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“We believe our findings can be useful for urologists in preoperative risk stratification and for guiding the intensity of postoperative surveillance,” added senior author Ben H. Chew, MD, MSc.

For the full article, turn to page 32

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Non–Muscle-Invasive Bladder Cancer: The revolution is here

Myriads therapies in the pipeline will change treatment landscape

Lisette Hilton / Urology Times® Correspondent

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Why the discovery phase is crucial

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Study highlights negative mental health impact of Peyronie disease

Overactive Bladder/Incontinence

Urinary incontinence prevalence is higher in women with diabetes

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IN THE PIPELINE

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SWOG S1602 phase 3 clinical trial is ongoing (NCT03091660)2

VICINEUM (VB4-845)
FDA currently reviewing a biologics license application for the treatment in patients with high-risk, BCG-unresponsive NMIBC3

CG0070
First patient dosed in December 2020 for phase 2 trial evaluating agent in combination with pembrolizumab (Keytruda)4

NADOFARAGENE FIRADENOVEC
Phase 3 data presented at 2020 Society of Urologic Oncology annual meeting and published in the Lancet Oncology, currently under FDA review5

N-803 (ANKTIVA)
Phase 2/3 data announced in December 20206

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Chairman’s Letter

NMIBC advancements spark anticipation and excitement

MIKE HENNESSY SR
Mike Hennessy Sr is chairman and founder of Urology Times® parent company, MJH Life Sciences™

T
day’s cover feature on current and future treatments in the non–muscle-invasive bladder cancer space is a fascinating look at an area within urology that had long been dormant but is now bursting with both available and forthcoming treatments, as Michael S. Cookson, MMHC, Urology Times® coeditor in chief, outlines in his accompanying editorial this month.

“Until recently, few breakthroughs were reported in the past several decades, and consequently, there had been not been much improvement in treatment-related outcomes....After a long period of stagnation and inertia, the bladder cancer space is alive and full of innovation and activation,” Cookson writes.

Switching gears to prostate cancer, look for a report on a recent discussion by Scott T. Tagawa, MD, MS, of the prostate-specific membrane antigen (PSMA)–targeted radiotherapeutic [12α-Lu-PSMA-617 (LuPSMA)]. As was evident from our cover feature in March,1 urologists can expect to hear quite a bit more about PSMA in the days to come. Tagawa discussed LuPSMA during the 2021 New York GU 14th Annual Interdisciplinary Prostate Cancer Congress® and Other Genitourinary Malignancies.2 During the discussion, Tagawa also gave an update on recent developments regarding the α particle–emitting radiotherapeutic radionuclide 223 (Xofigo) in patients with castration-resistant prostate cancer and bone metastases.

In benign prostatic hyperplasia, we report on recent 1-year follow-up data for the Optilume drug-coated balloon catheter system, as well as a presentation from Tobias S. Kohler, MD, MPH, on the UroCuff test. Kohler discussed the test at the recent Society of Benign Prostate Disease’s virtual meeting. For sexual dysfunction, look for coverage of a study pointing to the feasibility of sticking to your investment strategy, even during times of record-high markets. In Speak Out, 3 urologists share their thoughts on the COVID-19 pandemic–prompted rise in virtual conferences and meetings.

“I expect we’ll continue to see a hybrid system in that there will be in-person as well as Zoom lectures,” Ross Moskowitz, MD, predicts. Finally, in Malpractice Consult, Kenton H. Steele, Esq, gives a detailed breakdown of the discovery phase of a malpractice lawsuit and the importance of sticking to your investment strategy, even during times of record-high markets. In Speak Out, 3 urologists share their thoughts on the COVID-19 pandemic–prompted rise in virtual conferences and meetings.

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FDA approves sacituzumab govitecan for urothelial cancer
The FDA has granted an accelerated approval to sacituzumab govitecan (Trodelyv) for the treatment of patients with locally advanced or metastatic urothelial cancer (mUC) who previously received a platinum-containing chemotherapy and either a PD-1 or PD-L1 inhibitor.1,2

The approval of the antibody-drug conjugate (ADC) was based on the final data from cohort 1 of the phase 2 TROPHY-U-01 trial (NCT03547973), which showed that sacituzumab govitecan induced an overall response rate of 27.0% in heavily pretreated patients with mUC following the failure of both platinum-based chemotherapy and checkpoint inhibition. There were 31 responders, including 6 (5%) complete responses and 22 (22%) partial responses, according to findings presented during the 2020 European Society for Medical Oncology Congress.3 The median response duration with the ADC was 7.2 months.

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Vibegron is officially launched in US overactive bladder market
Vibegron (Gemtesa) is now commercially available in the United States for the treatment of adult patients with overactive bladder with symptoms of urge urinary incontinence (UUI), urgency, and urinary frequency, according to Urovant Sciences, the developer of the β3-adrenoceptor agonist.1

The FDA approved vibegron on December 23, 2020, for use in this setting based on the phase 3 EMPOWUR trial. In the primary study analysis at 12 weeks, vibegron showed a mean change in baseline in the average daily number of micturitions of −1.8 compared with −1.3 for placebo and −1.6 for tolterodine (P < .001).1,2 The mean change from baseline in UUI episodes was −2.0, −1.4, and −1.8, respectively.

REFERENCES
Bladder cancer research enters a renaissance period

MICHAEL S. COOKSON, MD, MMHC
Cookson, professor and chair of urology at the University of Oklahoma Health Sciences Center in Oklahoma City, is co-editor in chief of Urology Times®.

This issue of Urology Times® provides a timely update on the current and future state of improvements in the management of non–muscle-invasive bladder cancer (NMIBC). The high prevalence of disease translates to more than 700,000 individuals in the United States with bladder cancer, and the majority of those cases are noninvasive.1 Further-more, bladder cancer care has been tagged with the dubious distinction of being the most expensive cancer to treat over a patient’s lifetime.2 Until recently, few breakthroughs were reported in the past several decades, and consequently, there had not been much improvement in treatment-related outcomes.

Given the magnitude and burden of disease on the health care system, the problem begs for solutions in the form of improved detection and more effective treatment for both early- and late-stage disease. However, one of the most important reasons for the lack of advancements in treatment has been disproportionately low funding for research in bladder cancer. This underfunding has resulted in fewer quality studies and novel developments.3 Some of the pivotal breakthrough studies include the use of pembrolizumab (Keytruda), a PD-1 immune checkpoint inhibitor, which received FDA approval in 2020 after benefit was demonstrated in patients with BCG-unresponsive CIS.4 There is also great anticipation over targeted drug delivery (COMBAT) in superficial bladder cancer: initial results.5

Both of these novel intravesical therapies have resulted in complete response rates of greater than 40% at 12 months in patients with CIS. These and other agents used alone or in combination will revolutionize the treatment of patients who until recently had few bladder-preserving options and were often relegated to radical cystectomy. So, after a long period of stagnation and inertia, the bladder cancer space is alive and full of innovation and activation.6

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Bladder cancer research enters a renaissance period

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[BCG]-unresponsive disease and stimulating activity in this space. Now, the majority of clinical trials in non–muscle-invasive bladder cancer include patients with BCG–unresponsive disease,” Dinney said.

Transurethral resection of the bladder tumor (TURBT) remains the standard for the initial management of NMIBC, according to Leonard G. Gomella, MD, the Bernard W. Godwin Jr Professor of Prostate Cancer and chair of the Department of Urology at Sidney Kimmel Medical College at Thomas Jefferson University in Philadelphia, Pennsylvania.

“It is very important to get clear margins. What we have been finding is [that] to get good margins, there is a lot of variation in the technique and some limitations to standard white light detection,” Gomella said.

A major limitation of standard cystoscopy and TURBT when using white light is that it can miss 20% to 30% of flat, papillary, or carcinoma in situ (CIS) lesions, resulting in early recurrence,7 according to Badar M. Mian, MD, professor of surgery in the Division of Urology at Albany Medical College in New York.

“Two of the most commonly used modalities to improve the diagnostic and therapeutic yield endoscopic resection include photodynamic diagnostic, or blue light, cystoscopy and nar...
row band imaging. In single-arm studies, both modalities have demonstrated improved cancer detection rates and decreased recurrence rates. Blue light cystoscopy appears to be more efficacious, but there are no studies of direct head-to-head comparison of these enhanced imaging modalities,” Mian said.

Most low-grade bladder tumors do not need intravesical therapy. However, intravesical therapy is recommended for high-grade superficially invasive T1 bladder cancer with or without CIS. A repeat TURBT several weeks later is recommended in most settings with the presence of high-grade Ta or T1 disease. In the presence of any CIS, the patient is automatically classified as high risk. Guidelines always suggest that radical cystectomy or clinical trials be considered in these patients. However, in clinical practice it is reasonable to attempt to control the cancer with intravesical therapy initially, according to Gomella.

BCG remains today’s standard of care immunoncology agent for NMIBC. US clinicians tend to use BCG according to the Southwest Oncology Group (SWOG) regimen, which is an induction course of intravesical BCG for 6 weeks and then maintenance courses of 3 weekly doses at 3 months and every 6 months thereafter for up to 2 to 3 years, for both T1 and CIS disease, according to Gomella.

“There are many different variations on this schedule,” Gomella said.

Unfortunately, 30% to 40% of patients with NMIBC fail to respond to BCG therapy, and there is a need to better define BCG failure, according to Michael S. Cookson, MD, MMHC, professor and chairman of the Department of Urology and the Donald D. Albers Endowed Chair in Urology at the University of Oklahoma Health Sciences Center in Oklahoma City.

“Historically, patients treated with intravesical BCG who recurred were not properly identified, and so the decision as to when to discontinue BCG or move on to second-line treatments was difficult,” Cookson said. “Furthermore, the lack of a standard definition of BCG-unresponsive disease confounded results from these ‘salvage treatments’ and resulted in both overly optimistic response rates due to treatment of patients at lower risk and poor results sometimes due to delayed recognition of patients who were subjected to too many rounds of ineffective BCG. To be clear, patients identified as BCG unresponsive should not receive further BCG. So, it is important to clearly define BCG-unresponsive disease.”

It is defined in patients who recur with high-grade noninvasive disease who have persistent or recurrent CIS alone or with recurrent Ta/T1 disease within 12 months of completion of adequate BCG therapy, recurrent high-grade Ta/T1 disease alone within 6 months of completion of adequate BCG therapy, or T1 high-grade disease at the first evaluation following an induction BCG course. According to the FDA, adequate BCG is defined as at least 5 of 6 doses of an initial induction course plus at least 2 of 3 doses of maintenance therapy or at least 5 of 6 doses of an initial induction course plus at least 2 of 6 doses of a second induction course.

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“Non–muscle-invasive bladder cancer [that] has recurrent or persisted despite intravesical BCG is destined to progress to more advanced disease,” Mian said. “Delay in identifying BCG-unresponsive disease and moving to radical cystectomy is associated with worse overall survival, especially when non–muscle-invasive cancer is allowed to progress to muscle-invasive disease. Radical cystectomy remains the only curative option for BCG-unresponsive non–muscle-invasive bladder cancer, but some patients are not optimal candidates for, or refuse, a major surgical procedure.”

Another consideration is the worldwide BCG shortage, which is expected to continue for at least the next year, according to Gomella.

SUO and AUA recommend not using BCG for low-risk disease and to consider using an alternative chemotherapy agent or reduced-dose BCG for intermediate or high-risk disease.11

“The suggestion right now of using a half dose for induction and possibly a third of a dose for maintenance appears to be very reasonable. So far, we have not seen any major changes in disease recurrence or progression, although this is an area of ongoing research,” Gomella said.

Intravesical therapy is used not only in the salvage setting but also postoperatively.

“Historically, we have found that a single dose of chemotherapy within 24 hours of a TURBT, with 6 hours or less being the optimum time, can reduce 5-year recurrence rates. Right now, gemcitabine used in a 2000-mg dose and mitomycin C used in the 40-mg dose12 are the preferred agents,” Gomella said.

Currently, the only FDA-approved intravesical chemotherapy agents are thiotepa and valrubicin. Thiotepa is no longer used due to toxicity concerns, and valrubicin’s label is specific for BCG-refractory CIS in patients who cannot undergo radical cystectomy, Gomella said.

“We are using many intravesical agents now mostly off-label. Agents such as gemcitabine [and] docetaxel [are examples],13 and one of the mainstays that we have used for many years is mitomycin C,” Gomella said. “There are many trials using different methods seeking to improve the effectiveness of intravesical therapy. One of the biggest areas right now is the use of combination intravesical chemotherapy, and one of the most exciting areas that has been reported is the sequential use of gemcitabine and docetaxel. There have been some nonprospective randomized institutional studies that have shown using this combination of gemcitabine and docetaxel sequentially can have a recurrence-free survival [rate] at [approximately] 60% at 1 year and [approximately] 46% at 2 years in BCG-refractory disease.”

A big development last year was the approval of systemic pembrolizumab for BCG-refractory NMIBC.

“Pembrolizumab, a PD-1 immune checkpoint inhibitor, received approval14 after a single-arm study (KEYNOTE-057; NCT02625961) of high-risk, BCG-unresponsive non–muscle-invasive bladder cancer with carcinoma in situ,” Mian said. “It demonstrated complete response in 41% of patients for a median duration of 16.2 months. These patients were either ineligible for or declined radical cystectomy and required intravenous pembrolizumab for up to 24 months.”

