheter rate,” which chronicles what percent require a catheter initiated within 1 week of treatment. Thereafter, if the patient continues to require a catheter, he contributes not only to the catheter rate and associated catheter duration calculation, but also to the retention rate. For example, if a patient is catheterized within a week, then successfully completes void trials and then goes into retention within 3 days, he should be included in the “catheter rate” and “retention rate,” and his total days on catheter be used in the mean duration calculations.

**Efficacy vs. effectiveness**
We all know that double-blinded, randomized, controlled trials (RCTs) are the least biased and most reliable way to determine the efficacy of a treatment. However, we also know from experience that RCT results do not always represent outcomes in real practice. It is important that we examine and report not just the efficacy of a treatment but also the effectiveness.

The pioneer epidemiologist Archie Cochrane defined these types of evidence as follows: Efficacy is the extent to which an intervention does more good than harm under ideal circumstances; ie, Can it work? Effectiveness assesses whether an intervention does more good than harm under usual circumstances of health care practice; ie, Does it work in the real world?

Retreatment rates are carefully tracked in efficacy studies, but BPH studies typically suffer from a significant number of patients lost to follow-up. The 10-year retreatment rates typically quoted for TURP were not derived from prospectively enrolled studies but from retrospective health system databases. Four to five years from now, a retrospective look at the Medicare database, for instance, will be our first opportunity to truly see if these retreatment rates hold up in the uncontrolled setting.
Today, two new MIST procedures are becoming even more widely used than prior MISTs. There are important differences between these treatment options, and time will tell how well they meet patients’ needs. Rather than be jaded by past attempts, the urologic community should be optimistic that more patients will find the solution they seek to improve their quality of life with reduced morbidity.

To compare how close these treatments come to our MIST goals, we can perhaps use a minimally invasive score sheet (table 3). Importantly, the data are presented separately for randomized efficacy trials and real-world effectiveness studies. It should be noted that effectiveness data for UroLift is more extensive and that the majority of the Rezum effectiveness data is derived from single-center studies. Both procedures are routinely performed in the office as well as in facilities depending on practice patterns and reimbursement variations.

Rezum appears to require modestly greater anesthesia in form of prostate block or IV sedation, whereas UroLift is routinely conducted with topical lidocaine. Both procedures avoid the important serious adverse events associated with BPH surgery. Efficacy results showed similar stability or improvement in mean sexual function scores, although only UroLift showed no evidence of de novo, sustained ejaculatory dysfunction.

The early effectiveness data appear to indicate an elevated infection rate with Rezum. This is possibly associated with the now more consistent use of postoperative catheter and/or temporary stent. UroLift, on the other hand, appears to be maintaining a low rate and duration of catheterization and UTI. Early UroLift efficacy studies reported 10% of patients required a misdeployed implant removed, whereas a recent effectiveness study of 1,413 patients showed this to be reduced to less than 1%. UroLift continues to show no de novo, sustained ejaculatory dysfunction, while a low rate of EjD persists apparent with Rezum.

One outlier study reported a 20% rate of anejaculation/retrograde ejaculation after Rezum (Yang et al, WCE 2018 [abstract UP3-33]). The investigators hypothesized that they are perhaps more aggressive in treating the central zone and bladder neck area. All effectiveness studies have been relatively short term, and real-world retreatment rates will only become available once health care system databases are populated over the coming years. From 1999 to 2005, the number of MIST procedures rose from 11,582 to 72,887, increasing the total number of U.S. BPH procedures 44% (J Urol 2008; 180:241-5). This rate later plummeted due to a disappointment with outcomes and reduced reimbursement. The marked increase in total procedures during the MIST heyday, however, indicated that large numbers of patients were looking for a solution between drugs and surgery.

How do today’s MISTs stack up?

Today we have available two new MIST treatments with excellent efficacy data and a growing level of effectiveness evidence (table 1). Both treatments consider the failures of the MIST of the ‘90s and attempt to address them in different directions.

The Rezum steam injection treatment is based on the assumption that thermal ablation works but needs to be delivered more efficiently. Because steam is rapidly dispersed in tissue and also rapidly heats as it condenses, it is far more efficient than inducing tissue necrosis. The steam injection procedure entails on average five injections at 9 seconds each, which compares favorably to the 20 to 60 minutes required for TUNA and TUMT (J Urol 2016; 195:1529-38).

The UroLift is based on the assumption that only mechanical opening of the prostate results in rapid recovery and relief, avoidance of a catheter, and reliable preservation of sexual function. Unlike stents, when PUL implants are properly placed in the prostate lobe, encrustation and migration are unlikely. Because PUL does not rely on necrosis and tissue reabsorption, it is rapid acting and typically does not require postoperative catheterization (Can J Urol 2014; 21:7094-101).

Both MIST treatments have been carefully studied for efficacy, showing similar outcomes of approximately 10-point improvement in AUA-SI and over two-point improvement in QoL (table 2). These outcomes were largely sustained at 4 and 5 years. Surgical retreatment for recurring LUTS has been reported at 13.6% for UroLift at 4 and 5 years and 4.8% for Rezum at 4 years. While it appears that Rezum may be more durable, this must be viewed with caution as 19% patients were no longer in the study versus 9% for UroLift.

To compare how close these treatments come to our MIST goals, we can perhaps use a minimally invasive score sheet (table 3). Importantly, the data are presented separately for randomized efficacy trials and real-world effectiveness studies. It should be noted that effectiveness data for UroLift is more extensive and that the majority of the Rezum effectiveness data is derived from single-center studies. Both procedures are routinely performed in the office as well as in facilities depending on practice patterns and reimbursement variations.

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Today, two new MIST procedures are becoming even more widely used than prior MISTs. There are important differences between these treatment options, and time will tell how well they meet patients’ needs. Rather than be jaded by past attempts, the urologic community should be optimistic that more patients will find the solution they seek to improve their quality of life with reduced morbidity.

### TABLE 3 MINIMALLY INVASIVE SCORE SHEET

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>UroLift</th>
<th>Rezum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Office compatible</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Local anesthesia</td>
<td>Topical or block</td>
<td>Block</td>
</tr>
<tr>
<td>Serious adverse events</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfusion, stress incontinence</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Stricture</td>
<td>0%-0.7%</td>
<td>0%</td>
</tr>
<tr>
<td>Efficacy</td>
<td>0%-0.2%</td>
<td>0%-3.9%</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>2.9%-7%</td>
<td>6.6%</td>
</tr>
<tr>
<td>UTI</td>
<td>0%-4.6%</td>
<td>17.1%</td>
</tr>
<tr>
<td>Efficacy</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>0%</td>
<td>0%-3.1%</td>
</tr>
<tr>
<td>Post-op catheter (% patients; mean duration)</td>
<td>32%*; 0.7 days</td>
<td>75%; 3.4 days</td>
</tr>
<tr>
<td>Efficacy</td>
<td>7.7%-16%; 1 day</td>
<td>100%; 4.4 days</td>
</tr>
<tr>
<td>Urinary retention (after post-op catheter)</td>
<td>0.7%-9%</td>
<td>3.7%</td>
</tr>
<tr>
<td>Efficacy</td>
<td>1.9%-4.8%</td>
<td>10.7%-14%</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Erectile dysfunction</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>Ejaculatory dysfunction</td>
<td>0%</td>
<td>0%-3.1%</td>
</tr>
<tr>
<td>Efficacy</td>
<td>0%</td>
<td>0%</td>
</tr>
<tr>
<td>MSHQ-EjD Function*</td>
<td>1.3, p&lt;.001</td>
<td>5.1%</td>
</tr>
<tr>
<td>MSHQ-EjD Bother**</td>
<td>-0.8, p&lt;.001</td>
<td>-0.7, p=.0017</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>0%</td>
<td>3.1%-20%</td>
</tr>
</tbody>
</table>

*Failed void trial

**Mean change from baseline at 1 year. Improvement is positive for function and negative for bother.

Are you doing everything you can to preserve kidneys in your patients with low-risk UTUC?

