Slumping pay, burnout drive retirement

58% of urologists participate in MIPS, 19% in APMs

Richard Kerr / Content Channel Director

More than one-fourth of urologists say they have specific plans to retire within the next 2 years. An ongoing drop in reimbursement, feeling burned out, and government mandates are the primary factors affecting when they will retire, according to the 13th annual Urology Times State of the Specialty survey.

The results are in stark contrast to those of the survey 10 years ago, when urologists were asked whether their 5-year plan included retirement. Only 7% of 2008 survey respondents said retirement was in their plans; that number jumped to 28% in the 2013 survey.

As urologists test the waters of Medicare’s new Quality Payment Please see SURVEY, on page 22

For the full article, please turn to page 26

“Can’t wait to get out… because this is killing me”

“Actively searching for a way out of medicine”

More Survey Results

Read about urologists’ top concerns, 2019 plans, practice size, and more See pages 22-24

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Medicare final rule: How E/M changes help urologists

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Radiology report errors prove costly

How AI may reshape urologic practice

Over the past several years, there has been an explosion in artificial intelligence (AI) in health care. AI is already being applied to urologic practice in the areas of radiologic and pathologic diagnosis, patient monitoring and telemedicine, and automating repetitive tasks. Daniel Au, MD, and J. Brantley Thrasher, MD, examine the uses of AI as well as its benefits and shortcomings. For the full article, please turn to page 26

MIPS and APMs

Is your practice currently participating in MIPS?

58% 32% 10%

Yes No I am exempt from MIPS

Is your practice currently participating in an APM?

19% 81%

Yes No

Source: All graphics based on Urology Times State of the Specialty survey results
Significantly reduced nighttime urine production\(^3\)

Gave patients over 4 hours of uninterrupted sleep\(^3\)

Significantly increased the number of nights with 0 or 1 void\(^1\)

**IMPORTANT SAFETY INFORMATION**

**WARNING: HYPONATREMIA**

*See full prescribing information for complete boxed warning.*

- NOCTIVA can cause hyponatremia. Severe hyponatremia can be life-threatening, leading to seizures, coma, respiratory arrest, or death.
- NOCTIVA is contraindicated in patients at increased risk of severe hyponatremia. See Important Safety Information below for full contraindications.
- Ensure serum sodium is normal before starting or resuming NOCTIVA. Measure serum sodium within 7 days and approximately 1 month after initiating therapy or increasing the dose, and periodically during treatment. More frequently monitor patients ≥65 years of age and those at increased risk of hyponatremia.
- If hyponatremia occurs, NOCTIVA may need to be discontinued.

**INDICATIONS AND USAGE**

NOCTIVA is a vasopressin analog indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void.

**Limitation of Use:** Not studied in patients younger than 50 years of age.
THE SIMPLICITY OF

ONE spray
ONE nostril
ONE time a night

With NOCTIVA™ (desmopressin acetate) Nasal Spray, you can give your patients relief tonight and better functioning tomorrow.¹

Order samples at NoctivaHCP.com/UT

CONTRAINDICATIONS
NOCTIVA is contraindicated in patients with the following conditions: hyponatremia or a history of hyponatremia, polydipsia, primary nocturnal enuresis, concomitant use with loop diuretics or systemic or inhaled glucocorticoids, estimated glomerular filtration rate <50 mL/min/1.73 m², syndrome of inappropriate antidiuretic hormone secretion (SIADH), during illnesses that can cause fluid or electrolyte imbalance, congestive heart failure (New York Heart Association Class II-IV), and uncontrolled hypertension.

WARNINGS AND PRECAUTIONS
• Fluid retention: Not recommended in patients at risk of increased intracranial pressure or history of urinary retention. Monitor volume status in patients with NYHA Class I congestive heart failure.
• Nasal conditions: Discontinue in patients with concurrent nasal conditions that may increase absorption, until resolved.