Safety, however, could be an issue for some patients, as approximately 13% of those treated with pembrolizumab in trials reported 3 to 5 adverse events, according to Dinney.

“It is important to point out that the long-term disease control, or cure, rates of bladder salvage options such as combination intravesical chemotherapy or PD-1 inhibitors are not comparable to radical cystectomy,” Mian said. “Thus, the treatment options for potential avoidance of radical cystectomy should be discussed with sufficient equipoise and in the appropriate patient population.”

Pipeline update

There is a tremendous amount of work being done in BCG-refractory cancer, with dozens of trials looking at novel intravesical agents, according to Gomella.

“These novel agents include things such as the Tokyo strain of BCG. The SWOG 1602 Prime trial15 is actually looking at intradermal BCG priming when using the Tokyo strain of BCG,” Gomella said.

The FDA granted priority review to Vicineum (VB4–845), a recombinant fusion protein that targets epithelial cell adhesion molecule antigens on the surface of tumor cells to deliver a potent protein payload, Pseudomonas exotoxin A.16

“A recent trial17 showed this is a very safe approach and that patients with non–muscle-invasive bladder cancer in situ had reasonable complete response rates of [approximately] 40% at 3 months and [approximately] 28% at 6 months,” Gomella said. “What is important in that trial, known as the VISTA trial18, is that 75% of patients were able to remain free of cystectomy at a period of over 2 years.”

In late-stage trials, the oncolytic adenovirus CG0070, which contains a GM-CSF transgene, selectively killed cancer cells through the cells’ dysfunctional retinoblastoma pathway. Developer CG Oncology announced in December that the first patient with BCG-unresponsive
NMIBC was dosed in a phase 2 clinical trial of CG0070 in combination with pembrolizumab. The FDA also is reviewing the investigational gene therapy nadofaragene firadenovec. Investigators with the SUO Clinical Trials Consortium reported that in high-grade, BCG-unresponsive NMIBC, nadofaragene firadenovec resulted in a 46% complete response rate in CIS at 12 months, with or without Ta or T1 disease.

According to Dinney, who is part of the team that developed nadofaragene firadenovec, the goals of the therapy are to alter the natural history of this disease and prevent recurrence and progression to provide bladder preservation with acceptable morbidity.

“If you look at the studies that have been reported, it seems patients have [approximately] 1 year to try other therapies before their survival is compromised by avoiding cystectomy,” Dinney said. “If you look at Vicineum and nadofaragene, the clinical responses are similar. Vicineum has a more intense induction and maintenance schedule. Nadofaragene is a gene therapy that is given intravesically once every 3 months. And the safety profile of nadofaragene is favored over pembrolizumab.”

One other promising investigational agent for BCG-unresponsive NMIBC is the IL-15 super-agonist known as N-803.

“The IL-15 is a superagonist antibody and cytokine fusion protein that targets and activates endogenous killing through NK [natural killer] cells and CD8+ T cells without inducing any type of T-regulatory stimulation,” Gomella said. “It was reported...that in an early trial, almost 60% of the patients with carcinoma in situ had a complete response at 12 months with a very reasonable safety profile.”

The landscape is going to change dramatically in the next 2 years, according to Dinney.

“[Patients with] non-muscle-invasive bladder cancer will have a lot more choices,” he said.

Disclosures: Dinney developed nadofaragene firadenovec. Cookson has done consulting with FerGene.

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BADR M. MIAN, MD

COVER STORY / Bladder Cancer
BCG alternative shows promise in non–muscle-invasive bladder cancer

Hyperthermic intravesical therapy with high-dose mitomycin-C is safe and well tolerated

Cheryl Guttman Krader, BSPharm

Urology Times® Contributing Editor

Treatment for high-risk non–muscle-invasive bladder cancer (NMIBC) with hyperthermic intravesical chemotherapy (HIVEC) using high-dose mitomycin-C (MMC) is safe and well tolerated, and appears efficacious after short-term follow-up, according to a report from Duke University urologists.1 In a paper presenting term follow-up, according to a report from Duke University urologists,1 In a paper presenting the first North American clinical experience with this modality, the investigators summarized outcomes from a cohort of 14 patients who received MMC HIVEC because of the BCG shortage. The median number of instillations received was 6, and the median follow-up for the series was 11 months.

“Our study demonstrates the feasibility of HIVEC MMC and suggests it is a reasonable substitute for BCG during global shortages.”

SCOTT P. CAMPBELL, MD

The MMC HIVEC was well tolerated by 11 (79%) patients. Seven patients (50%) developed adverse events (AEs), but all were grade 1 or 2. During the available follow-up, 2 patients (14%) experienced a cancer recurrence, but both had discontinued MMC HIVEC after only 2 treatments.

Scott P. Campbell, MD, third-year urology resident at Duke University Medical Center, Durham, North Carolina, told Urology Times®, “Given the limited supply of BCG and the lack of reliable treatments in the post-BCG setting, our biggest priority is to continue to identify therapies for bladder cancer that are safe and effective alternatives to BCG. Our study demonstrates the feasibility of HIVEC MMC and suggests it is a reasonable substitute for BCG during global shortages. We hope that clinical trials stem from this series to help the urologic oncology community better understand how to optimize HIVEC, including testing alternative agents to MMC.”

The 14 patients included in the MMC HIVEC series comprised 4 with intermediate-risk disease and 10 with high-risk NMIBC. Twelve patients had recurrent tumors, of which 11 had been previously treated with intravesical BCG (median, 6 treatments). Three patients were BCG naïve.

“There are multiple hyperthermia systems, but the convective system we chose is small, reliable, low maintenance, widely available, affordable, and easy to use. Therefore, it could be rapidly implemented into clinical practice in our cancer center.”

DOMINIC C. GRIMBERG, MD

The MMC HIVEC was administered at a concentration of 2 mg/mL (120 mg diluted in 60 mL sterile water) using a convective hyperthermia system (Combat BRS) with an induction course of 6 weekly instillations followed by up to 12 additional monthly treatments in the setting of a negative postinduction cystoscopy. Dwell time was 60 minutes heated and 30 to 60 minutes unheated following catheter removal. MMC was chosen because it had been used in nearly all clinical trials investigating hyperthermia and is a reasonable substitute for BCG during global shortages.

Many patients have already been seen at a 12-month visit, and preliminarily the data show that durable oncologic control is possible when patients are able to receive full induction courses of high-dose HIVEC MMC.”

BRANT A. INMAN, MD, MS

“Many patients have already been seen at a 12-month visit, and preliminarily the data show that durable oncologic control is possible when patients are able to receive full induction courses of high-dose HIVEC MMC.”

REFERENCES
A tale of 2 lymph node dissections

Due to the low sensitivity of imaging studies, pelvic lymph node dissection (PLND) remains the most effective method for staging of prostate cancer. Due to paucity of randomized controlled trials (RCT), the role of various PLND templates, in terms of prognostic and therapeutic benefits, has remained controversial. Some experts believe that standard or limited PLND (LPLND) is sufficient for staging, whereas others strongly support the use extended PLND (EPLND) for its potential to remove more lymph nodes and micrometastases. An RCT by Lestingi et al was detailed here a few months ago.

Now, Touijer et al report the results of an RCT that was designed to address the questions regarding the therapeutic benefits (ie, biochemical recurrence [BCR]-free survival) of EPLND compared with LPLND. From October 2011 to March 2017, of 1477 men undergoing radical prostatectomy and bilateral PLND, 700 men were randomized to the LPLND template and 740 to the EPLND template group. Instead of individual patient randomization, a cluster randomization strategy was employed for ease of consent and logistics of trial execution. The surgeons were cluster randomized every 3 months to perform either LPLND or EPLND.

Among the randomized patients, no PLND was performed in 42 and 55 patients in the LPLND and EPLND groups. Thirty-seven patients were excluded either due to withdrawal of consent (n = 8) or being lost to follow-up (n = 29). In the LPLND and EPLND groups, respectively, the distribution of biopsy Gleason scores (GS) was 18% and 22% for GS of 8 or higher, 19% and 17% for GS 4 + 3, 52% and 52% for GS 3 + 4, and 10% and 9.4% for GS 6.

In terms of lymph node yield, a median of 12 lymph nodes were removed in the LPLND group compared with 14 in the EPLND group. The rate of lymph node metastasis (pN1) was 12% in the LPLND arm and 14% in the EPLND arm (P = .3).

After a median follow-up of 3.1 years, 388 (26.9%) BCR events occurred in the entire cohort. Regardless of how the data were analyzed, there was no difference in the BCR rates between the LPLND and EPLND (P = .5) groups. Overall, the rates of Clavien-Dindo grade 2 and grade 3 complications (including deep vein thrombosis or lymphocele) were similar in the LPLND and EPLND groups at 7.3% and 6.4%, respectively. There were no grade 4 or 5 complications.

Similar lack of therapeutic effect of EPLND was noted in another RCT reported by Lestingi et al a few months ago. Although these 2 trials cannot be compared directly, there are several baseline differences among the trials worthy of consideration. The current trial was sufficiently powered with 1477 patients, compared with 300 patients in the earlier study. One main difference among the trials was in the EPLND template. The earlier trial by Lestingi et al included the common iliac nodes in the EPLND template, which yielded median 17 lymph nodes, but not in the current trial, which yielded median 14 lymph nodes. Conversely, the median lymph node count with LPLND in the current trial was much higher than in the earlier trial (12 lymph nodes vs 3 lymph nodes, respectively), and the rate of pN1 in the LPLND group was 12% in the current trial and only 3.4% in the earlier trial.

Although studies have reported variability in the correlation between more lymph nodes removed and higher rate of pN1, none have demonstrated a difference in BCR rates between LPLND and EPLND groups. Further, the benefit of any PLND in patients with intermediate-risk prostate cancer, which make up the majority cohort in both of the RCTs, is subject to debate. A recent report by Alrok et al evaluated the impact of omitting the PLND in cases with biopsy GS of 3 + 4 or lower, T1-2 who are subsequently upgraded to prostatectomy GS 4 + 3 or lower, or stage pT3a. They noted that omission of PLND in appropriately matched cases did not alter the rate of BCR compared with those who underwent PLND (regardless of template). The current trial did not report the outcome of 97 patients in whom a PLND was omitted.

The authors of this RCT estimated that the complication rates were similar in the LPLND and EPLND groups, which is similar to what has been reported by other nonrandomized studies, and is reflective of this author’s experience. Yet a recent large, systematic review and meta-analysis of this subject suggests otherwise. A study by Cacciamani et al reviewed 176 studies (77,303 patients) undergoing PLND.2 Intraoperative complications were noted in 1.8% and postoperative complications in 14.1%. The limited or standard PLND group experienced fewer complications (risk ratio, 0.55; P = .01), especially lymphoceles and thromboembolic events, compared with EPLND. EPLND was an independent predictor of increased complications, especially lymphocele formation (risk ratio, 1.77; P < .001).

When comparing this trial with other studies, the median lymph node count in the LPLND cohort was higher; in the EPLND cohort, it was lower than expected. The lymphatic and fibrofatty tissue removed during PLND are contiguous and not anatomically compartmentalized based on the arbitrary template boundaries assigned by surgeons. The surgical technique and tissue handling by various surgeons can easily result in variations in lymph node count within the same template.

The lack of difference in the lymph node yield between the LPLND and EPLND templates noted in this RCT raises interesting questions about surgical technique, trial design, compliance with instructions, and surgical bias. This is illustrated by the fact that surgeons retrieved more lymph nodes from patients with high-risk prostate cancer even when they were assigned to perform LPLND. Knowledge of tumor characteristics and the awareness that their work is being reviewed may have influenced the surgical technique, resulting in higher-than-expected lymph node counts in the LPLND group and thus obscuring any potential differences in node count, pN1, or BCR rates.

It is common practice in uro-oncology to perform EPLND for high-risk prostate cancer. It remains unclear whether...
Expert outlines the latest data for the prostate-specific membrane antigen–targeted radiopharmaceutical

**PSMA theranostic** ¹⁷⁷Lu-PSMA-617 approaches prime time in mCRPC

The prostate-specific membrane antigen (PSMA)–targeted radiopharmaceutical ¹⁷⁷Lu-PSMA-617 (LuPSMA) is rapidly advancing through the pipeline in metastatic castration-resistant prostate cancer (mCRPC), Scott T. Tagawa, MD, MS, explained during the 2021 New York GU Hub Annual Interdisciplinary Prostate Cancer Congress and Other Genitourinary Malignancies.

In a session covering all radiopharmaceutical developments in mCRPC, Tagawa, a professor of medicine and urology at Weill Cornell Medicine and an attending physician at NewYork-Presbyterian/Weill Cornell Medical Center in New York, New York, spent a key segment focusing on LuPSMA, which is poised to become one of the first PSMA theranostics approved by the FDA.

Tagawa started the session by highlighting the first prospective study of LuPSMA, which was a single-arm phase 2 trial (ANZC-TR12615000912383) conducted exclusively at the Peter MacCallum Cancer Centre in Melbourne, Australia. The investigators enrolled men 18 years or older with mCRPC and disease progression. Patients had received taxane-based chemotherapy and second-generation androgen drugs, such as abiraterone acetate (Zytiga) and enzalutamide (Xtandi).