Kidney preservation should be a top priority when treating low-risk UTUC

Finding the right balance of cancer risks with the morbidity of surgery is challenging. The age and inherent comorbidities of patients with upper tract urothelial carcinoma (UTUC) add further difficulties for urologists to consider. 1-3

“Although radical nephroureterectomy (RNU) has been the gold standard for UTUC treatment, removing a kidney for low-risk UTUC can be overkill in many cases” said Brian Hu, MD, assistant professor of urologic oncology at Loma Linda University.

GUIDELINES RECOMMEND ACCURATE GRADING AND STAGING PRIOR TO TREATMENT SELECTION
Tumor grade, according to guidelines from both the European Association of Urology and National Comprehensive Cancer Network, is a primary factor when determining the best course of treatment. 1,4 Although tumor staging may be difficult to assert clinically in UTUC, grading can be conducted with a high level of accuracy. In 90% of cases, ureteroscopic biopsies can determine tumor grade with a low false-negative rate—regardless of sample size. For high-grade tumors, including carcinoma in situ, selective urinary cytology has high sensitivity. In addition to histopathology, urologists can utilize the full spectrum of clinical tools, including high-quality axial imaging, such as computerized tomography urogram or magnetic resonance urogram, retrograde pyelography, endoscopic evaluation, and cytology. 1

“Combining these modalities help give a full picture of each patient’s oncologic risk. This cancer risk can then be weighed against the risks of surgery and loss of renal function to help in guiding treatment decisions,” noted Hu.

GUIDELINES RECOMMEND KIDNEY-SPARING APPROACHES FOR LOW-RISK UTUC AND BEYOND
Kidney-sparing surgery is considered the standard of care for low-risk UTUC. However, guidelines recommend kidney-sparing treatment, even in patients with a normal contralateral kidney. 1,4

“Kidney-sparing surgery should also be strongly considered in high-risk UTUC when patients have impaired renal function, comorbid conditions limiting major surgery, a solitary kidney, or genetic predisposition to UTUC,” Hu added.” However, the benefits of kidney-sparing surgery must be weighed against higher recurrence rates and more intense cancer surveillance. Given improvements in the diagnosing and risk stratifying of UTUC, we are better able to identify patients who have low-risk disease.” 4

RNU DOESN’T ALWAYS LEAD TO BETTER OUTCOMES
RNU is a standard treatment for most high-risk cases. However, distal ureterectomy is an option in patients with high-risk tumors of the distal ureter. 1 Interestingly, there are retrospective data that demonstrate similar oncologic outcomes in patients with low-risk UTUC managed with RNU versus kidney-sparing strategies. 5,6 Endoscopic resections or ablations have demonstrated a lower rate of morbidity when compared with RNU. 7 The loss of nephrons with RNU can be deleterious to patients’ health, especially since studies have shown that approximately 50% of patients who undergo RNU for UTUC have already advanced to stage ≥3 chronic kidney disease. 2,3

EVIDENCE SUPPORTS A DIFFERENT APPROACH
In low-risk UTUC specifically, it’s time to reconsider traditional treatment approaches. With the latest tools and technologies, urologists may be better equipped to prioritize kidney preservation in these fragile patient populations.

Stay informed of the latest technologies and dialogue in UTUC. Read more at UTUCIntactivism.com.

References:
Q&A

OAB/INCONTINENCE

AUA, SUFU offer guidance on incontinence after prostate treatment

Earlier in 2019, the AUA and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) published a joint guideline on the subject of incontinence after prostate treatment. In this interview, Jaspreet S. Sandhu, MD, a member of this guideline’s panel, explains the rationale behind the guideline and summarizes its key points. (To read the guideline, see bit.ly/AUASUFUincontinenceguide.)

Q: Please explain the rationale behind this guideline.
A: As you know, male incontinence is quite prevalent, particularly after prostate treatment. There are a lot of different ways of treating male incontinence. Unfortunately, these have never been evaluated thoroughly. We also have many studies that tell us what happens to continence recovery after prostate treatment, particularly after radical prostatectomy and radiation therapy. The AUA Practice Guidelines Committee decided, in partnership with SUFU, to come up with a guideline that codifies what happens to continence recovery after prostate treatment, and gives current evidence as to the best way to treat this particular malady.

The variability is incredible when it comes to treating incontinence and, depending on where you go, there are different modes of treatment that are favored. There is a reasonable amount of evidence out there now that can help clinicians determine which modalities work better for which types of patients. That was the main rationale behind this guideline.

Another reason behind developing this guideline is the length of time many men wait to receive surgical treatment for incontinence. We say that if patients continue to have incontinence even then, should they have severe incontinence. As you and I know, there’s a group of patients that are never told about possible treatments for incontinence. This is just a way of making sure everybody knows there are treatments available, and hopefully that knowledge will allow some of these patients to be offered or referred for treatment sooner.

The 6-month time frame is to make sure people realize there are things available even then, should they have severe incontinence. As you and I know, there’s a group of patients that are never told about possible treatments for incontinence.

How does the guideline address the period between prostatectomy and surgical treatment for incontinence?

The guideline has sections on pre-prostate treatment, post-prostate treatment, and evaluation of incontinence after prostate treatment.

Q: How does the guideline address the period between prostatectomy and surgical treatment for incontinence?
A: The guideline has sections on pre-prostate treatment, post-prostate treatment, and evaluation of incontinence after prostate treatment. Generally, that applies to radical prostatectomy, but it can apply to patients who’ve had radiation therapy followed by a TURP or, in rare cases, after BPH surgery. Before treatment, the guideline says you should counsel patients about risk factors for incontinence. Following and sometimes even before treatment, pelvic floor muscle exercises and pelvic floor muscle therapy are definitely two options that can help hasten continence recovery. Beyond that, if patients continue to have incontinence after prostate treatment, then they can go on to evaluation and possibly surgical treatment.

Q: Are there any pharmacologic aids that you recommend to patients while they’re waiting to see if they have established incontinence?
A: Before presentation for incontinence after prostate treatment, there are really no medicines available. Now, if it’s primarily urgency urinary incontinence, which can be determined based on history—generally leakage at night or leakage associated with urgency and not necessarily associated with activity—then you should follow the overactive bladder guideline, which has a very good algorithm as to how to treat these men primarily with pharmacologic therapy.

There is also a guideline statement that specifically says if urgency urinary incontinence or urgency predominant mixed urinary incontinence is suspected, those patients should be evaluated and treated, whenever they present, as overactive bladder patients. That particular group of patients can be treated with anticholinergics or beta-3 agonists as needed.

Q: Are there any off-label pharmacologic treatments you would recommend?
A: The guideline does not address off-label treatment. There are off-label treatments in Europe and Japan. Duloxetine is available for stress urinary incontinence. Some people use treatments like imipramine for stress incontinence. Beyond that, there aren’t a whole lot of options. Most of these, as you know, are psychotropic medicines. For that reason,
Q: Do you ever use bulking agents while a patient is waiting for definitive therapy?

A: That's a very good question. One of the bases for this guideline was the fact that bulking agent use is rampant. The problem with bulking agents is twofold. One, they're not FDA approved for male incontinence. Two, their effect is generally fleeting; they're not durable.

JASPREET S. SANDHU, MD

Q: Duloxetine has never been considered for FDA approval as treatment for urinary incontinence in the U.S., primarily due to litigation risk. But if you want to provide something off-label, that may be an option.

A: Although this guideline is meant to deal with incontinence after prostate treatment, there are certainly statements that apply to patients who develop incontinence on their own. As you know, roughly 30% of men over the age of 70 will have some degree of urinary incontinence. If this is determined to be male stress urinary incontinence, then the evaluation and treatment is essentially the same as for those with incontinence after prostate treatment and the guideline statements related to evaluation, treatment, and surgical complication (of anti-incontinence surgery) apply to these patients as well.