ADVERSE REACTIONS
Common adverse reactions in clinical trials (incidence >2%) included nasal discomfort, nasopharyngitis, nasal congestion, sneezing, hypertension, back pain, epistaxis, bronchitis, and dizziness.

DRUG INTERACTIONS
Monitor serum sodium more frequently when NOCTIVA is concomitantly used with drugs that may cause water retention and increase the risk for hyponatremia.

USE IN SPECIFIC POPULATIONS
• Pregnancy: Use of NOCTIVA is not recommended.
• Pediatric: Do not use NOCTIVA for primary nocturnal enuresis in children.

To report SUSPECTED ADVERSE REACTIONS, contact Avadel at 1-877-638-4579 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see full Brief Summary on the following pages.

NOCTIVA™ (desmopressin acetate) Nasal Spray

The following is a brief summary. Please consult Full Prescribing Information for complete details.

**WARNING: HYponATREMIA**

- NOCTIVA can cause hyponatremia. Severe hyponatremia can be life-threatening, leading to seizures, coma, respiratory arrest, or death.
- NOCTIVA is contraindicated in patients at increased risk of severe hyponatremia, such as patients with excessive fluid intake, illnesses that can cause fluid or electrolyte imbalances, and in those using loop diuretics or systemic or inhaled glucocorticoids.
- Ensure serum sodium concentrations are normal before starting or resuming NOCTIVA. Measure serum sodium within 7 days and approximately 1 month after initiating therapy or increasing the dose, and periodically during treatment. More frequently monitor serum sodium in patients 65 years of age and older and in patients at increased risk of hyponatremia.
- If hyponatremia occurs, NOCTIVA may need to be temporarily or permanently discontinued.

**INDICATIONS AND USAGE**

NOCTIVA is indicated for the treatment of nocturia due to nocturnal polyuria in adults who awaken at least 2 times per night to void.

Nocturnal polyuria was defined in the NOCTIVA clinical trials as nighttime urine production exceeding one-third of the 24-hour urine production.

Before starting NOCTIVA:

- Evaluate the patient for possible causes for the nocturia, including excessive fluid intake prior to bedtime, and optimize the treatment of underlying conditions that may be contributing to the nocturia.
- Confirm the diagnosis of nocturnal polyuria with a 24-hour urine collection, if one has not been obtained previously.

**CONTRAINDICATIONS**

NOCTIVA is contraindicated in patients with the following conditions due to an increased risk of severe hyponatremia:

- Hyponatremia or a history of hyponatremia. [see Warnings and Precautions]
- Polydipsia
- Primary nocturnal enuresis [see Use in Specific Populations]
- Concomitant use with loop diuretics [see Warnings and Precautions]
- Concomitant use with systemic or inhaled glucocorticoids [see Warnings and Precautions, Drug Interactions]
- Renal impairment with an estimated glomerular filtration rate (eGFR) below 50 mL/min/1.73 m² [see Use in Specific Populations]
- Known or suspected syndrome of inappropriate antidiuretic hormone (SIADH) secretion
- During illnesses that can cause fluid or electrolyte imbalance, such as gastroenteritis, salt-wasting nephropathies, or systemic infection

NOCTIVA is contraindicated in patients with the following conditions because fluid retention increases the risk of worsening the underlying condition:

- Congestive heart failure (New York Heart Association Class II to IV) [see Warnings and Precautions]
- Uncontrolled hypertension

**WARNINGS AND PRECAUTIONS**

**Risk of Hyponatremia:** NOCTIVA can cause hyponatremia. [see Boxed Warning and Adverse Reactions]. Severe hyponatremia can be life-threatening if it is not promptly diagnosed and treated, leading to seizures, coma, respiratory arrest, or death.

NOCTIVA is contraindicated in patients at increased risk of severe hyponatremia, such as those with excessive fluid intake, those who have illnesses that can cause fluid or electrolyte imbalances, and in those using loop diuretics or systemic or inhaled glucocorticoids [see Boxed Warning, Contraindications, and Drug Interactions].