High PSMA expression was confirmed through a PSMA screening. Patients received a maximum of 4 cycles of intravenous LuPSMA. The primary end point of a 50% or more decline in PSMA from baseline was reached by 57% (n = 17) of 30 evaluable patients. Hofman et al also observed clinically meaningful improvements in pain severity and interference scores.

Regarding safety, the most frequently occurring adverse events (AEs) among the 30 evaluable patients were grade 1 dry mouth (87%), grade 1/2 nausea (50%), and grade 1/2 fatigue (50%). The investigators also reported that 4 patients (13%) had grade 1/4 thrombocytopenia potentially related to LuPSMA treatment.

The next key study of LuPSMA was the open-label phase 2 TheraP trial (NCT03924280). This study randomized men with mCRPC to LuPSMA or cabazitaxel (Jevtana).

“This was a postdocetaxel population, and a majority also happened to have received a hormone therapy, but that was not required. A PSA [prostate-specific antigen] of 20 ng/mL was required to enroll—so, higher than most of our CRPC studies that had a primary end point of PSA,” said Tagawa.

Overall, the TheraP trial enrolled 200 patients who received imaging with Gallium 68 PSMA-11 and fludeoxyglucose F 18 (¹⁸F-FDG) PET/CT confirming high PSMA expression and no sites of FDG-positive/PSMA-negative disease. More than 90% of patients in each arm had received abiraterone acetate, enzalutamide, or both.

Patients were randomized in a 1:1 ratio to LuPSMA (n = 99) or cabazitaxel (n = 101), and study treatment occurred at 11 clinical locations in Australia. PSA response rate was the primary study end point; a PSA response was defined as a 50% or more reduction.

The results showed that the PSA response rate was 66% with LuPSMA compared with 37% with cabazitaxel, representing a 29% absolute greater PSA response rate (P < .0001). For sensitivity analysis per protocol, the difference observed was 23% (P = .0016).

LuPSMA delayed progression versus cabazitaxel (HR, 0.63; P = .0028), with a comparable benefit observed in radiographic progression-free survival (PFS; HR, 0.64; P = .0070) and PSA PFS (HR, 0.60; P = .0017).

“This was an open-label study, and patients randomized to cabazitaxel sometimes did not accept therapy. But the sensitivity analysis still showed a [PSA response] benefit with LuPSMA and also a PFS benefit,” Tagawa said.

The safety analysis included 98 men in the LuPSMA arm and 85 men in the cabazitaxel arm. Grade 3/4 AEs occurred in 33% (n = 32) and 53% (n = 45) of the 2 arms, respectively.

Summarizing the main safety takeaways from TheraP and other early prospective assessments of LuPSMA, Tagawa said, “Prospectively, all studies [of LuPSMA] have shown that the majority of patients get some xerostomia, meaning greater than 50%. And you can see that dry mouth as well as thrombocytopenia were the toxicities that were higher with LuPSMA [vs] cabazitaxel. Luckily, the vast majority of these were grade 1, and most got better. But grade 3 is really bad…so just kind of keep that in mind.”

During his presentation, Tagawa mentioned that the next milestone for LuPSMA would be the eagerly awaited results of the phase 3 VISION trial (NCT03511664). Following Tagawa’s presentation, it was reported that findings from the VISION study showed that adding LuPSMA to best standard of care (BSC) improved overall survival (OS) in patients with progressive PSMA-positive mCRPC.

The open-label VISION trial accrued patients with progressive PSMA-positive mCRPC who received at least 1 novel androgen axis drug (eg, enzalutamide or abiraterone acetate) and were previously treated with 1 to 2 taxane regimens. Patients were randomized to LuPSMA plus BSC or BSC alone. The coprimary end points of the trial were OS and PFS.

Beyond OS, LuPSMA also extended PFS when added to BSC versus BSC alone. No new safety signals emerged in the trial.

Data from the study will be presented at a future scientific conference, according to Novartis, the developer of LuPSMA. The company also plans to submit the findings to regulatory authorities to receive approval of LuPSMA for patients with mCRPC.

For a list of references, visit: https://bit.ly/3qTG15H

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the increased lymph node yield or increased pN1 rates have any therapeutic effect on BCR. Neither the current nor the previous RCTs (and several nonrandomized studies) have reported any improvement in BCR rates with the use of EPLND. However, the median follow-up in both RCTs was relatively short and most patients harbored low- or intermediate-risk disease, which makes it difficult to draw firm conclusions. Three decades into prostate-specific antigen screening–detected prostate cancer, the prognostic and therapeutic impacts of various types of pelvic lymph node dissection remain unclear. The role of PLND will be further challenged when more sensitive imaging and staging modalities become readily available. Although it’s likely that the urologists will continue to utilize EPLND despite unclear prognostic value, this will have to be balanced with the lack of therapeutic advantage, additional surgical time and cost, and possible increase in complications associated with EPLND.

For a list of references, visit: https://bit.ly/3v6w57V

**For list of references visit.**

Rucaparib plus enzalutamide shows early promise in metastatic CRPC

The combination of rucaparib (Rubraca) and enzalutamide (Xtandi) was shown to be safe with early signs of efficacy in patients with metastatic castration-resistant prostate cancer (mCRPC), according to findings from the phase Ib RAMP study presented during the American Association for Cancer Research Annual Meeting 2021.1

The doublet of the PARP inhibitor rucaparib and the androgen receptor (AR) inhibitor enzalutamide induced a prostate-specific antigen (PSA) decline in three-fourths of patients and a confirmed PSA response in half of the patients enrolled in the small study.

“A combination of enzalutamide and rucaparib had an acceptable safety profile and no clinically significant drug-drug interactions. In this small patient set, patients previously treated with AR-directed therapies showed responses to the combination even in the presence of AR alterations and in the absence of [DDR] gene alterations,” wrote the investigators, led by Arpit Rao, MBBS, of the University of Minnesota, Minneapolis.

Of the 8 patients, 75% (n = 6) had a PSA decline. Four (50%) patients had a confirmed PSA response, defined as a 50% or more decline in PSA level from baseline.

The investigators also conducted an exploratory analysis to assess the association between genomics and clinical activity. For this analysis, the researchers used a Foundation Medicine assay to profile plasma and/or tissue samples for genomic alterations. Of the 8 patients, genomic data were available for 6, all of whom had received prior AR-directed therapy.

The combination led to a PSA decline from baseline in 3 of the 4 patients with 1 or more somatic AR alteration (−99%, −22%, and −17%, respectively). No PSA decline was observed in the 1 patient with a DDR gene mutation (a subclonal alteration of CHEK2). Of note, genomic testing did not identify any alterations in BRCA1/2 or PALB2.

The investigators concluded that the early efficacy signals and genomic data support additional trials exploring the combination of rucaparib and enzalutamide in mCRPC. One such study, the CASPAR trial (NCT04455750), has already been launched.2 The phase 3 trial is exploring the combination as a frontline treatment in biomarker-unselected men with mCRPC.

Rucaparib is approved by the FDA for the treatment of patients with deleterious BRCA1 mutation (germline and/or somatic)–associated metastatic mCRPC who have been treated with AR-directed therapy and a taxane-based chemotherapy.

REFERENCES

CTC mutations may predict hormone therapy outcomes in mCRPC

Genetic alterations were linked to response or resistance to abiraterone acetate and enzalutamide

Audrey Sternberg
Managing Editor, Oncology®

Certain genetic alterations in circulating tumor cells (CTCs) were associated with treatment outcomes with the androgen receptor (AR) inhibitors enzalutamide (Xtandi) and abiraterone acetate (Zytiga) in patients with metastatic castration-resistant prostate cancer (mCRPC), according to findings published in Molecular Cancer Research.3

Specifically, gains of BRCA2, APC, KDM5D, CYP11B1, and SPARC and losses of CHD1, PHLPP1, EKB, ZFHX3, and NCOR2 detected by CTCs were associated with primary resistance to abiraterone and enzalutamide. In contrast, gains in ATM, NCOR2, and HSD17B4 detected by CTCs were associated with sensitivity to the AR inhibitors.

“We were surprised to observe that a gain of BRCA2 was associated with worse outcomes in mCRPC resistant to AR inhibitors, as that has not been described before. Typically, loss of BRCA2 has been associated with poorer outcomes,” study author Andrew Armstrong, MD, MSc, medical oncologist at the Duke Cancer Institute Center for Prostate and Urologic Cancers at Duke University in Durham, North Carolina, said in a news release.2 “Our finding may explain some resistance to DNA-damaging agents and AR therapies that have not been well understood and requires further mechanistic investigation.”

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CPC MUTATIONS
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The retrospective secondary analysis of the prospective PROPHECY trial (NCT02269982) of men receiving either enzalutamide or abiraterone was conducted to identify somatic genomic alterations associated with acquired resistance. Seventy-three samples from 48 patients were analyzed over time for pooled CTCs and whole-genome copy number alterations by germline DNA; additionally, CTCs and germline whole-exome sequencing before and after progression on AR-targeted therapy were assessed in 22 paired samples.

The PROPHECY study had previously revealed that the presence of androgen receptor splice variant 7 (AR-V7) in CTCs in this patient population was associated with a lower response rate and poorer survival outcomes with either enzalutamide or abiraterone.1

“While these findings were encouraging, only about 5% to 40% of patients with mCRPC have CTCs that are positive for AR-V7, depending on the disease context, suggesting that other genetic alterations may play a role in drug resistance.”

ANDREW ARMSTRONG, MD, MSC

splice variant 7 (AR-V7) in CTCs in this patient population was associated with a lower response rate and poorer survival outcomes with either enzalutamide or abiraterone.1

“While these findings were encouraging, only about 5% to 40% of patients with mCRPC have CTCs that are positive for AR-V7, depending on the disease context, suggesting that other genetic alterations may play a role in drug resistance,” Armstrong said.

Research confirms prior data

The research was also able to confirm prior data indicating that poor outcomes with AR inhibition are associated with PTEN loss, MYC gain, AR gain, and TP53 mutations in CTCs.

Patients benefiting the most from treatment with enzalutamide or abiraterone were more likely to have alterations in genes associated with DNA repair, steroid metabolism, lineage plasticity, and PI3K and WNT signaling by CTCs. Benefits with therapy were more likely in patients with chromatin and epigenetic gains correlated with loss of CHD1 and gains of KDM5D, whereas progression was more often seen in those with clonal evolutions with gains in ATM, FOXA1, UGT2B17, KDM6A, CYP11B1, and MYC and/or acquired losses of NCOR1, ZFHX3, and ERG.

“Our study reinforces that analyzing CTC genomics has potential for identifying and tracking disease resistance or efficacy with AR inhibitors over time,” Armstrong said. “The novel alterations we identified will need to be validated by further research but may represent priority candidates for new drug targets.”

The investigators acknowledged the small sample size as a limitation to the study and pointed out that differences in sensitivity of assays at different time points may bias the findings.

REFERENCES

"While these findings were encouraging, only about 5% to 40% of patients with mCRPC have CTCs that are positive for AR-V7, depending on the disease context, suggesting that other genetic alterations may play a role in drug resistance."

ANDREW ARMSTRONG, MD, MSC
Radium-223 in metastatic CRPC: Where are we in 2021?

Research points to importance of using bone health agents with the prostate cancer treatment

Jason M. Broderick
Associate Editorial Director, Urology Times®

At the 2021 New York GU 14th Annual Interdisciplinary Prostate Cancer Congress® and Other Genitourinary Malignancies, which was held virtually in March, Scott T. Tagawa, MD, MS, discussed the latest developments with the alpha particle–emitting radioactive therapeutic agent radium-223 (Xofigo) in patients with castration-resistant prostate cancer (CRPC) and bone metastases.1

**ALSYMPCA trial**

Based on results from the phase 3 ALSYMPCA trial (NCT00699751), the FDA approved radium-223 in 2013 for the treatment of patients with CRPC, symptomatic bone metastases, and no known visceral metastatic disease.

The double-blind ALSYMPCA trial randomized 921 patients with CRPC and bone metastases 2:1 to best standard of care plus either 6 doses of radium-223 or placebo.2 Radium-223 reduced the risk of death by 30%, with median overall survival (OS) of 14.9 months compared with 11.3 months in the placebo arm (HR, 0.70; P < .001). The median time to first skeletal-related event was 15.6 months versus 9.8 months, respectively (HR, 0.66; P < .001).

“A 30% improvement in overall survival is right in line with the 20% to 30% improvement we typically see with successful agents, so this led to an FDA approval,” said Tagawa, professor of medicine and urology at Weill Cornell Medicine and an attending physician at New York-Presbyterian/Weill Cornell Medical Center in New York, New York.

**Radium-223 combinations**

Following the ALSYMPCA study and prior to the FDA approval of radium-223, investigators conducted a phase 3b trial that was an early access, open-label, single-arm study of radium-223 in patients with CRPC with bone metastases.1

Among the findings from this nonprospective early access data set was that median OS was longer among patients treated with radium-223 plus abiraterone acetate (Zytiga), enzalutamide (Xtandi), or both agents, versus the median OS in patients not receiving these treatments. Combination therapy with radium-223 plus denosumab also was associated with a longer median OS compared with median OS in patients receiving radium-223 without denosumab.3

“It looked [as though] there was a fairly clear difference in overall survival for patients who got radium-223 with either abiraterone or enzalutamide at the same time, and similarly for those [who] received denosumab at the same time,” Tagawa said.