Further, the fact that 30% of men develop incontinence without any prostate intervention provides a good baseline. I use this figure when counseling patients who are undergoing post-prostatectomy anti-incontinence surgery. It’s a good normalizing technique and a good way of telling people that, after artificial urinary sphincter placement, you will likely still leak a little bit.
The much-anticipated proposed rule for the Medicare physician fee schedule was finally released on July 29, 2019. The bottom-line impact to urology for 2020-based changes to relative value units (RVUs) is a projected +1% additionally. The Centers for Medicare & Medicaid Services is projecting a minor 0.14% increase in the conversion factor from $36.04 to $36.09.

While the overall impact on the specialty for 2020 is minor, there are a few changes of note that we will address in this article. The more newsworthy information in the proposed rule surrounds changes to coding effective Jan. 1, 2021.

First, we will address the changes for 2020.

**MIPS changes.** In the area of the Quality Payment Program (QPP), Medicare is proposing to increase the requirements for the Merit-based Incentive Payment System (MIPS) program. The threshold for physicians to avoid penalties for payments in 2022 will require a minimum score of 45 for performance in 2020, up from 30 in 2019. The percentage assigned to the Quality and Cost categories will be adjusted to 40% and 20%, respectively. The minimum score for exceptional performers will be raised to 80 points.

CMS did not change the eligibility requirements for reporting year 2020. The maximum penalty for those failing to meet MIPS requirements has been increased to –9%, up from –7%. Penalties and bonuses will be applied to payments in 2022 based on 2020 reporting. We encourage you to further review the proposed changes for the QPP program as CMS continues to change this program to increase the incentives to participate.

**Supervision of advanced practice providers.** CMS is proposing to modify regulation of physician supervision of physician assistants (PAs) to give PAs greater flexibility to practice more broadly in the current health care system in accordance with state law and state scope of practice. The proposal includes a provision that, in the absence of state law governing physician supervision of PA services, the physician supervision required by Medicare for PA services would be evidenced by documentation in the medical record of the PAs’ approach to working with physicians in furnishing their services.

**Physical therapy/occupational therapy benefits.** CMS is proposing a change in per-beneficiary incurred expenses under physical therapy definitions. These benefit caps are no longer applied as limitations but as threshold amounts above which services require, as a condition of payment, inclusion of modifier –KX, and that use of modifier –KX confirms that the services are medically necessary as justified by appropriate documentation in the patient’s medical record. The definition of modifier –KX should assist in providing services to patients receiving benefit from ongoing physical therapy-type services for pelvic floor rehabilitation. Functionally, you will need to continue to document medical necessity and improvement and use modifier –KX to indicate the services provided are medically necessary.

**RVU changes.** Table 1 includes a few higher volume services for which the proposed RVU changes will result in increases of greater than or equal to 5% in the office setting beginning Jan. 1, 2020 if adopted. The majority of the changes reflect changes to the practice expense values based on adjustments to equipment valuation and/or disposables related to the procedure. Changes to specific high-volume codes are noteworthy. The work values for the Urolift system codes 52441 (initial implant) and 52442 were reduced from 4.5 to 4 and 1.2 to 1.01, respectively. However, the non-facility value for

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Percent increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>51610</td>
<td>Injection for bladder x-ray</td>
<td>7.1%</td>
</tr>
<tr>
<td>51715</td>
<td>Endoscopic injection/implant</td>
<td>5.0%</td>
</tr>
<tr>
<td>51725</td>
<td>Simple cystometrogram</td>
<td>6.5%</td>
</tr>
<tr>
<td>51792</td>
<td>Urinary reflex study</td>
<td>7.6%</td>
</tr>
<tr>
<td>51797</td>
<td>Intraabdominal pressure test</td>
<td>17.1%</td>
</tr>
<tr>
<td>52000</td>
<td>Cystoscopy</td>
<td>11.1%</td>
</tr>
<tr>
<td>52281</td>
<td>Cystoscopy and treatment</td>
<td>7.5%</td>
</tr>
<tr>
<td>52287</td>
<td>Cystoscopy chemodenervation</td>
<td>5.6%</td>
</tr>
<tr>
<td>52310</td>
<td>Cystoscopy and treatment</td>
<td>6.7%</td>
</tr>
<tr>
<td>52441</td>
<td>Cystourethro w/ implant</td>
<td>6.8%</td>
</tr>
<tr>
<td>53620</td>
<td>Dilate urethra stricture</td>
<td>11.8%</td>
</tr>
<tr>
<td>76872</td>
<td>US transrectal</td>
<td>12.7%</td>
</tr>
</tbody>
</table>

Source: Adapted from CMS proposed rule by Ray Painter, MD, and Mark Painter

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Percent decrease</th>
</tr>
</thead>
<tbody>
<tr>
<td>51798</td>
<td>US urine capacity measure</td>
<td>7.1%</td>
</tr>
<tr>
<td>55874</td>
<td>Trnp/ plnt biodegrdabl mtr/l</td>
<td>5.0%</td>
</tr>
<tr>
<td>64561</td>
<td>Implant neuroelectrodes</td>
<td>6.5%</td>
</tr>
<tr>
<td>96372</td>
<td>Ther/proph/diag inj sc/im</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

Source: Adapted from CMS proposed rule by Ray Painter, MD, and Mark Painter

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**TABLE 1** HIGH-VOLUME SERVICES WITH PROPOSED RVU INCREASES (>5% INCREASE)

**TABLE 2** HIGH-VOLUME SERVICES WITH PROPOSED RVU DECREASES (>5% DECREASE)
In the last decade, there has been a marked increase in the number of prostate cancer treatments being developed, as well as the speed in which they are trialed and approved. Although prostate cancer continues to be the second leading cause of cancer death in men in the U.S., these treatment advancements are improving the quality of care and long-term survival rates for these men. While the suppression of testosterone and use of oral androgens can be a constant part of treatment for men with castrate resistant prostate cancer, let’s not lose sight of the fact that they are only one piece of the puzzle. The reality is that these methods are only part of the solution for the more than 40,000 men in the U.S. who will see their disease become castrate resistant and metastatic.  

Although metastatic castrate-resistant prostate cancer (mCRPC) is not curable, the number of treatments that become available in just the last 10 years have given urologists the tools to control the cancer for prolonged periods of time. A paradigm shift in how we treat mCRPC began in 2010 with the introduction of an immunotherapy for mCRPC. When sipuleucel-T was FDA-approved, it prolonged overall survival (OS) among men with mCRPC by 4.1 months. Reported in the pivotal IMPACT trial in the New England Journal of Medicine, this was very significant at a time when patients in the later stages of prostate cancer virtually had no options aside from chemotherapy.  

Urology was one of the first specialties to adopt immunotherapy, dating back to the use of Bacillus Calmette-Guérin (BCG) in the late 1990s. While sipuleucel-T has become an increasingly vital cancer treatment option for mCRPC patients, it remains largely underutilized in part because it differs mechanistically from other prevailing forms of cancer treatment that affect familiar prognostic biomarkers, such as PSA. Instead, sipuleucel-T stimulates the body’s immune system to target and attack prostate cancer cells that express PAP (prostatic acid phosphatase) – a protein present on 95% of prostate cancer cells. As we come to understand more about how immunotherapy works, research indicates that this type of treatment may have a more profound effect earlier in the disease progression when the tumor volume and associated immunosuppressive mechanisms are lower.  

At the time of the IMPACT trial (2003–2007), men with a PSA of <22.1 ng/mL accounted for a mere 25% of the mCRPC population in the study. In those days there was simply no clinical advantage to closely monitoring PSA unless a patient was experiencing cancer-related pain. In my practice today, PSA values for most patients at the time of mCRPC diagnosis is well below that <22.1 ng/mL level thanks to treatment protocols that require close monitoring of PSA changes, and routine radiographic assessments to ensure we identify the crucial time window when a patient’s cancer metastasizes. When considering immunotherapy for my mCRPC patients, I am thinking about the potential to extend life by more than a year for certain patients, not 4.1 months as originally reported in all cohorts. There is immense excitement around immunotherapy across various tumor types, however, its use in treating mCRPC remains low, despite a demonstrated survival benefit and generally manageable safety profile. Additionally – and people may not think about this as often as they should – an entire course of PROVENGE therapy is just three infusions in as little as six weeks. We know from earlier data that while immunotherapy takes some time to generate an immune system response, that response can be long lasting. The addition of sipuleucel-T as the foundation of mCRPC treatment provides us with a unique ability to offer therapies with differing mechanisms of action to maximize the available treatment options for our patients. As other specialties wait patiently for immunotherapy to become a clinical reality, urologists have an effective option today, and we should use it.