Before starting or resuming NOCTIVA, ensure that the serum sodium concentration is normal. Consider the 0.83 mcg dose as the starting dose for patients who may be at risk for hyponatremia.

When NOCTIVA is administered, fluid intake in the evening and nighttime hours should be moderated to decrease the risk of hyponatremia. Monitor the serum sodium concentration within 7 days and approximately 1 month of initiating NOCTIVA or increasing the dose, and periodically thereafter. The frequency of serum sodium monitoring should be based on the patient’s risk for hyponatremia. For example, more frequent monitoring is recommended for patients 65 years of age or older or those on concomitant medications that can increase the risk of hyponatremia, such as tricyclic antidepressants, selective serotonin reuptake inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDs), chlorpromazine, carbamazepine, and thioule diuretics [see Drug Interactions].

If hyponatremia occurs, NOCTIVA may need to be temporarily or permanently discontinued, and treatment for the hyponatremia instituted, depending on the clinical circumstances, including the duration and severity of the hyponatremia.

**Fluid Retention:** NOCTIVA can cause fluid retention, which can worsen underlying conditions that are susceptible to volume status. Therefore, NOCTIVA is contraindicated in patients with New York Heart Association Class II to IV congestive heart failure or uncontrolled hypertension [see Contraindications]. In addition, NOCTIVA is not recommended in patients at risk for increased intracranial pressure or those with a history of urinary retention, and should be used with caution (e.g., monitoring of volume status) in patients with New York Heart Association Class I congestive heart failure.

**Concurrent Nasal Conditions:** Discontinue NOCTIVA in patients with concurrent nasal conditions that may increase systemic absorption of NOCTIVA (e.g., atrophy of nasal mucosa, and acute or chronic rhinitis), because the increased absorption may increase the risk of hyponatremia. NOCTIVA can be resumed when these conditions resolve.

**ADVERSE REACTIONS**

The following adverse reaction is described elsewhere in the labeling:

- Hyponatremia [see Boxed Warning and Warnings and Precautions]

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

Two randomized, double-blind, placebo-controlled, multicenter trials conducted in adults 50 years of age and older evaluated the efficacy and safety of NOCTIVA nasal spray compared to placebo. At baseline, 1045 patients treated with NOCTIVA 0.83 mcg or 1.66 mcg, or placebo, had nocturia due to nocturnal polyuria, waking at least 2 times per night to urinate. Nocturnal polyuria was defined as nighttime urine production exceeding one-third of the 24-hour urine production. The mean age of the patients studied with nocturia due to nocturnal polyuria was 67 years with 42% between 50 and 64 years of age, and 58% aged 65 years and older. Fifty-seven percent were men and 43% were women. Caucasians comprised 79%, Blacks 12%, Hispanics 6%, and Asians 2% of the trial population.

During these trials, serious adverse reactions were reported in 2%, 2%, and 3% of patients with nocturia due to nocturnal polyuria treated with NOCTIVA 0.83 mcg, NOCTIVA 1.66 mcg, and placebo, respectively. There was one case of hyponatremia in the 1.66 mcg group and one case in the placebo group classified as serious adverse reactions.

**Adverse Reactions Leading to Discontinuation:** Among patients with nocturia due to nocturnal polyuria, the discontinuation rate due to adverse reactions was 4.0% with NOCTIVA 0.83 mcg, 4.4% with NOCTIVA 1.66 mcg, and placebo, respectively. Table 1 displays the most common adverse reactions leading to discontinuation in patients with nocturia due to nocturnal polyuria.