**In summary, radium-223 will lead to an overall survival benefit in men with metastatic castration-resistant prostate cancer to the bone with limited extraosseous disease. We should not start abiraterone/prednisone and radium-223 at the same time, and we should use a bone health agent when we use this drug.”**

SCOTT T. TAGAWA, MD, MS

The subsequent ERA 223 trial (NCT02043678) randomized 806 patients with CRPC and bone metastases to abiraterone acetate and prednisone/prednisolone plus either radium-223 (n = 401) or placebo (n = 405).4 The primary results showed that the median symptomatic skeletal event-free survival was 22.3 months with radium-223 plus abiraterone compared with 26 months for placebo plus abiraterone (HR, 1.122; P = .2636).

“Surprisingly to many of us, this was a flat, negative trial. The trends were actually in favor of placebo, both for the primary end point of symptomatic skeletal-related events, [and] overall survival,” Tagawa said.

Tagawa did note, however, that an unplanned analysis from ERA 223 underscored the importance of using bone health agents (BHAs) with radium-223. In both the intervention and control arms, frequency of fractures was lower when patients received BHAs along with their assigned therapy. In the radium-223/abiraterone/prednisone arm, the rate of symptomatic bone fracture was 15% in patients who did not receive accompanying BHAs versus 1.3% in those receiving BHAs. The rates were 4.7% versus 2.4%, respectively, in the placebo plus abiraterone/prednisone arm.

This finding “strengthened evidence and recommendations to use bone-protective agents when using radium-223,” Tagawa said.

Despite the setback of ERA 223, other combination regimens with radium-223 are currently being explored. The randomized phase 3 PEACE III trial (NCT02194842) is comparing radium-223 plus enzalutamide versus enzalutamide alone in patients with asymptomatic or mildly symptomatic CRPC metastatic to bone. The phase 3 DORA trial (NCT03574571) is randomizing patients with metastatic CRPC to radium-223 plus docetaxel or docetaxel alone.

**Is radium-223 benefit enhanced with a higher dose?**

A key question that emerged following the ALSYMPCA trial was whether higher doses of the radiopharmaceutical would produce a greater benefit. However, results from a phase 2 trial showed that symptomatic skeletal event-free survival was not improved in patients with bone-metastatic CRPC with either a higher dose of radium-223 than that used in the ALSYMPCA trial (HR, 1.06; P = .70) or an increase in the number of doses compared with the standard 6 doses used in the ALSYMPCA trial (HR, 1.26; P = .31).5

**Conclusions**

“In summary, radium-223 will lead to an overall survival benefit in men with metastatic castration-resistant prostate cancer to the bone with limited extraosseous disease. We should not start abiraterone/prednisone and radium-223 at the same time, and we should use a bone health agent when we use this drug,” Tagawa said.

Looking ahead, beyond the search for optimal radium-223 combinations, Tagawa said another key question concerns retreatment.

“If a patient who was treated a couple of years ago did well, now has progressive disease/symptomatic disease restricted to bone, and has been through all the other agents, can we [treat him again with radium-223] safely?” he asked. “We do not know, at least not yet.”

For list of references visit, https://bit.ly/3aA1r3b
Partnership launches novel test for hereditary prostate cancer risk

Test examines a 14-gene panel to detect mutations linked to hereditary prostate cancer

Jason M. Broderick  
Associate Editorial Director, Urology Times®

NorthShore University HealthSystem and GoPath Laboratories have partnered to launch the ProstateNow genetic test for determining an individual’s inherited risk of developing prostate cancer.¹

Using a blood or saliva sample, ProstateNow employs a 3-pronged approach for assessing risk: family history (FH), rare pathogenic mutations (RPMs), and a genetic risk score (GRS) that was developed by NorthShore. Results of the test, which are available within 10 to 14 days, can be used by urologists to make recommendations on screening and treatment.

“Family history, rare pathogenic mutations, and genetic risk score each measure risk independently,” Brian T. Helfand, MD, PhD, chief of the Division of Urology and director of the John and Carol Walter Center for Urological Health at NorthShore, said in a news release. “Combining all 3 tools provides the most comprehensive inherited risk assessment for patients and their families.”

Importantly, African Americans have a higher incidence of prostate cancer than the general population, but comprehensive genetic tests have been less available to [individuals] who are not Caucasian,” Helfand added. “We’re thrilled to offer this innovation to our patients—including Black members of our community—who can benefit from more informed treatment plans and the potential for more targeted prostate cancer therapies.”

Published data support test

Study results recently published in European Urology support the 3-pronged ProstateNow approach for predicting prostate cancer incidence and mortality.² The study consisted of a large prospective cohort of 208,685 patients from the UK Biobank database who had not received a diagnosis of prostate cancer at the time of recruitment. The investigators compared GRS with FH and RPMs as predictors of prostate cancer incidence and mortality.

Across the study population, there were 6890 cases of prostate cancer identified and 419 prostate cancer–related deaths at a median follow-up of 9.67 years. Univariate analyses showed that all 3 measures were significantly associated with the incidence of prostate cancer. The rate ratios were 1.88, 2.89, and 1.97 for FH, RPMs, and GRS, respectively (P < .001 for all). Multivariable analyses showed that the associations were independent. The measures of FH and RPMs determined that 11% of participants had higher prostate cancer risk, and the addition of GRS identified another 22% of participants with higher prostate cancer risk.

The investigators also used C-statistic as a marker of comparison. For predictive models, the C-statistic value ranges from 0.50 to 1.00 and higher are indicative of better models. The investigators showed that adding GRS to FH and RPM increased the C-statistic from 0.58 to 0.67 (P < .001) and from 0.65 to 0.71 (P < .002) for differentiating incidence and differentiating mortality, respectively.

“[Results of] this population-based prospective study suggest that GRS complements 2 guideline-recommended inherited risk measures (FH and RPMs) for stratifying the risk of prostate cancer incidence and mortality,” the investigators wrote. “These results provide critical data for including GRS in prostate cancer risk assessment.”

ProstateNow can be accessed online on GoPath’s website. Medicare covers the test for qualifying patients, but they must first receive a referral from a urologist or other physician.³

REFERENCES


NOVEL FOCAL ABLATION SYSTEM SHOWS PROMISE

Jason M. Broderick | Associate Editorial Director, Urology Times®

The NanoTherm therapy system continues to show promise as a novel technique for the focal ablation of intermediate-risk prostate cancer, according to updated data from a pivotal trial announced by MagForce AG, the developer of the therapy.¹

In the 2-stage pivotal trial of NanoTherm, a streamlined procedure that enables treatment completion in 1 day is being used in stage 2, compared with a longer procedure used in stage 1. MagForce reported in a news release that multiple safety analyses have now found no new safety signals with the 1-day process used in the 10 patients enrolled in the stage 2a cohort, compared with the patients in the stage 1 cohort. The company specifically noted that treatment-related adverse effects observed in stage 2a were minimal and similar to those reported in stage 1.

Reference


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Drug-coated balloon catheter sustains efficacy in BPH at 1-year follow-up

Jason M. Broderick
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One-year results of the EVEREST-I study showed sustained efficacy and safety with the Optilume drug-coated balloon catheter system in patients with lower urinary tract symptoms (LUTS) related to benign prostatic hyperplasia (BPH), according to findings published online in Prostate Cancer and Prostatic Diseases.1

At the cutoff date for the data analysis, 75 men had completed 1 year of follow-up. At 1 year, the percentage of patients with an improvement of 40% or more in International Prostate Symptom Score (IPSS) from baseline was 81%. This was identical to the rate achieved at the 3-month mark, which was the primary end point of the study.

“Treatment with the minimally invasive Optilume BPH Catheter System is safe and showed subjective and objective improvements in LUTS. Benefits were rapid and persisted through 1 year. The initial results warrant further evaluation of this therapy as a treatment option for patients with LUTS related to BPH,” wrote principal investigator Steven A. Kaplan, MD, director of the Men’s Wellness Program at Mount Sinai Health System and a professor of urology at Icahn School of Medicine at Mount Sinai in New York, New York.

The Optilume system consists of a dilation catheter that exerts radial force to dilate the prostatic urethra, which results in a commissurotomy. The distal end of the catheter has a semi-compliant, inflatable double-lobe balloon with a proprietary coating that contains paclitaxel.

The EVEREST-I trial (NCT03423979) enrolled 80 men with BPH across 6 investigative sites in Latin America. The study investigated 3 sizes of the balloon, described as small, medium, and large. Beyond meeting the primary end point, the results showed that the mean IPSS score was 22.3 at baseline and had improved to 8.3, 8.0, and 7.9 at 3 months, 6 months, and 1 year, respectively. Mean maximum flow rate (Qmax) was 10.9 mL/sec at baseline and 18.4 mL/sec at 1 year. Improvements in both IPSS and Qmax were statistically significant.

Analyses performed with men stratified by balloon size showed that the level of symptom improvement and its durability were similar regardless of balloon size. However, maximum symptom relief was achieved by day 30 using the small balloon, whereas it took 6 months to achieve maximum symptom relief with the large balloon.

Analyses of improvements in Qmax showed that the large balloon was associated with significant improvement within the first 30 days but a slight deterioration in benefit at 1 year. Qmax improvements were relatively smaller using the small and medium balloons, but peak flow still increased to approximately 17 mL/sec and remained stable throughout the 1-year follow-up.

Safety was favorable, with no changes in sexual function, according to the investigators. Only 1 major device/procedure-related adverse event occurred: At 3 months, 1 patient developed stress urinary incontinence, which resolved by the 30-day follow-up.

“Postprocedural complications included common urologic events, and the rate of complications was significantly impacted by device diameter,” noted the investigators.

In addition, IPSS quality of life improved from 4.6 to 1.3 at 1 year.1

REFERENCE

UroCuff makes it easier to assess bladder function in patients with BPH

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In an era of ever-increasing treatment options for benign prostatic hyperplasia (BPH), the UroCuff test is useful for assessing bladder function in patients.

Tobias S. Köhler, MD, MPH, discussed the UroCuff test in a presentation at the 2021 Society of Benign Prostate Disease Annual Meeting, which was held virtually in March. Köhler, professor of urology and chair of Mayo Men’s Health at Mayo Clinic in Rochester, Minnesota, began his talk by discussing challenges in BPH care and the importance of assessing bladder function.

“Men often will be lost to follow-up, especially if their symptoms are mild,” Köhler said. Other patients may choose to delay surgical intervention and instead take medications. Then, by the time patients seek management of BPH, permanent bladder damage often has occurred. In addition, patients with severe symptoms frequently have unrealistic expectations for symptom relief, he said.

The UroCuff test, he explained, is a noninvasive pressure-flow study that is easy to use and is similar to a uroflow test. It does not require catheters and can be ordered the same day.

“This is a huge advantage in the day where brick-and-mortar visits are decreasing and video visits are increasing,” Köhler said. “Imagine getting all the information you need in 1 visit instead of having to reschedule the patient to come back on a different day for their urodynamics, etc.”

Patients taking the UroCuff test should have an urge of 8, 9, or 10 on a scale of 1 to 10 in order to obtain good data, according to Köhler. Neurogenic bladder and failed prior intervention are factors he considers when ordering the test, and he also pointed out the 2019 amendment to the American Urological Association (AUA) clinical guidelines for surgical management of lower urinary tract symptoms (LUTS) attributed to benign prostatic hyperplasia, which states, “Clinicians should consider pressure flow studies prior to surgical intervention for LUTS attributed to BPH when diagnostic certainty exists (Expert Opinion).”1

Köhler also highlighted the recently added AUA guideline statement that states, “Clinicians should inform patients of the possibility of treatment failure and the need for additional or secondary treatments when considering surgical and minimally invasive treatments for LUTS secondary to BPH (Clinical Principle).” With the UroCuff test, Köhler said, clinicians

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UroCuff

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can assess whether a second procedure would benefit patients.

UroCuff has been extensively reviewed in the literature, with 92 peer-reviewed papers on the subject. One key finding from the literature, Köhler said, is that “the UroCuff test is highly correlated with catheterized [urodynamic] studies, so you can be fairly confident that the UroCuff readings that you get will mimic those that you would get with standard urodynamics.”

How it works

The UroCuff system works on Pascal’s principle, which states that—per Encyclopedia Britannica definition—“in a fluid at rest in a closed container, a pressure change in 1 part is transmitted without loss to every portion of the fluid and to the walls of the container.”

“So, if you can measure the pressure in the urine at the tip of the urethra, you can get a better idea of the pressure inside the bladder,” Köhler said.

UroCuff is available in 2 patient connection types: the Classic and DC (direct compression). With the Classic connection, an adapter is wrapped around the penis and acts as a blood pressure cuff. With the DC connection, the adapter gently seals to the glans, creating an extended urethra, according to Köhler. The newer DC connection offers the advantages of maintaining a natural voiding pattern and recording pressure throughout the void, Köhler said. Patients who have to sit to void or who have hypospadias, however, cannot use the DC type. The report generated by the test is similar to that from catheterized flow studies, Köhler said.