INDICATION  
PROVENGE® (sipuleucel-T) is an autologous cellular immunotherapy indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone-refractory) prostate cancer.  

IMPORTANT SAFETY INFORMATION  
Acute Infusion Reactions: Acute infusion reactions (reported within 30 minutes of infusion) are possible and include nausea, vomiting, fatigue, fever, rigors or chills, respiratory events (dyspnea, hypoxia, and bronchospasm), syncope, hypotension, hypotension, and tachycardia.  

Thromboembolic Events: Thromboembolic events, including deep venous thrombosis and pulmonary embolism, can occur following infusion of PROVENGE. The clinical significance and causal relationship are uncertain. Most patients had multiple risk factors for these events. PROVENGE should be used with caution in patients with risk factors for thromboembolic events.  

Vascular Disorders: Cerebrovascular events (intracranial hemorrhage, ischemic strokes and transient ischemic attacks) and cardiovascular disorders (myocardial infarctions) have been reported following infusion of PROVENGE. The clinical significance and causal relationship are uncertain. Most patients had multiple risk factors for these events.

Handling Precautions: PROVENGE is not tested for transmissible infectious diseases.  
Concomitant Chemotherapy or Immunosuppressive Therapy: Chemotherapy or immunosuppressive agents (such as systemic corticosteroids) given concurrently with the leukapheresis procedure or PROVENGE has not been studied. Concomitant use of immunosuppressive agents may alter the efficacy and/or safety of PROVENGE.  

Adverse Reactions: The most common adverse reactions reported in clinical trials (≥ 15% of patients receiving PROVENGE) were chills, fatigue, fever, back pain, nausea, joint ache, and headache.
INDICATIONS AND USAGE: PROVENGE® (sipuleucel-T) is an autologous cellular immunotherapy indicated for the treatment of asymptomatic or minimally symptomatic metastatic castrate-resistant (hormone-refractory) prostate cancer.

DOSEAGE AND ADMINISTRATION
- For autologous use only.
- For intravenous use only.
- The recommended course of therapy for PROVENGE is 3 complete doses, given at approximately 2-week intervals.
- Premedicate patients with oral acetaminophen and an antihistamine such as diphenhydramine.
- Before infusion, confirm that the patient’s identity matches the patient identifiers on the infusion bag.
- Do not initiate infusion of expired product.
- Infuse PROVENGE intravenously over a period of approximately 60 minutes.
- Do not use a cell filter.
- Interrupt or slow infusion as necessary for acute infusion reactions, depending on the severity of the reaction.

To report SUSPECTED ADVERSE REACTIONS, contact Dendreon Pharmaceuticals LLC at 1-877-336-3736 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Table 1  Incidence of Adverse Events Occurring in ≥5% of Patients Randomized to PROVENGE

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>PROVENGE (N = 601)</th>
<th>Control* (N = 303)</th>
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<tbody>
<tr>
<td>All Grades n (%)</td>
<td>All Grades n (%)</td>
<td>All Grades n (%)</td>
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<tr>
<td>Abdominal Cramps</td>
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<td>Chest Pain</td>
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<td>Insomnia</td>
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<td>Dyspnea</td>
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<td>Fatigue</td>
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<tr>
<td>Headache</td>
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<td>Nausea</td>
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<tr>
<td>Rash</td>
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<tr>
<td>Thromboembolic events</td>
<td></td>
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<tr>
<td>Thrombosis</td>
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<tr>
<td>Pulmonary embolism</td>
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</tbody>
</table>

*Control group received non-activated autologous peripheral blood mononuclear cells.

Postmarketing Experience
The following adverse reactions have been identified during post-approval use of PROVENGE. 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.

- Nervous system disorders: syncope, transient ischemic attack, stroke (see Warnings and Precautions)
- Cardiovascular disorders: myoccardial infarction (see Warnings and Precautions)
- Thromboembolic disorders: deep vein thrombosis and pulmonary embolism (see Warnings and Precautions)
How to improve patients’ access to their health information

In most states, the physician may own the physical medical record, but the patient owns all of the underlying information. HIPAA clearly established a right to access that information. In 2014, the Department of Health and Human Services finalized a rule that allows patients to request test results from CLIA-certified labs and amended the HIPAA Privacy Rule to compel those same labs to furnish that information directly to patients (bit.ly/privacyruleamendment). (Urologists who own their own CLIA-certified lab should take special note.) Patient access to health information—whether it resides in a medical record, a lab company’s system, or an insurance company records—is a right firmly protected by federal laws and regulations.

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Notwithstanding these rights, neither the custodians of this information nor the health information technology vendors whose products store this information have rapidly facilitated electronic access. The federal EHR incentive program once known as “meaningful use” initially included a core objective to provide patients an ability to view, download, and transmit their health information, as well as two measures to reward eligible clinicians for performance under this objective. As with other aspects of meaningful use, many physicians found the objective to be burdensome and their EHRs unable to easily meet the measures.

Eventually, this program and its incentives and regulations, along with market forces and consumer demand have pressured EHR vendors and their users to adopt a usable patient portal and facilitate patients’ access to their own information. In 2019, the incentives for providing such access are contained in the Promoting Interoperability category of the Merit-based Incentive Payment System (MIPS). Forty percent of the category score is based upon the measure, “Provide Patients Electronic Access to their Health Information”—essentially the fraction of unique patients seen in the measurement period who have successfully registered for the portal.

Practices who have not yet mastered the art of registering all patients for portal access are simply not meeting the expectation of most patients and payers—including Medicare—and will see this reflected in their MIPS scores this performance year.

The government has also created the “Blue Button” initiative to allow Medicare beneficiaries, veterans, and those insured through the Federal Employees Health Benefit Program to download certain information about their health (bit.ly/Blue-button). Blue Button is powered by new standards that allow systems to “talk with each other,” known as interoperability. Many commercial insurers have Blue Buttons for their beneficiaries, and you should look for this functionality to expand to all payers, pharmacies, provider organizations, and others in the health care information ecosystem.

Taking access to health records one step further is the mission of the “open notes” movement. The idea of routinely giving every patient a copy of their medical record was proposed as early as 1973 as a way to address “four serious problems… maintaining high quality of care, establishing mutually satisfactory physician-patient relations, ensuring continuity, and avoiding excessive bureaucracy” (N Engl J Med 1973; 289:688-92).

Early adopters of the open notes concept (think progress notes, office visits) included MD Anderson Cancer Center, Beth Israel Deaconess Medical Center, Geisinger Health System, the VA, and the University of Washington Harborview Medical Center. Today, more than 40 million Americans have access to their notes. The case for open notes is largely proven in research and publications at this point: Allowing patients to review their actual visit notes improves accuracy and safety (patients can report errors), improves medication adherence, builds trust and satisfaction with physicians, improves outcomes in chronic disease, and supports those caring for patients (scheduling visits, reconciling medications).

Open notes concerns debunked

Physicians have concerns about this type of “patient engagement,” many of which have been debunked by experience: open notes has not increased email traffic, has not lengthened patient portal.

Robert A. Dowling, MD

Dr. Dowling is the president of Dowling Director Services, a private health care consulting firm specializing in quality improvement, clinical informatics, and health care policy affecting specialty care. He is the former medical director of a large, metropolitan single-specialty urology group in Ft. Worth, TX.