**Table 1: Most Common Adverse Reactions (≥2 Incidences) Leading to Discontinuation in Patients With Nocturia Due to Nocturnal Polyuria in 2 Double-Blind, Placebo-Controlled Clinical Trials**

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>NOCTIVA 1.66 mcg (n=341)</th>
<th>NOCTIVA 0.83 mcg (n=354)</th>
<th>Placebo (n=340)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyponatremia/Blood Sodium Decreased</td>
<td>4 (1.2%)</td>
<td>3 (0.9%)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Nasal Discomfort</td>
<td>2 (0.6%)</td>
<td>0</td>
<td>3 (0.9%)</td>
</tr>
<tr>
<td>Nasal Congestion</td>
<td>2 (0.6%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Atrial Fibrillation</td>
<td>2 (0.6%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Dizziness</td>
<td>0</td>
<td>2 (0.6%)</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>Dysuria</td>
<td>1 (0.3%)</td>
<td>2 (0.6%)</td>
<td>0</td>
</tr>
</tbody>
</table>

**Most Common Adverse Reactions:** Table 2 summarizes the most common adverse reactions reported by patients with nocturia due to nocturnal polyuria. This table shows adverse reactions reported in at least 2% of patients treated with NOCTIVA and at a higher incidence with the 1.66 mcg dose than with placebo.
Table 2: Common Adverse Reactions (Reported by ≥2% of NOCTIVA-Treated Patients and at a Higher Incidence With the 1.66 mcg Dose Than With Placebo) in 2 Double-Blind, Placebo-Controlled Clinical Trials in Patients With Nocturia Due to Nocturnal Polyuria

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>NOCTIVA 1.66 mcg (n=341)</th>
<th>NOCTIVA 0.83 mcg (n=354)</th>
<th>Placebo (n=349)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal Discomfort</td>
<td>20 (5.9%)</td>
<td>12 (3.4%)</td>
<td>17 (4.9%)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>13 (3.8%)</td>
<td>8 (2.3%)</td>
<td>10 (2.9%)</td>
</tr>
<tr>
<td>Nasal Congestion</td>
<td>10 (2.9%)</td>
<td>5 (1.4%)</td>
<td>5 (1.4%)</td>
</tr>
<tr>
<td>Sneezing</td>
<td>9 (2.6%)</td>
<td>8 (2.3%)</td>
<td>5 (1.4%)</td>
</tr>
<tr>
<td>Hypertension/Blood Pressure Increased</td>
<td>9 (2.6%)</td>
<td>6 (1.7%)</td>
<td>4 (1.1%)</td>
</tr>
<tr>
<td>Back Pain</td>
<td>8 (2.3%)</td>
<td>4 (1.1%)</td>
<td>3 (0.9%)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>7 (2.1%)</td>
<td>7 (2.0%)</td>
<td>4 (1.1%)</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>7 (2.1%)</td>
<td>3 (0.8%)</td>
<td>3 (0.9%)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>6 (1.8%)</td>
<td>7 (2.0%)</td>
<td>5 (1.4%)</td>
</tr>
</tbody>
</table>

No overall changes were observed in the safety profile during the open-label, uncontrolled extension trial with up to 126 weeks of follow-up.

Hyponatremia: Table 3 shows the incidence of serum sodium concentrations below the normal range reported in the 2 placebo-controlled trials.

Table 3: Hyponatremia in 2, Double-Blind, Placebo-Controlled Clinical Trials in Patients With Nocturia Due to Nocturnal Polyuria

<table>
<thead>
<tr>
<th>Serum Sodium Concentrations (mmol/L)</th>
<th>NOCTIVA 1.66 mcg (n=341)</th>
<th>NOCTIVA 0.83 mcg (n=354)</th>
<th>Placebo (n=349)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤125</td>
<td>5 (1.5%)</td>
<td>0</td>
<td>1 (0.3%)</td>
</tr>
<tr>
<td>130-134</td>
<td>42 (12.3%)</td>
<td>33 (9.3%)</td>
<td>18 (5.2%)</td>
</tr>
<tr>
<td>126-129</td>
<td>7 (2.1%)</td>
<td>8 (2.3%)</td>
<td>0</td>
</tr>
</tbody>
</table>

Of the 5 patients on NOCTIVA 1.66 mcg with serum sodium ≤125 mmol/L, all were 65 years of age or older. Four were men. The onset of the hyponatremia ranged from 6 days to 12 weeks after the start of dosing. Four of these patients were taking a concomitant systemic or intranasal glucocorticoid and 3 were taking an NSAID.