Köhler discussed results of a study he co-authored that was recently published in Journal of Urology. The study evaluated data from more than 50,000 patients across 103 urology practices who had undergone UroCuff testing. Patients were categorized by Newcastle Noninvasive Nomogram quadrants. The results showed that 24% of patients had unobstructed flow, 32% had high pressure/high flow, 29% had obstructed flow, and 15% had low pressure/low flow. Köhler also discussed data from his experience with the first 50 patients on whom he performed the UroCuff test. In this group, 44% of patients had unobstructed flow, 9% had high pressure/high flow, 41% had obstructed flow, and 6% had low pressure/low flow. In addition, 15 of the patients had undergone a previous procedure, and of these patients, 9 had unobstructed flow and 6 had obstructed flow.

“I think, all in all, UroCuff...can really help with stratifying our patients and making informed decisions with them to help them pick...the best option for them,” Köhler concluded.

Disclosures: Köhler has no BPH-related disclosures. He is a member of the AUA BPH guidelines committee but does not serve as a spokesperson for the group.

REFERENCES


Study highlights negative mental health impact of Peyronie disease

Depression appears to be common in patients, retrospective data indicate

Cheryl Guttmann Krader, BSPharm
Contributing Editor, Urology Times®

Depression is common among individuals with Peyronie disease (PD), according to findings of a retrospective study.

The study, which was reported in an article published online by The Journal of Sexual Medicine, aimed to identify factors that could predict depression among individuals seeking evaluation for early PD. Analyses comparing depressed and nondepressed cohorts categorized by scores on the validated Center for Epidemiologic Studies Depression Scale (CES-D) found no statistically significant differences between the 2 groups in any of the demographic-, bother-, or curve-related characteristics that were assessed as potential predictors. Notably, however, the depressed cohort represented 27% of the 408 study participants.

“There have been just 2 previous reports investigating the direct impact of PD on mental health, and they only briefly explored potential predictors of mental illness in this patient population. Given the limited data and the importance of this association, we undertook this study to determine if there were any characteristics that might help clinicians identify men with PD who are [experiencing] depression,” said Nahid Punjani, MD, MPH, first author of the published report, in an interview with Urology Times®.

“Although we did not identify any demographic-, bother-, or curve-related risk factors, we hope our study will lead urologists to acknowledge there is a high prevalence of depression in men with PD and to initiate an appropriate referral to a mental health care professional when indicated,” added Punjani, who is a fellow in male sexual medicine at Memorial Sloan Kettering Cancer Center and a fellow in reproductive medicine and an instructor of urology at Weill Cornell Medical College in New York City, New York.

The investigators retrospectively reviewed prospectively collected data from patients with documented PD seen by a single provider, John P. Mulhall, MD, director of the Male Sexual and Reproductive Medicine Program at Memorial Sloan Kettering Cancer Center.

To be eligible for inclusion, participants needed to have undergone a curvature assessment upon intracavernosal injection at the time of duplex ultrasound and have completed 3 questionnaires that all patients with PD are asked to fill out at initial presentation: the Self-Esteem and Relationship (SEAR) questionnaire, which assesses the psychosocial impact of erectile dysfunction (ED); the Peyronie’s Disease Questionnaire (PDQ), which assesses the psychosexual consequences of PD; and the CES-D, which is used to screen for depression/depressive disorder. Patients with a CES-D score of 16 or higher were categorized as having clinically meaningful depression and comprised the depressed group.

“Dr. Mulhall uses the CES-D as part of a highly structured, standardized intake for patients seeking evaluation for PD. Urologists, however, may employ any validated depression screening questionnaire to identify men with PD who may be depressed. They might also consider closely

See PEYRONIE DISEASE page 32
The Management of Biochemical Recurrence in Prostate Cancer

KEY TAKEAWAYS:

- After radical prostatectomy, a rise in prostate-specific antigen (PSA) level to 0.2 ng/mL or greater is considered recurrence. For patients with high-risk disease, consecutive rises in PSA level prior to reaching 0.2 ng/mL is also considered a recurrence.
- It is important to look at the surgical pathology because in some cases, benign glands at the margin can result in low levels of PSA that are not cancer related. Identifying recurrence is more challenging after definitive radiotherapy because the prostate gland remains in situ, and therefore some level of PSA is detectable.
- Therapy should be initiated for patients with Gleason scores of greater than 8 at the time of surgery, if biochemical recurrence is less than 3 years and if the PSA doubling time is less than 9 to 12 months.
- The recommended imaging modality is a positron emission tomography (PET) CT or PET MRI. The most widely available agent is fluciclovine, a fluorine 18-based agent, used to localize recurrent disease in patients who are presenting with increased PSA levels.
- There are multiple agents and combinations currently under investigation that may become available over the next few years. 18F-DCFPyL, a second-generation prostate-specific membrane antigen PET agent, is furthest along in the FDA review process and will most likely be considered as the next agent for approval.
- Overall, the greatest unmet need for patients with prostate cancer is the ability to localize disease reliably with current imaging modalities at very low PSA levels.

New imaging technologies improve early detection of biochemical recurrence (BCR) after definitive treatment for prostate cancer, but the clinical role of these imaging modalities and management based on these results continue to have unanswered questions, according to experts who participated in a recent CancerNetwork® Around the Practice virtual presentation, moderated by Raoul Concepcion, MD, of the Comprehensive Prostate Center in Nashville, Tennessee. The presentation featured an interactive online platform in which audience members answered several polling questions, which were discussed by the panelists.

Follow-up After Definitive Treatment for Prostate Cancer

The first polling question asked the audience to estimate the percentage of patients definitively treated for prostate cancer who would subsequently have BCR. Of the respondents, 40% estimated a BCR rate of 30% to 50% in this group of patients, whereas 20% estimated rates of less than 10%, 10% to 30%, and more than 50%, respectively. The second polling question asked for a true or false response to the following statement: “For patients who do have a BCR, initial therapy should always be androgen deprivation therapy (ADT).” Of the respondents, 60% answered “false,” and 40% answered “true.”
For patients who received initial definitive therapy, the National Comprehensive Cancer Network (NCCN) guidelines recommend measuring prostate-specific antigen (PSA) every 6 to 12 months for 5 years and then annually thereafter, along with an annual digital rectal examination (which may be omitted if PSA is undetectable). Judd Moul, MD, of the Duke Cancer Center in Durham, North Carolina, said that after radical prostatectomy, he typically sees his patients every 3 months for the first year. If their features are particularly high-risk, he will continue to see them every 3 to 4 months for up to 3 years, and if lower risk, he will decrease visits to every 6 months for the next 2 to 3 years and annually thereafter up to 10 years.

Although various PSA cutpoints have been used to define BCR, Brian Helfand, MD, of NorthShore University Health System and University of Chicago in Chicago, Illinois, said that he uses a PSA level of 0.2 ng/mL as the cutoff following radical prostatectomy, as results from one study showed that most (86%) postoperative patients with PSA level greater than the lowest PSA level reached, which had a sensitivity and specificity of 64% and 74%, respectively, for predicting clinical failure in one study. He added that consecutive rises in PSA level taken at least 1 month apart also increase suspicion for recurrence.

Although the PSA nadir usually occurs within 3 to 6 months following define ADT (androgen deprivation therapy) plus radiation therapy, Moul said that it can take up to 18 months to reach the PSA nadir following radiation therapy without ADT. Moul added that detectable PSA unrelated to cancer may be observed in a subset of patients who have benign glands at the surgical margin after radical prostatectomy.

When deciding whether to initiate treatment with a BCR, the panelists said that the timing of recurrence is important to consider, and Helfand added that a rapid rate of PSA doubling is particularly concerning. Results from a study of 379 men with BCR showed that a pathological Gleason score of 8 or higher, 3 or fewer years from radical prostatectomy to recurrence, and PSA doubling time less than 3 months or 3.0 to 8.9 months were independently associated with shorter time to disease-specific mortality. Concepcion said that a patient with these risk factors would be at risk for succumbing to his disease if therapy were not initiated.

Case 1: The panelists discussed the case of a White man, age 58 years, who presented in 2010 with a PSA level of 15 ng/mL. Transrectal ultrasonography-guided biopsy showed that 5 of 12 core biopsies were positive and classified as Gleason group 2, and staging work-up was negative. Surgical pathology after robotically assisted radical prostatectomy showed pathologic stage of T3a. The PSA level was 0.8 ng/mL 6 months after surgery, but follow-up was not done for another 3 years when he had a PSA level of 8.3 ng/mL. The patient was asymptomatic and had no signs of metastatic disease on bone scan and CT.
The first polling question regarding case 1 asked the audience whether they would start this patient on ADT. Of the respondents, 66% answered yes, 17% answered no, and 16% said there was not enough information to decide.

Munir Ghesani, MD, of the Icahn School of Medicine at Mount Sinai in New York, New York, pointed out that the current standard of care for work-up has changed since 2013 and includes several imaging options beyond the conventional bone scan and CT (summarized in the NCCN guidelines).1

18F-fluciclovine is a positron emission tomography (PET)–CT radiotracer that, according to Ghesani, is currently available at most commercial radiopharmacies across the United States. The LOCATE trial (NCT02680041) showed that 18F-fluciclovine PET-CT detected lesions in the pelvic region or prostate bed in 52% of patients with negative or equivocal pelvic CT and changed management plans in 59% of all patients.2

According to Ghesani, 11C-choline is also an approved radiotracer for PET, but its short half-life limits its availability to sites that have a cyclotron. In December 2020, the FDA approved Gallium-68 PSMA-11 (68Ga-PSMA-11) for PET for men with suspected metastases of prostate cancer that are potentially curable by surgery or radiation therapy or suspected recurrence of prostate cancer based on PSA levels, although Ghesani noted that the approval is currently limited to University of California, Los Angeles, University of California, San Francisco, and sites performing studies that have approached the FDA about cross-referencing the investigational new drug.6

A poll of the audience revealed that 47% of respondents would use 18F-fluciclovine PET-CT to image and restage the case patient, whereas 30% would use 68Ga-PSMA-11 PET-CT and 23% would use technetium bone scan. However, the panelists noted that many insurance carriers cover only 18F-fluciclovine PET-CT after a bone scan and CT have been performed, and some even limit coverage to patients with a minimum PSA level of 2.0 ng/mL. Furthermore, Ghesani said that bone scan and CT have low sensitivity for detection of BCR and often fail to show the extent of disease when recurrence is detected, which can lead to suboptimal targeting of treatment. He stressed the importance of collaborating with insurance providers and societies to eliminate the requirements for bone scans and CT prior to more sensitive imaging modalities in the near future.

In the first polling question about the case, the majority (approximately 90%) of the audience members recommended restaging the patient. In the next question, 56% of respondents said that they would use CT and technetium bone scan to restage the patient. Other answer choices receiving responses included18F-fluciclovine PET-CT...
(30%) and $^{68}$Ga-PSMA-11 PET-CT (14%). Moul said that his approach to the case patient would depend in part on the patient’s current health and life expectancy. “If he’s in poor health, I would probably observe him,” he said. “If he was in robust health, or…had a greater than 10-year life expectancy, I would work him up.” Moul added that $^{18}$F-fluciclovine PET-CT would be “an ideal imaging test” in the work-up.

Ghesani said that according to at least 1 study, $^{68}$Ga-PSMA-11 PET-CT may have better sensitivity for BCR than $^{18}$F-fluciclovine PET-CT in the setting of a very low PSA level. Findings from a prospective trial (NCT03515577) showed that the detection rates were significantly higher with $^{68}$Ga-PSMA-11 (56%) than with $^{18}$F-fluciclovine (26%) in 50 patients with PSA level of 0.2 to 2.0 ng/mL (odds ratio, 4.8; $P = .0026$). However, Ghesani said that $^{18}$F-fluciclovine PET is still considerably more sensitive than CT and bone scan. “If only fluciclovine PET is available, it will still be very appropriate to do that scan,” he said.

Ghesani added that patients are usually scanned sooner after injection with the $^{18}$F-fluciclovine PET-CT than with $^{68}$Ga-PSMA-11, and the lower degree of urinary excretion may be advantageous for identifying small areas of recurrence in the prostate bed. Results of a prospective study of patients with BCR after definitive primary therapy (N = 58) showed that detection rates of $^{18}$F-fluciclovine versus $^{68}$Ga-PSMA-11 varied by location of recurrence: $^{18}$F-fluciclovine had a higher rate of detection than that of $^{68}$Ga-PSMA-11 for local recurrence (37.9% vs 27.6%; $P = .03$), a similar rate for local pelvic lymph nodes (46.6% vs 50%; $P = .71$), and a lower rate for extrapelvic lymph nodes (41.4% vs 51.7%; $P = .26$) and bone (25.9% vs 36.2%; $P = .23$). The study authors concluded that further research is needed but suggested that the varying strengths of each tracer may complement each other.