Five years ago, I wrote a column for Urology Times describing contemporary initiatives allowing patients to gain access to their health information from providers and payers. Two pioneers of the modern movement empowering patients to access and share their information—Dave deBronkart and Regina Holliday (bit.ly/deBronkart, bit.ly/Reginaholliday)—were both touched by metastatic kidney cancer. As we consider how much has changed in the understanding and management of that disease in the last 5 years, it is worth revisiting what has changed—and what hasn’t—in granting patient access to their medical records.

Patients have rights to their health information. The Health Insurance Portability and Accountability Act of 1996 (HIPAA) protects the privacy and security of individuals’ health information, but also provides patients the legal and enforceable right to access and gain a copy of their health information—including but not limited to their medical records, x-rays, and lab tests. The only exceptions to this right of access are psychotherapy notes and insurance company records—is a right firmly protected by federal laws and regulations.

Patients have rights to their health information. The Health Insurance Portability and Accountability Act of 1996 (HIPAA) protects the privacy and security of individuals’ health information, but also provides patients the legal and enforceable right to access and gain a copy of their health information—including but not limited to their medical records, x-rays, and lab tests. The only exceptions to this right of access are psychotherapy notes and insurance company records—is a right firmly protected by federal laws and regulations.

PRACTICE POINTERS

- The “Blue Button” initiative allows Medicare beneficiaries, veterans, and those insured through the Federal Employees Health Benefit Program to download certain information about their health.
- Research shows that allowing patients to review their actual visit notes improves accuracy and safety, improves medication adherence, builds trust and satisfaction with physicians, improves outcomes in chronic disease, and supports those caring for patients.
- Implementing open notes in a practice can be as simple as adjusting a setting in an EHR and/or patient portal.
HEALTH INFORMATION
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visit times, and has not significantly changed documentation workflow. Some physicians worry their notes could confuse or even offend patients; an oft-cited example is documenting physical appearance (obese), sexual history, or mental status (anxious, angry). Patients have a right to access this information already, and best practices include professionally documenting under the assumption that others—referring physicians, patients, attorneys—may access the record in the future.

How do you implement “open notes?” It could be as easy as a setting in your EHR and/or patient portal. Some products have the ability to assign filters, rules about what sort of documents can be viewed (again, the patient has a right to all of it), and timelines. Another easy way to implement the concept is to simply print a copy of every visit and give/send to the patient as routinely as you send updates to their referring physician. A communication plan with your staff and your patients is an important factor in success. For more resources, go to www.opennotes.org.

PROPOSED RULE
continued from page 30
each code was increased, resulting in an overall increase when the service is performed in the office. For 52441, the increase in the office-based payment as proposed is 6.8% as noted in Table 1, and the increase in office-based payment for 52442 as proposed is 4.6%.

In addition, code 54640 (Orchiopexy, inguinal approach, with or without hernia repair) is proposed to have a reduction of 9.7% in the facility setting, reflecting a code change eliminating the “with or without hernia repair” language.

Looking ahead to 2021
E/M changes. The biggest news included in the proposed rule does not take effect on Jan. 1, 2020 but rather is scheduled to be effective Jan. 1, 2021. As noted in our August 2018 column (“Medicare proposed rule outlines significant changes,” page 26), CMS proposed a radical change to payment and documentation for E/M codes. In our December 2018 column (“Medicare final rule: How E/M changes help urologists,” page 31), we addressed the CMS finalized rule to change the payments and documentation requirements for E/M codes effective Jan. 1, 2021. The changes would have consolidated payments for new and established patient office visits to three levels for each category.

The news was met with a decidedly mixed reaction. In response to the proposed and final rule, the American Medical Association CPT Editorial Panel and Relative Value Update Committee convened work groups and expanded surveys to revise the structure of the E/M service codes. The results of these efforts were reported to CMS. In this proposed rule, CMS is proposing to accept the majority of the work done by the AMA.

Practices, EHRs, and other entities will now have a little over a year to adapt to the changes in office/outpatient E/M visits. We will spend more time addressing these changes over the next year but present a quick summary of the changes below. (Note that these changes will not affect coding, payment, or documentation requirements for 2020. For 2020, continue to follow rules adopted for 2019.)

• CPT code 99201 (Level 1 new patient office/outpatient E/M visit) is being eliminated.
• History and physical examination will no longer affect code selection but should be documented as appropriate. This change will likely require some changes to your EHR templates for both. Medicine reconciliation will still be required under MIPS, but review of systems and other portions relative to past medical, family, and social history can be changed to reflect more focused and relevant information with updates as needed for clinical reasons. For the physical examination, vitals will still be required for MIPS, but you will no longer need to include observations for eight systems or bullets as required by 1997 guidelines and instead can focus on documentation of only those issues relevant to patient care.
• Medical decision-making changes are subtle but will need to be addressed in how you think about the level of service you are charging. The AMA will eliminate some of the more ambiguous language from the table of risk. Data as noted in MDM will be revised to focus more on volume of relevant information and summation effort required and less on counting the amount of data reviewed.
• Time will be the other option for selection of service level. There are a number of changes surrounding time-based coding. Time will now be considered to be total time spent on that day, eliminating the face-to-face component with regard to time. In addition, the requirement for the visit to include 50% spent in counseling or coordination of care will be eliminated. Time can be used to document any visit if you document the time spent that day.
• CPT code definitions will include time ranges within the code definition, eliminating the ambiguity of the average visit time associated with current coding rules. The times for each code as noted in the rule are as follows: 99202 (15-29 minutes), 99203 (30-44 minutes), 99204 (49-59 minutes), 99205 (60-74 minutes), 99212 (10-19 minutes), 99213 (20-29 minutes), 99214 (30-39 minutes), and 99215 (40-54 minutes). A new code will be added to the CPT manual to report time for services that exceed level 5 services: 999XX for each additional 15 minutes over 74 minutes for 99205 and 54 minutes for 99215.
• CPT codes 99358-9 (Prolonged E/M without Direct Patient Contact) would no longer be reportable in association or “conjunction” with office/outpatient E/M visits.
• A new add-on code will be added to CPT to address patients who have chronic issues addressed during a visit. The code can be used by any specialty.
• All codes will be revalued with slight increases.

Bottom line: Urologists should prepare their practice to face new expectations around patient access to their health care information. New electronic standards, federally backed initiatives to support interoperability and information exchange, and a growing consumer demand will continue to fuel this “movement.” Patients desire a new level of transparency in what has been a system full of opaque costs and information, and health care is likely to see the same innovations in consumer access that have characterized banking, travel, and other service industries. UFT

The information in this column is designed to be authoritative, and every effort has been made to ensure its accuracy at the time it was written. However, readers are encouraged to check with their individual carrier or private payers for updates and to confirm that this information conforms to their specific rules.
Setting up a trust confers several financial advantages

Tool provides management of assets while minimizing probate expenses

Q: I’ve been told that I should create a living trust and start putting assets into it. Can you explain what this is and how it may be useful?

A: Trusts are frequently used in effective estate planning to provide management of assets as well as minimize probate expenses and estate taxes. Despite their apparent complexity, trusts can be extremely useful in many aspects of planning your estate.

To thoroughly understand trusts, you need to know the various roles of the parties affiliated with the trust in order to begin beneficial discussions with an estate planning attorney. First, there’s the grantor. This is the individual who establishes the trust and usually transfers funds into the trust. Next is the trustee, who makes certain the terms of the trust, as outlined by the grantor, are carried out. Finally, there is the beneficiary. The beneficiary is the individual (or individuals) for whom the trust has been created. Often a minor, the beneficiary can also be a surviving spouse, adult child, or any individual in need of financial assistance (or supervision) after the death of the grantor.

Knowing these basics, you can then focus on the different types of trusts most often used for estate planning purposes. The first is a testamentary trust. This trust is usually part of a will and comes into existence after death. With a testamentary trust, assets may pass through probate before being received by the trust. The trust can then help divide assets for each beneficiary, manage assets, or distribute assets as required by the directions of the trust.

A living trust, also sometimes referred to as an inter-vivos trust, is created during the life of the grantor. In addition, the grantor is usually also the trustee and beneficiary of the trust. Assets are transferred into the trust during the grantor’s life and avoid probate at death. As an added benefit, living trusts provide benefits during life, particularly in the event the grantor becomes incapable of effectively managing the assets due to reasons related to health or competency.

A living trust can identify contingent trustees who assume managerial responsibilities of the trust in the event the original trustee (usually the grantor) is unable to perform their duties. Such forethought will avoid the excessive legal costs involved if a grantor is declared incompetent, since in such cases, annual accountings to the court are required.

A trust can be a highly effective method of controlling the management and distribution of assets. However, a trust only works to the extent that assets have been transferred into the trust. Often, individuals spend hours in their attorneys’ offices creating what they hope will be the perfect trust arrangement for their estate. Unfortunately, many never get around to transferring their assets into the trust. If you create a trust for your estate plan, make certain your assets are titled in the way necessary for the trust to work, since asset titling and beneficiary designations take precedence over the directives of your will or trust.

For example, if you have a large life insurance policy naming your surviving spouse as beneficiary, a residence and summer home jointly titled with your spouse, and various investment accounts also jointly titled with your spouse, all of that will pass directly to your spouse, bypassing any trust arrangement you paid to put in place. Then, whatever plans the survivor has made (or may make) will be the controlling factor for all assets going forward.

To control the distribution and management of the assets and to minimize estate tax liability and ultimately probate expenses, it is necessary to revisit all titling and beneficiary designations. Your estate planning attorney, working in tandem with your investment and insurance advisers, can assist in this process to ensure a well-coordinated and effective estate plan.

Q: Who should I choose as trustee of my trust?

A: The answer really comes down to whom you trust to do a competent job. Many people choose their children, a family member, or a friend that they believe trustworthy. If you do not have anyone you think can handle the task, your estate planning attorney may be able to act as trustee or can recommend an attorney willing to act as trustee. If they decline, certain banks are willing to act as a corporate trustee; however, their services usually come at a higher cost.

Make certain your assets are titled in the way necessary for the trust to work, since asset titling and beneficiary designations take precedence over the directives of your will or trust.

FINANCIAL TIPS

- Under a living trust, assets are transferred into the trust during the grantor’s life and avoid probate at death.
- If you create a trust for your estate plan, make certain your assets are titled in the way necessary for the trust to work, since asset titling and beneficiary designations take precedence over the directives of your will or trust.
- The best person to choose as trustee of your trust is the one you believe will carry out your wishes as you have planned; otherwise, paying an attorney or corporate trustee is the next best option.

The information in this column is designed to be authoritative. The publisher is not engaged in rendering legal, investment, or tax advice.
Cover Feature

NMCRPC UPDATE
continued from page 1
toff, MD, chairman of medicine at Memorial Sloan Kettering Cancer Center, New York. “The clinical benefits for this subset of patients should be measured in delayed symptoms referable to their cancer or an improvement in overall survival.”

And while data from recent studies are very encouraging, “We don’t have the long-term data to say definitively that prolonged metastasis-free survival significantly increases overall survival,” Dr. Gomella said.

As a result, there is still a need to exercise caution in using these drugs in the context of treating nmCRPC patients, Dr. Kibel said.

“You’re treating patients who are asymptomatic, sometimes elderly, with drugs that have side effects. They’re going to feel less well than they did before they were treated with the hope that it eventually leads to clinical benefit,” Dr. KANTOFF said.

Early results from clinical studies show little difference among the drugs. While apalutamide and enzalutamide have a different chemical structure than darolutamide, each of these androgen inhibitors demonstrates similar rates of metastasis-free survival after 24 months as well as reduction in PSA. The populations studied—both in terms of size and patient characteristics (eg, patient age and PSA doubling time)—also are highly comparable.

But the drugs are not without side effects. While the improvements in metastasis-free survival rates are similar, studies show patients who take apalutamide and enzalutamide may suffer from profound fatigue and increased incidence of falls and fractures. Enzalutamide also has been linked to increased risk of seizures. Meanwhile, darolutamide appears to lack the central nervous system side effects associated with apalutamide and enzalutamide and results in less fatigue, but may prompt feelings of weakness, diarrhea, hot flushes, anemia, and decreased appetite.

How can physicians choose the right drug for their patients? “That’s a challenging question—one that hasn’t been fully addressed,” said Tomasz M. Beer, MD, professor of medicine, division of hematology/medical oncology, and Grover C. Bagby Chair of Prostate Cancer Research for the Oregon Health & Science University School of Medicine, Portland. Typically, these decisions are based on a physician’s experience with the drug and the patient’s health profile, Dr. Beer said.

“For somebody with a history of seizures, somebody with a risk of falls, someone on a blood thinner—those people are not good candidates for apalutamide or enzalutamide, but darolutamide might be a better choice,” said Adam S. Kibel, MD, Elliott Carr Curator professor of surgery in urology at Harvard Medical School and chief of urology, Brigham and Women’s Hospital and Dana-Farber/Brigham and Women’s Cancer Center, Boston.

Patients’ individual preference, too, is a factor. “Many patients have a robust response to these drugs,” Dr. Beer said. “Some patients are unable to tolerate the side effects, and they discontinue treatment.”

Cost is also an issue. “There are situations where patients have to pay $1,000 a month to be on a drug, and there are patients who can’t afford it,” Dr. KANTOFF said.

Researchers are exploring the “biology of resistance,” looking at biomarkers—such as androgen receptor variant-7 (AR-V7)—to help guide treatment. For example, AR-V7 can help predict resistance to hormonal therapies. But the incidence of AR-V7 mutations in patients with nmCRPC is low, Dr. KANTOFF said. Additionally, some physicians are reluctant to use biomarkers to guide treatment.

“We are finding biomarkers of resistance; we are understanding better what the resistance mechanisms are. But there’s a little bit of a gap between our knowledge and translating that to clinical utility or benefit,” Dr. KANTOFF said. As a result, “Most physicians have not used biomarkers to make a decision regarding, ‘Should I use this drug or something else?’”

Given the similarities among the drugs and the lack of definitive information on which treatment is best for specific patient profiles, Dr. Kibel said clinicians will need to be selective. “Each provider is going to have to pick their drug of choice and gain experience with it,” he said.

The advent of androgens to prolong metastasis-free survival is exciting, presenting options for treatment of a disease that formerly left physicians’ hands tied.

“One of the important points to remember is that the patients in these studies had a rapid PSA doubling time of less than 10 months. That meant these patients were doomed to rapidly develop metastatic disease,” Dr. Gomella said. “These drugs delay progression of metastases and slow PSA doubling time.”

But even with these advancements, there are still many questions to be answered about treatment of nmCRPC.

For example, the proper drug sequencing for prostate cancer that is progressing from hormone-sensitive nonmetastatic prostate cancer to nmCRPC is an open book,” Dr. Gomella said. In general, we believe certain patients may initially benefit from a next-generation androgen sequence inhibitor before they get chemotherapy. Others may benefit from upfront chemotherapy, depending on how much disease burden they have.

There’s also the question of how to best assist patients who find the side effects of the drugs difficult to bear. “Is there some way to add something—like an immunotherapeutic—for patients who have a difficult response? That’s an area that requires further exploration,” Dr. Beer said.

Additionally, it’s not clear how often patients should undergo diagnostic imaging tests or the impact that next-generation imaging scans will have on detection of nmCRPC and treatment.

“The clinical trials all looked at progression of disease based on a standard bone scan, CT scan, and MRI. When we start to use next-generation imaging scans such as PSMA scans, are we going to decree that patients are progressing toward metastasis earlier? If so, how will this impact the use of these drugs?” Dr. Gomella said.

Further, advancements in technology may change physicians’ perceptions of the state of disease in nmCRPC patients.

“I think the biggest question we have to ask is, ‘What is M0 CRPC?’” Dr. Kibel said. “We believe all of these patients have some form of metastatic disease. As new imaging agents do a better job of identifying metastatic disease, will we find that patients who were designated ‘M0 CRPC’ actually have micrometastatic disease that we just couldn’t pick up? Will the M0 designation go away?”