**Emerging Imaging Modalities and Future Directions**

Ghesani said that at least 5 combinations of 2 gallium-based and 3 fluorine-based radiotracer agents are in the pipeline, with the second-generation PSMA-PET agent $^{18}$F-DCFPyl, the furthest along in the FDA review process. However, Helfand noted that the ability to reliably localize disease with low PSA level remains the greatest unmet need regarding BCR and detection, and identifying the roles for recently approved and emerging radiotracers will be important moving forward. Moul concluded that although the new imaging modalities are clinically useful, care must be taken to avoid overly aggressive management, particularly in older patients. “Don’t forget to keep your doctor’s hat on and look at the patient, look what’s in front of you, and put it in context,” he said.

**Reference**


**Editor’s Note:** Interview quotes were slightly modified for readability.
**Meta-analysis generates surprising insights on postureteroscopy urosepsis**

Review of nearly 5600 patients found a 5% pooled incidence of postoperative urosepsis

Cheryl Guttmann Krader, BSPharm
Contributing Editor, Urology Times®

Findings from a systematic review and meta-analysis of urosepsis after ureteroscopy (URS) for stone management show that this serious complication occurs at an unexpectedly high rate and is associated with some surprising risk factors, according to investigators.

The research, which is the first systematic review with meta-analysis to specifically investigate risk factors for and incidence of urosepsis after URS, analyzed data from 13 studies that included 5597 patients.1 It found a 5% pooled incidence of postoperative urosepsis and determined that preoperative stent placement, positive preoperative urine culture, older age, diabetes, longer procedure time, and ischemic heart disease were each associated with a statistically significant increased risk.

“Ureteroscopy has become the leading approach for treating stone disease because of its efficacy and the perception that it is a very safe procedure and associated with minimal morbidity. Therefore, the 5% rate of urosepsis was surprising to us and to other urologists as well, judging from posted tweets,” lead author Naeem Bhojani, MD, told Urology Times®.

Bhojani and senior author Ben H. Chew, MD, MSc, pointed out that although their study identified associations between certain variables and urosepsis risk, it does not establish causal relationships. For that reason and in the absence of evidence about the efficacy of preventive strategies targetting these factors, it is not possible to make any recommendations for risk management. “Nevertheless, we believe our findings can be useful for urologists in preoperative risk stratification and for guiding the intensity of postoperative surveillance,” said Chew, an associate professor in the Department of Urologic Sciences at the University of British Columbia in Vancouver, Canada.

The 13 studies used for the meta-analysis included 5 prospective trials. Across the 13 studies, the rate of urosepsis ranged from 0.2% to 17.8%. The use of different criteria for urosepsis diagnosis and different durations of postoperative symptom surveillance (1 to 30 days) may, in part, account for the wide variability in rate, said Bhojani, a principal scientist, a urologist, and an associate professor at the University of Montreal in Canada.

Although surprisingly high, the 5% rate of urosepsis appears to be true. In a follow-up investigation, the investigators turned to the IBM MarketScan Commercial Database that contained information from over 110,000 URS procedures performed in the United States. In that large cohort of cases with prospectively collected data, they found a nearly identical 30-day postoperative sepsis rate of 4.9%.

**Preoperative stent placement, older age were among risk factors**

In the meta-analysis, preoperative stent placement, positive preoperative urine culture, and older age were the strongest risk factors for postoperative urosepsis. The effects of having a stent or a positive urine culture are easy to understand because patients with these findings are likely colonized with bacteria or have bacteriuria, Bhojani said.

“Moving forward with research to understand the association with ischemic heart disease, however, was particularly surprising and hard to rationalize. Explanations for the associations between urosepsis and older age, diabetes, and longer procedure time are also unclear, although Bhojani postulated that increasing procedure time could favor translocation of bacteria into the bloodstream because it would be accompanied by an increasing level of intrarenal pressure.”

“There are some observational data suggesting that exposure to a longer duration of increased intrarenal pressure can lead to infection being transmitted into the bloodstream, and we are currently studying that relationship further,” Bhojani said.

Chew noted that large prospective studies would be needed to determine effective ways for reducing urosepsis risk.

“Based on our study, we cannot say that patients with the risk factors we identified should be given more powerful antibiotics as prophylaxis or kept in the hospital longer so that they can be watched more closely for postoperative sepsis,” he said. “However, we think that urologists should remain aware that patients with 1 or more of the risk factors warrant more intensive monitoring because they may be at significant risk for urosepsis after URS.”

**REFERENCE**


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collaborating with a mental health professional at their institution,” Punjani said.

**Several factors compared among groups**

The 408 participants had a mean age of approximately 56.5 years and mean duration of PD of approximately 20 months. Features that differed significantly between the depressed and nondepressed groups included being partnered (83.9% vs 73.6%, respectively), having a history of depression (26% vs 11%, respectively), and mean degree of curvature (38° vs 33°, respectively). The latter difference, however, was not considered clinically meaningful, and the percentage of participants with a complex deformity was similar in the 2 groups. The depressed group also had significantly worse PDQ and SEAR scores than the nondepressed group.

Risk factors for depression were examined through logistic regression modeling. The multivariable models considered age, partner status, duration of PD, history of depression, complexity of deformity, PDQ domain scores, total SEAR score, and ED as potential predictors. Only the total SEAR score was independently associated with depression—having a higher (more favorable) SEAR score was protective against depression. The investigators noted that the SEAR questionnaire has not been validated in the PD population.

“Moving forward with research to understand the psychological and emotional impacts of PD, we hope to explore issues related to partner distress in this patient population,” Punjani said.

**REFERENCE**

Urinary incontinence prevalence is higher in women with diabetes

Odds of having UI were 56% higher in women with diabetes vs women without.

Cheryl Guttman Krader, BSPharm
Urology Times® Contributing Editor

Analyses of cross-sectional data from women participating in a Danish population-based study provide a reference for the prevalence of urinary incontinence (UI) among Western European women and support the hypothesis that because of disease-related complications, UI is more prevalent in women with diabetes than in women without diabetes, according to the investigators who published their results in a recent article.1

The research, which was conducted by Ea Lowenstein in Nykobing Falster Hospital, Nykobing Falster, Denmark and coauthors, included data collected through questionnaires and blood tests for 7906 adult women (aged ≥ 18 years) who were participants in the Lolland-Falster Health Study. The study population included 374 women with diabetes (4.7%) and 7322 women without diabetes (95.3%). UI, defined as any involuntary leakage of urine during the previous 4 weeks, was present in 188 (50.3%) of the women with diabetes and in 2958 (39.3%) of the women without diabetes.

An association between diabetes and UI was found in an unadjusted logistic regression analysis, with the odds of having UI being 56% higher among women with diabetes than in women without diabetes. Although no association was found between diabetes and UI in a multiple logistic regression analysis adjusting for confounders, there was an association between diabetes and more frequent UI in a subgroup multivariable logistic regression analysis. In addition, the results of another subgroup analysis with adjustment for confounders showed an association between having severe diabetes, identified based on use of multiple antidiabetic medications, and UI. The latter finding led investigators to comment that attention be given to UI when counseling women with severe diabetes.

Additional analyses evaluated associations between diabetes and UI subtypes: stress urinary incontinence, urgency urinary incontinence, and mixed urinary incontinence (MUI). When adjusting for confounders, diabetes was found to be significantly associated only with MUI. The investigators postulated this may be because women with diabetes have more severe UI than women without diabetes.

No clear patterns for risk are seen

Subgroup analyses stratifying women by hemoglobin A1c (HbA1c) level and duration of diabetes showed no clear patterns for risk. Age and body mass index were identified as the most important UI risk factors. Associations were also found between UI and parity, current smoking, and sedentary level of physical activity.

The investigators noted that previous studies have shown a link between diabetes and UI, and they hypothesized that such an association exists because diabetes-related microvascular complications and neuropathy would lead to bladder damage and/or affect detrusor muscle function.

Nevertheless, previous studies investigating diabetes as a risk factor for UI have generated conflicting findings. The investigators noted that the variable results may be explained by differences in study populations, methods, and UI definitions.

In the current study, women were identified as having diabetes if they self-reported the diagnosis or use of insulin or another antidiabetic medication, had an HbA1c level of 6.5% or higher, or met criteria for history of filling prescriptions for an antidiabetic medication prior to study enrollment. The presence of UI and its subtypes was identified based on information from the International Consultation on Incontinence Questionnaire—Urinary Incontinence Short Form.

According to the investigators, study strengths included a more than 90% questionnaire response rate and the ability to adjust for important confounders. They observed, however, that there was a risk of selection bias, as participation rates were lower for younger and older women. As another limitation, the investigators mentioned that the low number of women with diabetes and UI could have resulted in a type 2 error, and they reported that a post hoc sample size calculation revealed that the study had low power to detect an association.

REFERENCE

eCoin neurostimulator is effective in managing overactive bladder, data show

50% or greater improvement in urgency urinary incontinence was seen in 68% of participants.

Jason M. Broderick
Associate Editorial Director, Urology Times®

Pivotal data for eCoin, a leadless tibial nerve stimulator for managing overactive bladder (OAB), have been published online by Journal of Urology.1

Results from the primary efficacy analysis of an open-label, single-arm trial showed that eCoin met the primary end point of the study by achieving a 50% or greater improvement in urgency urinary incontinence (UUI) in 68% of participants after 48 weeks of treatment.

“eCoin demonstrated clinical benefit for treating OAB with automatic delivery of an intermittent low-duty cycle [stimulation] implanted with a minimally invasive, brief procedure,” wrote the investigators, led by Alexandra Rogers, MD, of Sansum Clinic Urology in Santa Barbara, California.

The eCoin device is a tibial neurostimulator that is the shape and size of a nickel. It is implanted in the lower leg—above the fascia over the tibial nerve—in an office or outpatient procedure by a urologist or urogynecologist. The procedure, performed under local anesthesia, takes approximately 20 minutes.

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NCCN adds lenvatinib/pembrolizumab to Category 1 recommendation

Panel based recommendation on findings from phase 3 CLEAR trial evaluating combination treatment

Kristie L. Kahl
Vice President, Content

The National Comprehensive Cancer Network (NCCN) has recommended the combination use of lenvatinib (Lenvima) plus pembrolizumab (Keytruda) for frontline treatment of renal cell carcinoma (RCC).1

“The urologist should be aware of these data...because of the question of whether cytoreductive nephrectomy is appropriate or not,” Eric Jonasch, MD, professor in the Department of Genitourinary Medical Oncology, Division of Cancer Medicine, at The University of Texas MD Anderson Cancer Center in Houston, and vice-chair of the NCCN Guidelines Panel for Kidney Cancer, said in an interview with Urology Times®.

“Even with less-powerful regimens, the role of cytoreductive nephrectomy has decreased, so that for individuals who have intermediate- and poor-risk disease, in particular, systemic therapy should be the frontline choice for most patients,” he said.

CLEAR trial
An NCCN panel based its Category 1 recommendation on findings from the phase 3 CLEAR trial (NCT02811861), which evaluated the combination of lenvatinib with either pembrolizumab or everolimus (Afinitor) compared with sunitinib (Sutent) for the treatment of patients with advanced RCC receiving therapy in the frontline setting.2

Patients were randomized 1:1:1 to receive 20 mg oral lenvatinib once daily plus 200 mg intravenous pembrolizumab once every 3 weeks (n = 355), 18 mg oral lenvatinib once daily plus 5 mg oral everolimus once daily (n = 357), or 50 mg oral sunitinib once daily for 4 weeks on and 2 weeks off (n = 357).

Progression-free survival (PFS) by Independent Review Committee (IRC) per RECIST v1.1 was the primary end point. Secondary end points included overall survival (OS), objective response rate (ORR) by IRC per RECIST v1.1, safety, and health-related quality of life.

The median PFS with lenvatinib and pembrolizumab was 23.9 months (95% CI, 20.8-27.7) compared with 9.2 months (95% CI, 6-11) with single-agent sunitinib (HR, 0.39; 95% CI, 0.32-0.49; P < .001).

The lenvatinib plus everolimus treatment arm achieved a median PFS of 14.7 months (95% CI, 11.1-16.7) compared with the 9.2 months in the sunitinib arm (HR, 0.65; 95% CI, 0.53-0.8; P < .001).

A median OS was not reached in any of the 3 treatment arms; however, the data indicated the end point was significantly longer in the lenvatinib and pembrolizumab arm compared with the sunitinib arm (HR, 0.66; 95% CI, 0.49-0.88; P = .005).

ORR was higher in both the lenvatinib plus pembrolizumab (71%; 95% CI, 66.3-75.7) and lenvatinib plus everolimus (53.5%; 95% CI, 48.3-58.7) treatment arms compared with sunitinib (36.1%; 95% CI, 31.2-41.1). In particular, Jonasch noted that the 16% complete response rate with lenvatinib plus pembrolizumab was impressive.

Lastly, patients in the lenvatinib plus pembrolizumab arm achieved the longest median duration of response at 25.8 months (95% CI, 22.1-27.9), compared with 16.6 months (95% CI, 14.6-20.6) in the lenvatinib plus everolimus arm and 14.6 months (95% CI, 9.4-16.7) in the sunitinib arm.

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Based on data from the trial, Valencia Technologies, the manufacturer of eCoin, previously submitted a premarket approval to the FDA for use of the device in patients with OAB.3

Overall, the open-label, single-group assignment pivotal trial of eCoin (NCT03556891) comprised 133 patients with OAB with UUI who were implanted with eCoin. eCoin was comprised 133 patients with OAB with UUI episodes as measured by a 3-day voiding diary at 48 weeks following activation of eCoin.