These are questions that will continue to be explored by researchers as well as groups such as the AUA, which has amended guidelines around nmCRPC based on recent advancements.

“Dr. KANTOFF has stock/other ownership interests in Context Therapeutics, Druggability Technologies, Placon, Ser, and Tarveda Therapeutics; and has a consulting or advisory role with Bayer Healthcare, Genentech/ Roche, Janssen, Merck, Metamark Genetics, New England Research Institutes, OncoCell MDx, Progenesis, Sanofi, Ser, Tarveda Therapeutics, and Therma Fisher Scientific. Dr. Gomella is a consultant/adviser to Astellas, Janssen, MDx Health, Merck, Bayer, and Strand Laboratories. Dr. Beer has stock/other ownership interests in Salarius Pharmaceuticals and has a consulting or advisory role with Albire, Astellas, AstraZeneca, Bayer, Boehringer Ingelheim, Clovis Oncology, GlaxoSmithKline, Janssen Biotech, Merck, and Pfizer. Dr. Kibel has received honoraria from Blue Earth Diagnostics, InSightec, Janssen, Merck, Pfizer, and Profound.

“We are finding biomarkers of resistance; we are understanding better what the resistance mechanisms are.”

PHILIP KANTOFF, MD

“These drugs fulfill an unmet need for treatment of nonmetastatic castration-resistant prostate cancer.”

LEONARD G. GOMELLA, MD
Proposals to mitigate ‘surprise billing’ affect all physicians

Barry a week goes by without a congressional hearing on drug pricing or a state legislature considering how to shed light on the true cost of health care services. Patients frequently blame providers, while providers point to payers. “Fixing” these high-profile problems requires a careful and nuanced approach—not a strong suit of the people and institutions responsible for making and enforcing the law.

One such issue is the payment of services by out-of-network physicians that are provided at in-network facilities. A study published in the New England Journal of Medicine (2016; 375:1915-8) reported 22% of emergency room visits included care from an out-of-network provider. Urologists’ understanding that these charges are not uncommon in elective inpatient admissions is backed up by a 2017 analysis that found 9% of scheduled stays at in-network hospitals led to an unexpected bill from an ancillary physician (Health Affairs 2017; 36:177-81).

Addressing so-called “surprise billing” is made even more complex because it requires action at the state and federal levels. States regulate commercial health insurance plans, but 61% of privately insured employees are in self-insured employer plans, which are administered by the federal government.

In a statement to Congress, America’s Health Insurance Plans, the trade group representing payers said, “The problem of surprise medical bills tends to be concentrated among certain medical specialties where providers are likely to charge substantially more than their peers in other specialties and not accept private insurance.” It’s widely understood that nobody wants to saddle patients with unexpected bills, particularly when the services are provided during an emergency.

AACU President Mark Edney, MD, MBA, pointed out, “Arriving at solutions that are acceptable to patients, providers, and payers is complex from an advocacy perspective because it requires advanced negotiating skills.”

“We must understand and appreciate the positions of the other parties at the table—patients and payers,” Dr. Edney said. “Threading the needle to get to a solution that is perceived as fair by all is a challenge but ultimately doable as long as we all continue to negotiate from an informed position and in good faith.”

The most complicated questions within surprise billing are how to determine a fair reimbursement rate for out-of-network services and whether to initiate an independent arbitration process if the payer or provider disputes that standard charge. There is cause for physicians to be concerned. The three most common reimbursement benchmarks—Medicare rates, billed charges, and contract rates—fail to truly cover the cost of providing a service. What’s more, in state after state and in federal legislation, insurers have resisted the inclusion of a dispute resolution process.

In June, a bipartisan majority of the Senate Health, Education, Labor and Pensions (HELP) Committee approved the Lower Health Care Costs Act (S.1895) by a vote of 20-3. The current bill is opposed by most physician organizations because it ties out-of-network payments to average in-network rates and does not include an independent payment arbitration process. The latter provision was strongly supported by Sen. Bill Cassidy, MD (R-LA) and a handful of colleagues, but the Trump administration has opposed arbitration.

Separately, Raul Ruiz, MD (D-CA) introduced bipartisan surprise billing legislation in the House of Representatives that is based on a New York law that contributed to a dramatic decline in the number of consumer complaints about balance bills. That model imposes “final-offer” arbitration in which both the payer and provider submit offers to an independent arbitrator who selects one or the other. The apparent logic behind this approach is that the threat of the arbitrator choosing the other party’s offer incentivizes each party to submit a reasonable offer or settle before going to that point.

States offer solutions

Similar arbitration solutions have been pursued in Illinois, New Hampshire, and New Jersey. Indeed, states are playing a leading role in addressing unexpected out-of-network billing. Four additional states have taken action this year to prohibit balance bills, institute arbitration processes, and promote pricing transparency among providers, payers, and patients “to avoid situations that lead to balance bills,” according to the National Academy for State Health Policy.

In Washington, for example, long-contesting parties came together to support an independent database to set out-of-network prices, followed by a procedure of binding arbitration between a provider and a carrier. “If you don’t like [the reimbursement],” said Insurance Commissioner Mike Kreidler, “challenge it and go to binding arbitration… It’s at your own peril.”

In Texas, the lead sponsor of a new law asserted, “We wanted to try to take the patients out of the middle of it because really it’s not their fight.” Instead, state officials will oversee arbitration between insurance companies and medical providers to negotiate a payment. This expands a law they already had on the books concerning emergency services.

Generally, when it comes to surprise billing, providers urge policymakers to consider binding arbitration to determine a fair payment. Payers say that will increase costs and slow the claims process and instead favor an approach based on rates defined as what similar providers accept as payment for their services. Policy and political questions abound, including the notion of Paul Clement, a former Republican solicitor general who said proposals to cap out-of-network rates would violate the takings clause of the Fifth Amendment.

The AACU, for one, will be keeping close tabs on all of these issues, promoting solutions based on principles outlined in a February letter to the House Committee on Ways and Means which concludes, “In addition to providing strong patient protections, we believe the principles set forth above would improve transparency, promote access to appropriate medical care, and avoid creating disincentives for insurers and health care providers to negotiate network participation contracts in good faith.”

Rosal E. Weber is state affairs manager, policy and engagement, for the American Association of Clinical Urologists.
What’s your biggest frustration with prior authorization?

One is the delay in delivering care. If I order surgery that requires prior authorization, it won’t always come through in a timely manner, and that impacts patients’ quality of life.

The second is the wear and tear on my nursing staff navigating the prior authorization process. It’s relatively thankless work, so it doesn’t enhance my team’s satisfaction.

Even minor issues, like having a procedure approved as an inpatient procedure, and if we do it outpatient (same hospital, same operating room, same staff), the insurance company can deny payment. Our hospital lost about $2.7 million one year because the status of admission was incorrect. The care is delivered, but they declined payment because the right box wasn’t checked.

We also get denials and have to appeal things that shouldn’t be necessary. For example, for a patient with relatively severe Parkinson’s disease with urge incontinence, the insurance company wants me to prescribe an anticholinergic, which unfortunately significantly impacts the severity of Parkinson’s. Insurance will deny medication that won’t impact Parkinson’s, and it has to be appealed. Even then, it will cost more out of pocket or the patient won’t get the medication, more commonly the latter.

The denial is not a denial because ‘we don’t think your medical decision was correct’; the denial is because ‘this medication is our preferred medication.’

DR. BOELTER

As with many urologists, I’m super busy. It takes weeks and weeks to get in to see me. I’ve had to limit the time my staff spends on prior authorizations, particularly medications. It takes too much time away from patient care; that’s much more important.

So we have patients handle their own pre-authorizations—contacting insurance companies themselves for medication approval. That actually works pretty well, but my staff still sits on the phone sometimes for 15 to 20 minutes for medication authorization.

Testing, CT scans, and surgery are things patients can’t do on their own, so my staff works on those.