A median UUI episodes was 4.3. Based on patient reporting, the mean number of daily UUI episodes was 4.3. Based on patient reporting, the mean history of OAB was 11 years.

The primary efficacy end point was the rate of participants having a 50% or greater improvement in UUI episodes as measured by a 3-day voiding diary at 48 weeks following activation of eCoin. At 28 and 52 weeks, the rate of device-related adverse events (AEs) was 15%. AEs related to device or procedure were generally considered to be mild to moderate. At 52 weeks post implantation, 19% of participants had AEs related to the procedure or the device. The specific incidence of device-related events at 52 weeks of treatment was 10%. There was 1 serious AE, consisting of an infection related to the study procedure. According to the investigators, this resulted in an explant, which investigators were able to resolve without sequelae.

“eCoin offers a novel OAB therapy with minimal [adherence] issues due to automatic therapy delivery and a well-tolerated, reproducible implantation procedure, all precipitating the potential for high adoption once available,” the authors wrote in their study conclusion.

REFERENCES
“This trial basically showed various, very strong results in all of these domains….All of these factors, together, show that this is one of the strongest regimens that’s been tested so far in advanced kidney cancer,” Jonasch explained. “And so the NCCN panel felt that these data deserve preferred status.”

Urological implications

Although systemic therapy is recommended, Jonasch continued, there could still be the integration of therapy, highlighting the need for a multidisciplinary approach.

“[With this recommendation], the integration of surgery and systemic therapy becomes even more important,” he said. “The timing of one versus the other is also important for the patient’s well-being, especially when you can get such rapid response with systemic therapy. But it doesn’t in any way diminish the role of the surgeon in the team. The team consists of the medical oncologist, the surgeon, the radiation oncologist, and the nursing staff, as it has before.”

Moreover, this recommendation highlights the need for open patient-physician communication, he said.

“The patient- or therapy-related details a skilled oncologist evaluates to make these decisions can prioritize those therapies, even within the preferred category. Or there might be some circumstances that will make a preferred regimen not appropriate for a particular patient,” Jonasch explained. “This is obviously a conversation that needs to occur between the patient and the physician. The physician can then explain what the different regimens are in these various categories, [as well as] explain why one would be chosen over the other and whether there may be other choices that are not preferred but that might actually be ideal for that particular patient for various reasons.”

REFERENCES


NIVOLUMAB/CABOZANTINIB COMBO APPROVED IN EU FOR RCC

Jason M. Broderick | Associate Editorial Director, Urology Times

The European Commission has approved the combination of nivolumab (Opdivo) and cabozantinib (Cabometyx) as a frontline treatment for patients with advanced renal cell carcinoma (RCC), Ipsen announced in a news release. In the United States, nivolumab/cabozantinib was approved by the FDA on January 22, 2021, as a frontline treatment for patients with advanced RCC.

Reference

What can you do about rising medical record review requests?

Physician involvement in responses to payer audits is crucial

We decided to head in a different direction with this month’s column. We have done our best in many of our articles to impress upon the reader the importance of accurate and complete documentation, as the medical record serves as both the key to appropriate ongoing care for your patient and proof of services provided. Documentation is important to communicate what you are thinking, what you have done, and what you are planning in relation to each patient’s treatment, and therefore it is the key to being reimbursed for the work provided. Unfortunately, sometimes even thorough and complete documentation does not result in payment by an insurance company for quality medical care.

What insurance companies decide is or is not covered does not always make sense. Keeping up with coverage decisions for all your payers requires a coordinated effort by your entire staff. An efficient urology office will invest in this process. It is frustrating and takes time to develop and maintain, but once in place it will pay immediate dividends. The goal is to know if you are going to be paid before you provide the service and who is responsible for what portion of the amount owed to the practice.

You can do everything as planned and still run into frustrating delays and roadblocks and even the unexpected outright denial. These roadblocks, delays, speed bumps, and administrative/technicality denials seem to be on the rise. Even with well-documented charts, it may seem that insurers aren’t being true to their word of coverage or don’t have enough trust that the provider is using their skills and judgment for the best possible patient outcomes.

In addition, medical record requests prior to payment are all too commonplace, leading to frustrating delays in patient care. We also have seen an increase in reviews for services already paid, which further increases the expense of running a practice. Often, there is seemingly little method to this madness of requests. The requests that do not fit a clear pattern are what we would classify as probe audits.

Regardless of which type of request you receive, make sure you send all relevant portions of the medical record requested.

Include supporting documentation with records

Regardless of which type of request you receive, make sure you send all relevant portions of the medical record requested. We have seen many medical records sent for review that support an evaluation and management service or procedure but are missing lab or imaging service reports that also were billed. Before sending in medical records, ensure that each service that was reported has the supporting documentation included. If the documentation cannot be found, explain the circumstance and, if appropriate, addend the medical record, but do so in a manner that clearly acknowledges the addendum. Certainly, this is nothing like it used to be. There has never been a time when so much scrutiny has been placed on providers and practices. The obvious primary driver of medical record requests is money. The payers monitor billing patterns of providers and groups and will select notes for review based on billing patterns that do not conform to other urology groups. If your group demonstrates in a review that you are documenting well and understand the rules, you are less likely to be investigated further. If they find a problem that they were looking for based on your coding patterns (eg, uroflow test on a higher percentage of patients than average) or based on a random chart audit, you are likely to receive a request for repayment.

Although many payers will limit the takeback to the records reviewed with problems that have been identified, others will extrapolate the problem as a percentage of all claims with the same coding pattern and request a settlement in a larger amount. It is important to scrutinize any payers’ findings in these chart reviews.

We have been involved in a number of chart reviews. Most reviewers in these types of audits do not understand urology, and we have been able to get many “mistakes” overturned. To do so, it is extremely important to have the physician involved in the process. Although a coder/auditor should make the first pass in analyzing the payer audit, it is important to find out physician intent and prepare a response understood and signed by the physician. If your chart review agrees with the payer findings, you should admit the mistake and communicate any corrective actions that you are going to take to stop the practice. If these communications are verbal, record the conversations, if possible, or summarize the communication in a letter or email back to the payer. We do not recommend simply paying the requested takeback in any case. Respond to each finding, even if you agree with them and pay in full.

The record requests for individual services based either on the type of service provided or a seemingly random record request either prior to or after payment are similar. The process of gathering and submitting the medical record should not change; submit the entire record and check for support of all services reported. We recommend that you review and check with physicians regarding documentation only if needed instead of holding records for physician review. What
FROM THE PAGES OF:

**Medical Economics**

**Health Policy**

**Fauci: Addressing health care access disparities will take decades**

**KEITH A. REYNOLDS**

Reynolds is an associate editor for Medical Economics®.

Anthony Fauci, MD, director of the National Institute of Allergy and Infectious Diseases (NIAID), says that addressing disparities in health care access disparities will likely take decades.

Fauci was taking part in a question-and-answer session during the opening plenary of the American College of Physicians (ACP) Internal Medicine Meeting 2021 along with Gregory Kane, MD, treasurer of ACP, and Darlyn Moyer, MD, executive vice president and CEO of ACP.

Fauci said the pandemic has shown a bright light on the inequities of the health care system, particularly in the rates of hospitalization seen among racial and ethnic minorities. According to Fauci, these inequities are tied to social determinants of health that put Black, Hispanic, and Native American citizens into educational and economic situations that limit their ability to receive medical care.

“We have to start committing now to something that’s going to take decades to change,” he said. “Because it took centuries to get here, it’s going to take decades to change. But if we don’t make the commitment now to do it, we’re never going to do it.”

When asked whether COVID-19 could be eradicated globally, Fauci seemed more confident that it will be eradicated in some countries and controlled in others, but the process will take years and vaccinating a large portion of the world’s population.

“We’re going to be continually threatened by variants that will come from other countries, which tells us the obvious solution to that is to make sure that we get the entire world vaccinated against [COVID-19],” Fauci said. “Until we do that, I don’t think we’re going to eliminate this infection. I think it’ll be there at a low level; we’ll be protected. We may need to get boosted every once in a while, to keep the level of protection up. But we have to look at it as a global problem; otherwise, we’re never going to truly eliminate it.”

Fauci said that early in the pandemic, the US response was hamstrung by the dismantling of the local health infrastructure, failure to mobilize the private sector early for diagnostics, and the rapidly evolving situation with little transparency from China. The transmission method of the virus also caught the world by surprise.

“We’ve never had any pathogen of any note of seriousness in which...50% and 60% of the transmissions occur from a person who never will get symptomatic, or who was in the pre-symptomatic stage,” he said. “That broke all the paradigms of infectious disease because, prior to that, transmissions were always a little bit asymptomatic but dominated by the symptomatic person.”

As for the United States’ successes in responding to the pandemic, Fauci highlighted the Trump administration’s Operation Warp Speed that invested billions in vaccine development and pre-purchase as well as the Biden administration’s rollout of the vaccines.\[7\]

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.
Increased drug costs and spending for Medicare beneficiaries have been an area of concern for patients, their physicians, policy makers, and regulators for several years. Medicare pays for most drugs through either the Part B program (generally injectable medications purchased by providers and administered in a clinical setting) or the Part D program (generally prescribed oral and patient-administered medications). A previous article discussed the most common Part D drugs prescribed by urologists from a program and cost perspective. This article discusses them from a prescribing (and sometimes dispensing) perspective.

The Centers for Medicare & Medicaid Services (CMS) recently released detailed provider Part D drug prescribing and utilization data for 2018. It is important to remember that only approximately two-thirds of Medicare beneficiaries are enrolled in Part D, and prescribing patterns in this program may not be generalizable to all patients in your practice. Total spending in 2018 for the Part D program was $168 billion, up more than 10% from 2017. The total cost is based on the amount paid by the Part D plan, the Medicare beneficiary, government subsidies, and any other third-party payers. Total cost for 9944 unique urologists’ prescribed Part D drugs was more than $1.5 billion, or 0.9% of the total program cost. Eleven drugs account for 80% of this spending. The drugs most frequently prescribed by urologists (measured in 30-day fills) were tamsulosin (7,462,775), followed by finasteride (4,791,306), oxybutynin (1,557,233), and mirabegron (1,060,529). The drug with the highest urology spend was mirabegron ($188.million, 8%), followed by solifenacin succinate ($182 million, 7%), tolterodine (Detro LA, Detryl) (6%), and others (Table 1). From a payer perspective (CMS, in this case), mirabegron is the largest spend across all specialties ($1.06 billion; 4% of dollars), followed by solifenacin succinate ($692 million, 29%), oxybutynin ($255 million, 11%), tolterodine ($188 million, 8%), and others (Table 2). From a specialty perspective, urologists prescribe only 27% of dollars in this class: 35% of mirabegron, 22% of solifenacin succinate, 17% of oxybutynin, 29% of fesoterodine fumarate (Toviaz), and 27% of trospium chloride (Sanctura). Finally, 57% of the urology prescribing Part D costs for these OAB drugs was “spent” on mirabegron (Table 3). The patient’s perspective is difficult to generalize, as there are many different plans with different formularies and different cost-sharing structures; generally, the more expensive drugs will cost the patient more and propel them faster to the “coverage gap” (also known as the doughnut hole). In 2018, the spending threshold to enter the gap was $3750, and the patient then assumed 35% of brand-name drug costs until they reached...
Medical liability insurance premiums are on the rise

More than 30% of premiums increased in 2020, AMA analysis indicates

TOBY SHRYOCK
Shryock is managing editor for Medical Economics.

Medical liability insurance premiums are increasing after a decade of mostly steady rates, according to a new analysis from the American Medical Association. In 2020, more than 30% of premiums reported on a survey of liability insurers increased from the previous year, the highest percentage since 2005.

For a second consecutive year, there has been an exceptional surge in the size of the increase. Between 2010 and 2018, the share of premiums that increased ranged from 12% to 17%. In 2019, that proportion almost doubled to 26.5% and went up again in 2020 to 31.1%. According to the AMA analysis, although some 2020 premiums may have been set after the onset of the COVID-19 pandemic, it was still too early for them to be affected by it.

“Increases in medical liability premiums compound the economic stress on medical practices as the COVID-19 pandemic resulted in significant reductions to patient volume and revenue, and higher expenses for scarce medical supplies,” said AMA President Susan R. Bailey, MD, in a news release. “Practice revenue has not fully recovered as the pandemic has stretched on, and a protracted upward trend in medical liability premiums will threaten the viability of many practices that already face a difficult road to recovery.”

The analysis identified the 14 states that had premium increases of 10% or more. Those states and their shares of reported premiums that increased by such magnitude in 2020 are: Kentucky (29.6%), South Carolina (27.8%), Maryland (18.8%), Nebraska (16.7%), Oregon (16.7%), Montana (16.7%), Georgia (14.8%), Missouri (14.8%), New Hampshire (13.3%), Illinois (11.9%), Michigan (11.6%), Texas (9.2%), North Carolina (6.7%), and Virginia (1.3%).

“Keeping medical liability premium growth in check is imperative to ensure patient access to care is not jeopardized by unaffordable liability insurance costs that make it impossible for physicians to remain in practice,” said Bailey.

“This concern is particularly pressing given the negative impact that the COVID-19 pandemic has had on access and practice viability, as many physicians have had to suspend patient visits or elective procedures, and some have had to close their practices,” Bailey added.

Together with state medical societies, the AMA is pursuing both traditional and innovative medical liability reforms to preserve premium stability and meet the needs of millions of Americans who need affordable, accessible medical care. This includes limited and targeted emergency protections for physicians who continue to treat patients during the pandemic without adequate resources and support.

The newly released AMA analysis on medical liability insurance premiums is based on an annual survey of professional liability insurers conducted by the Medical Liability Monitor. The MLM reports base premiums for 3 specialties in each state where the responding insurers provide coverage.

REFERENCES

PART D

continued from page 38

$5000. Individuals enrolled in Medicare Part D plans typically know a lot about the cost of their prescription drugs—because they pay a share.

Surprising trends

Urologists might be surprised to know that in 2018, they collectively prescribed less than 5% of sildenafil (Viagra), 10% of abiraterone acetate, and less than 20% of enzalutamide in the Part D program. These are drugs that are commonly dispensed in some urology practices, and urologists are recognized as the experts in prostate cancer, OAB, and men’s health. The drug-prescribing data reflect the reality that urologists prescribed a minority of the medical treatments for these conditions in the Medicare Part D program in 2018.

Did you know you can find your own data? Go to https://data.cms.gov/d/mhdd-npiz/visualization. In the filter area, type in either your name or your national provider identifier number. Your detailed prescribing data are available so you can see how your numbers compare with the aggregate statistics.

Bottom line: Drug costs to the Medicare Part D program as a whole continue to increase each year, but urology accounts for less than 1% of the spending in this program in the most recent available data (2018). Expensive oral drugs are under close scrutiny—especially if there are generic equivalents—and urologists prescribe and, in some cases, dispense some of these drugs. Urologists should be familiar with the costs under their direct or indirect control and their contribution to this important part of health care expenditures in the Medicare program.

REFERENCES
With the markets pushing record highs, how should you react?

Sticking to your investment strategy can help avoid emotion-driven decisions.

Q: The markets seem to be pushing record highs. Are there adjustments I should be making to my portfolio?

A: As the COVID-19 vaccine rollout continues and another stimulus package has been approved, the equity markets have again pushed against all-time highs. These moments tend to elicit 2 very different responses from investors: euphoria and fear. Some investors view this as a sign to get more money in the market and hope the wave continues moving upward. Others see this as a sign that we are due for a pullback and start taking money off the table. Both of these actions are emotional responses. Investing with emotion is a risky endeavor and can lead to costly mistakes.

Removing emotion when investing is never easy. However, successful investing requires exactly this level of discipline. What can you do during these moments when markets are pushing highs and there is uncertainty about their future direction?

Have an investment strategy and stick to it. Every investor should have an investment strategy printed out and pinned to their desk. An investment strategy keeps you disciplined. It will tell you when to buy, what types of investments to buy, and when it is acceptable to sell. An investment strategy allows you to block out the noise in the markets and media and focus on growing your wealth in a disciplined way.

Rebalance. Often when markets are performing well, there are specific asset classes that drive that performance. This often leads to these categories becoming overweight compared with their target percentages because they have grown significantly. If this is true for your portfolio, now may be a good time to rebalance. Keeping your asset allocation in line with its target percentages is key to long-term investing. If your equity categories are overweight, the risk in your overall portfolio has increased, since these tend to be the most volatile asset classes.

Keeping your asset allocation in line with its target percentages is key to long-term investing.

There are 2 ways to rebalance. You can sell the category that is overweight and reallocate the proceeds to underweight categories such as bonds and real estate. This will add more downside protection in the event markets turn negative. However, the tax implications of selling must be considered. Rebalancing in tax-advantaged accounts such as 401(k)s and IRAs is easy to do; you can sell investments without having to worry about capital gains taxes. That is not the case with taxable accounts such as individual, joint, and trust accounts. Selling an investment with a significant gain in these accounts may result in owing a hefty capital gains tax. For these types of accounts, the second rebalancing strategy typically works best. Add more money to the account and apply that money to the underweight categories.

Stockpile cash to invest if the markets experience a correction. The markets will experience a correction. Knowing exactly when is impossible without a crystal ball. However, corrections provide excellent buying opportunities, as some investments may be trading at a discount. By having cash on hand, you can be prepared for when that moment comes.

Determine what amount you feel comfortable with having in reserves and eventually investing. When a market correction occurs, use this stockpile to invest in categories trading at a discount. You do not typically want to invest your entire cash reserve at once. If the markets continue to move downward, you will have gone all in before the investment hit bottom. To avoid this risk, use a dollar-cost averaging strategy to invest incrementally over a set period of time. Buying incrementally as investments go down will allow you to get in at good prices, but removes the risk of going all in at the wrong time.

When markets are pushing highs, everyone wants to know if they will keep going or if they are due for a pullback. No one can know for sure. The best thing you can do is have a plan in place so you know how to react regardless of which direction the markets go, remain well allocated and diversified across asset classes, and have cash available in case a buying opportunity arises.

JEFF WITZ, CFP

Witz is educational program director at MEDIQUIS Asset Advisors, Inc in Chicago, Illinois. He welcomes readers’ questions and can be reached at 800-883-8555 or witz@mediqus.com.

The information in this column is designed to be authoritative. The publisher is not engaged in rendering legal, investment, or tax advice. If you would like assistance with your individual investment strategy, please email witz@mediqus.com.
This faculty member will serve as an Assistant, Associate or full Professor and be responsible for high-volume clinical activity within the realm of urology at the Salt Lake City Veterans Medical Center. He or she would work 50%-80% in this capacity balanced with clinical work or research at the University of Utah. Multiple specialty focus could be possible at both clinical sites, such as Oncology, Reconstructive Urology, or Endourology. This faculty member would be expected to develop a strong regional program focused upon the urologic care of veterans.

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What is your impression of virtual meetings and conferences?

ROSS MOSKOWITZ, MD / Orange, California

“I haven’t attended virtual conferences; however, our department at [the University of California] Irvine does all our Grand Rounds on Zoom. They usually entail scientific lectures, with outside speakers 2 to 3 times a month.

The only meeting I commonly attend is the Western Section, but haven’t gone since returning to California.

In the past 2 years, I attended a billing conference and the Society of Academic Urologists [SAU annual meeting]. I wouldn’t have gone back to the billing conference so soon, anyway. The SAU went virtual in January, but my clinical schedule had started picking up, so I didn’t want to take time off. If we took time off when the [operating rooms] were opening up for elective procedures, I’d have felt bad about time away from patients, even if we weren’t traveling to attend.

“My main complaint about virtual lectures is the loss of camaraderie of seeing colleagues face-to-face and having casual conversations.”

NATHANIEL BARNES, MD / Houston, Texas

“I just attended the Society for Benign Prostatic Disease [virtual meeting], and maybe a bit of 1 or 2 AUA [American Urological Association] meetings.

It’s a good way to access the general content, probably easier than being there in person, in some ways. For a plenary session or something, it’s just as good, if not better, to do it virtually—having the slide right in front of you while you’re sitting at a desk. It’s easier to take notes on your computer and to look things up while you’re watching.

I certainly miss interacting with colleagues, talking to people about new ideas and new practices. The industry portions are less useful virtually than in-person where we can walk around the booths and see new products and talk to people from the companies.

Post pandemic, I would like to see a return to in-person meetings. They’re more engaging overall. Being able to interact with your colleagues is better in person. Portions of the meetings could be done virtually in a very effective manner, which might help with the space considerations. They might have combination meetings where some content is virtual, and some is in person.

I think they’ll offer content virtually for people who might not be able to travel easily for logistical reasons having nothing to do with the pandemic—people who can’t go to every meeting but would still like access the content.”

WILLIAM JAFFE, MD / Philadelphia, Pennsylvania

“I didn’t participate in virtual conferences this year, although I’ve done a ton of virtual meetings, speaker trainings, [and] advisory boards, but not 1 [continuing medical education] or AUA [American Urological Association] meeting. I’m one of the senior physicians in our organization and have both clinical and system-level responsibilities. When COVID-19 hit, my responsibilities grew. I’m also co-chair of our new system-wide Cancer Center of Excellence.

We did most hospital-system meetings virtually. After the pandemic, I hope we incorporate that into our operation because Houston is a very spread-out city—54 miles across—and we have 13 hospitals. When we had a system meeting, we’d have it centrally and everybody had to drive there. But attendance at virtual meetings is through the roof because everybody participates. Even if they’re in the [operating room], between cases they go to the doctors’ lounge and sign in. People are actively engaged in the discussion. Sitting in their office, people don’t feel threatened chiming in and giving an opinion. Meetings also start and end on time because we’re not waiting for stragglers. I would find it deleterious to eliminate them after the pandemic.

AUA meetings could become a hybrid for a couple reasons, [such as] revenues involved for the convention centers, the hotels, and vendors. Secondly, certain things can be harder to do virtually. Vendors find it harder to demonstrate their products. On the other hand, we had a list of big group courses and some were at the same time. They can video everything, so later you watch whatever courses you missed.”

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Malpractice Consult

Discovery phase could hold key to malpractice case

Any aha moments usually happen before a trial begins

Most of us are familiar with the trope of a fictional legal drama in which a key witness or piece of evidence is revealed for the first time at the critical moment of a trial. However, a “Perry Mason moment” rarely occurs in real legal disputes. The reason is simple. In most lawsuits, including cases involving alleged medical malpractice, the parties must exchange all information they will use as evidence well before the trial begins, a process known as discovery. This column provides an overview of the discovery process, the different types of discovery, and why the process is important.

What is the discovery process?

During discovery, each party can request information and documents from the other parties. This process prevents “trial by ambush,” where one side does not learn what information will be presented against them until it is too late to gather evidence to rebut the accusation. Discovery is necessary for achieving fair outcomes in legal disputes.

Although there are some limits on what information can be requested, the standard for whether a discovery request is permissible is broad. Generally, a discovery request is proper when it is “reasonably calculated to lead to the discovery of admissible evidence.” In other words, parties can ask for information that cannot be used as evidence if the party can show the request might lead to uncovering admissible facts.

What are the different types of discovery?

The exchange of information in a lawsuit consists of different forms of discovery requests, including:

Initial disclosures. Some jurisdictions have enacted rules requiring parties to voluntarily produce basic information to opposing parties even before that information is requested. Typically, a party must reveal the identity of witnesses with relevant information, documents supporting a party’s claims, and any insurance policy that may cover the cost if the plaintiff is awarded damages.

Interrogatories. These are open-ended questions sent to the other parties. In a case involving allegations of medical malpractice, a plaintiff may ask the defendant to provide the names of all staff members who provided care, information about the defendant’s education and work experience, and other information concerning the defendant physician’s practice. On the other side of the case, a defendant will typically request information about any medical conditions that predate the care at issue, prior lawsuits filed by the plaintiff, and details of the injuries the plaintiff claims the defendant caused.

Request for production. These requests are used to obtain relevant documents or physical evidence. In a medical malpractice lawsuit, the plaintiff will request all medical records related to the care at issue. Although producing a medical record may seem simple, things are rarely as easy as providing a printed copy of a patient’s chart. Plaintiffs often request the original files from the electronic record platform. These electronic files will show when information was added to the patient’s record and whether entries have been altered. A defendant can request records from care providers who treated the plaintiff before and after the care at issue. Through these records, a defendant can gain a complete picture of a patient’s medical history and the course of a plaintiff’s recovery after an injury allegedly caused by the defendant’s negligence.

Requests for admissions. These requests consist of carefully worded factual contentions that parties must either “admit” or “deny.” This type of request can narrow the scope of a dispute. For instance, a plaintiff may ask a defendant to admit that an injury occurred. If the defendant admits the truth of the request, the parties focus on whether the injury was caused by the defendant’s actions.

Depositions. In a deposition, a witness provides sworn responses to questioning by counsel for one of the parties. Depositions are used to obtain all relevant information a witness may have. Depositions allow a party to learn everything a witness will say if they testify at trial. Moreover, if a witness’s testimony at trial is different from their deposition, the witness’ credibility can be attacked. The question will become, “Is the witness lying now, or were they lying in their deposition?”

Unlike other forms of discovery where the attorney representing a party can help craft a response, depositions involve directly questioning an opposing party. Before a defendant physician is deposed, they will typically meet with the lawyer defending the case to prepare for all questions opposing counsel is likely to ask.

Conclusions

Very few of the malpractice cases filed each year are ever presented to a jury. However, every lawsuit will involve discovery. The information obtained and admissions made during discovery are often the deciding factors in resolving a case. As such, an understanding of the purpose and mechanisms in the discovery process is critical for any urologist involved in a legal dispute.
I am a urologist.
I am a patient.

I can genuinely say the benefits of the UroLift® System are real and the procedure and recovery were easy to tolerate.

Edward Cohen M.D., F.A.C.S.*
Chief Executive Officer
and Chairman Genesis Healthcare Partners

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*Dr. Cohen is a paid consultant of NeoTract | Teleflex. Results may vary.
**No instances of new, sustained erectile or ejaculatory dysfunction**1-6


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