We have a big military educational presence in Monterey, so I see a lot of military personnel and they’re all TRICARE patients. Their prior authorization routine is even more onerous.

Over the years, I’ve taken care of several high-ranking officers at the Presidio and asked why we have to go through prior authorization every time. In the last 15 years, I can’t recall ever being rejected. Every request for CT scans, surgery, or MRIs has been approved. So what’s the point of prior authorization, if they’re all going to be approved, other than to drive my office staff crazy?

Sometimes, I get fed up and get on the phone myself. When a retired family practitioner is on the other end, not only do they not know much about urology, they’ve never seen the patient. Within 30 seconds, it’s approved.

At one point, every staff member spent ½ to 2 hours a day on prior approvals. I have a solo practice and can’t afford to pay these people to play these insurance games.

David Flemming, MD / Monterey, CA

Just the sheer amount of time it takes to get prior authorizations for routine care. We need standard workflows for standard things that fall under guideline recommendations. We should do prior authorizations to filter out unique or maybe not appropriate treatments. But often, we’re requesting prior authorizations for things that get approved 95% of the time or more. If it’s standardized, guideline-driven care that gets approved most of the time, why does it still require prior authorization?

Insurance companies have no automated way to screen normal care, and our staff must still spend time filing paperwork. It seems like a delaying tactic to spread out payments to providers, and it delays patient care.

I also struggle, as a specialist who’s an expert—I’m a reconstructive urologist by training—when we call for prior authorizations, and the physicians we’re dealing with—especially peer to peer—are not experts in the field. They’re going off a ‘cookbook’ in terms of what to approve or not to approve. That’s frustrating.

A peer-to-peer review gets really time consuming. The reviewers may not be available when you call, and you can’t schedule in advance. You have to hang on the line a significant amount of time—20 minutes to a half hour—to get these coordinated.

Even a regular prior authorization can take a half hour on the phone just to reach somebody. It’s significant and means we have to hire more personnel to handle the paperwork. That increases the cost of care.

Joshua Broghammer, MD / Kansas City, KS

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Dr. Underwood: Health system must work for all

Dr. Underwood expressed the AMA’s policy position that enacting a Medicare for All plan would be fraught with problems, reducing coverage options, eliminating patient freedom of choice, injecting partisan politics into coverage policy, threatening access to mental health and contraceptive coverage, and more.

“It would destabilize coverage for 150 million people who already have insurance coverage. Health care is 20% of our economy, and Medicare for All would destabilize that,” he said, noting that such a plan would really not be a panacea, considering that millions of Medicare patients also pay for Part D drug coverage and supplemental plans to cover the gaps left by the health care plan for the elderly.

“We need to make sure that the health system works for the rich and the poor,” he stressed. “Your economic status, what you are born into, should not limit your quality of life. Poor black people have less than 10 to 12 years of life expectancy than whites, and it looks like Hispanics will be the same. That is wrong and somewhat criminal in a society that is as wealthy as ours.”

These issues must be addressed as health care policy is developed for the future.

“You’re only as strong as your weakest link,” he said, noting that in Buffalo there are five zip codes, dominated by African-American residents, where the mortality rate from disease is 300% higher than the rest of Erie County and the state of New York.

“You have a medical school, a law school, a school of public health, a dental school. Yet there is no strategic plan to fix this,” Dr. Underwood said. “These are some of the things we have to address, and I don’t think Medicare for All will fix that. We can send people to the moon and probes to Mars. We can do whatever we want to do. So, we can fix that. I think if we do, we will be a stronger nation for it.”

There are other key issues of particular concern to Dr. Underwood, such as physician burnout, which he said increased by some 40% in 2017, with some 300 to 400 physicians committing suicide last year.

“A lot of it has to do with the way our system doesn’t work for us,” he said.

Some of that involves such practice issues as requirements for electronic medical records and increased paperwork requirements that result in 2 hours of paperwork compared to 1 hour of patient care.

“We need to fight that.” He said. “We are working harder with less reimbursement. Private practices are being run out of business and urologists are being forced into either large practice groups or hospital health systems. Many who are working in health systems are finding themselves less satisfied with their positions, in contracts they didn’t really understand, and are having to move out of the area if they break away from the hospital system.”

Many smaller practices and groups are in trouble, said Dr. Underwood, because they are unable to create the infrastructure necessary, such as electronic medical records technology, and all the things they need to pay for performance indicators, etc., so that increases the burden, and they find themselves in the position where they have to get out of the business, sell their practice to a hospital, or join a large urology group if one is in their area.”

### AMA fights proposed mergers

Dr. Underwood said efforts by the AMA that helped result in proposed mergers between Aetna and Humana and Cigna and Anthem Health failing to be finalized saved physicians upwards of $500 million a year because “they would have had a monopoly and would have imposed contracts that would have reduced reimbursement rates to providers.

“It’s all about making more money, not improving care,” he said. “That’s what these mergers are all about.”

Still in play is CVS’s acquisition last year of Aetna, which is being held up by U.S. District Court Judge Richard Leon in Washington.

The AMA and its Council on Legislation, chaired by Dr. Underwood, brought together legal and academic experts and determined that the merger would have been anticompetitive and would have had “deleterious effects on both patients and physicians.”

After the U.S. Justice Department approved the merger, the AMA filed comments to Judge Leon and then filed an amicus brief explaining why Aetna’s proposed divestiture would fail to restore competition in the prescription drug plan market to premerger levels, one of the concessions CVS/Aetna needed to make to win government approval.

Dr. Underwood said he welcomes the opportunities offered by his new position on the AMA Board of Trustees, which he feels will allow him to make a real difference for patients and physicians alike.

“Urologists are cleaning up records at night,” he said. “We are working harder with less reimbursement. Private practices are being run out of business and urologists are being forced into either large practice groups or hospital health systems. Many who are working in health systems are finding themselves less satisfied with their positions, in contracts they didn’t really understand, and are having to move out of the area if they break away from the hospital system.”
Below is a review of a recent court case where the defendants were found to have deviated from the standard of care during a surgical procedure. This case helps to highlight important considerations around the level of involvement and supervision for trainees, and perhaps more importantly, what the patient knows.

The plaintiff had long-standing problems with urinary frequency and difficulty emptying his bladder, lasting nearly 30 years. He had undergone two transurethral resections of the prostate 2 years apart that provided some relief, in addition to taking a 5-alpha-reductase inhibitor.

The plaintiff sought treatment with a new urologist some 25 years after the TURPs had been done with complaints of nocturia, frequency, and urgency. A GreenLight laser procedure was recommended and performed. Postoperatively, the plaintiff experienced significant pain and bleeding, and more importantly, complete urinary incontinence. The plaintiff testified to soaking numerous adult incontinence pads per day.

A few months after the procedure, the plaintiff obtained his medical records from the hospital where the procedure was performed and learned that it had been performed by a third-year resident and not the physician he saw at the outpatient visit. In the complaint, the plaintiff alleged that the resident performed an unnecessary procedure, and that he performed it negligently.

The appropriate standard of care in medical malpractice litigation is proven—or not—by way of expert testimony. In the jurisdiction where this case was tried, the applicable rule is that expert testimony must explain what a medical professional of ordinary skill, judgment, care, and diligence in the same medical specialty would do in similar circumstances.

As in most any medical malpractice case, the court and/or jury often must be educated by expert witnesses about the involved anatomy, pathophysiology, and surgical procedures, along with other medical jargon, to fully understand the issues at trial.

As in most any medical malpractice case that reaches trial, the court and/or jury often must be educated by expert witnesses about the involved anatomy, pathophysiology, and surgical procedures, along with other medical jargon, to fully understand the issues at trial.

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Plaintiff’s expert covers key points
The plaintiff’s expert witness, a board-certified urologist, testified to a few key points:
• He explained the anatomy of the male urinary system.
• Performance of the GreenLight laser procedure deviated from the standard of care.
• The GreenLight laser procedure was not the appropriate treatment for the plaintiff.

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