Sex: The incidence of hyponatremia with NOCTIVA was similar in men and women.

Age: Patients 65 years of age and older treated with NOCTIVA had a higher incidence of hyponatremia compared to those younger than 65 years of age (see Table 4).

Table 4: Hyponatremia, Based on Age, in 2 Double-Blind, Placebo-Controlled Clinical Trials in Patients With Nocturia Due to Nocturnal Polyuria

<table>
<thead>
<tr>
<th>Serum Sodium Concentrations (mmol/L)</th>
<th>NOCTIVA 1.66 mcg &lt;65 years (n=146)</th>
<th>NOCTIVA 1.66 mcg ≥65 years (n=195)</th>
<th>NOCTIVA 0.83 mcg &lt;65 years (n=148)</th>
<th>NOCTIVA 0.83 mcg ≥65 years (n=206)</th>
<th>Placebo &lt;65 years (n=144)</th>
<th>Placebo ≥65 years (n=205)</th>
</tr>
</thead>
<tbody>
<tr>
<td>130-134</td>
<td>14 (9.6%)</td>
<td>28 (14.4%)</td>
<td>8 (5.4%)</td>
<td>25 (12.1%)</td>
<td>7 (4.9%)</td>
<td>11 (5.4%)</td>
</tr>
<tr>
<td>126-129</td>
<td>0</td>
<td>7 (3.6%)</td>
<td>2 (1.4%)</td>
<td>6 (2.9%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>≤125</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1 (0.5%)</td>
</tr>
</tbody>
</table>

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

Risk Summary: There are no data with NOCTIVA use in pregnant women to inform any drug-associated risks. No adverse developmental outcomes were observed in animal reproduction studies with administration of desmopressin during organogenesis to pregnant rats and rabbits at doses approximately <1 and 31 times, respectively, the maximum recommended human dose based on nasal surface area (see Data).

NOCTIVA is not recommended for the treatment of nocturia in pregnant women. Nocturia is usually related to normal physiologic changes during pregnancy that do not require treatment with NOCTIVA.

In the U.S. general population, the estimated background rate of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal Data: Desmopressin acetate did not cause fetal harm in teratology studies in rats and rabbits at doses of 0.05 to 10 mcg/kg/day, which is approximately <1 times (rat) and 31 times (rabbit) the maximum recommended human dose based on nasal surface area.

Lactation: Desmopressin is present in small amounts in human milk and is poorly absorbed orally by an infant. There is no information on the effects of desmopressin on the breastfed infant or on milk production. The development and health benefits of breastfeeding should be considered along with the mother’s clinical need for NOCTIVA and any potential adverse effects on the breastfed infant from NOCTIVA or from the underlying maternal condition.

Pediatric Use: NOCTIVA is contraindicated for the treatment of primary nocturnal enuresis because of reports of hyponatremic-related seizures in pediatric patients treated with other intranasal formulations of desmopressin. Studies of NOCTIVA have not been conducted in pediatric patients (see Contraindications).

Geriatric Use: Patients 65 years and older treated with NOCTIVA had a higher incidence of hyponatremia compared to patients less than 65 years old treated with NOCTIVA (see Warnings and Precautions, and Adverse Reactions).

Renal Impairment: Desmopressin is mainly excreted in the urine. The area under the concentration-time curve (AUC) and terminal half-life of desmopressin in renally impaired patients with an eGFR below 50 mL/min/1.73 m² is 3- to 4-fold greater than in patients with an eGFR above 50 mL/min/1.73 m². Therefore, NOCTIVA is contraindicated in patients who have renal impairment with an eGFR below 50 mL/min/1.73 m² (see Contraindications).

Hepatic Impairment: The effect of hepatic impairment on the pharmacokinetics of desmopressin has not been studied.

**OVERDOSAGE**

Signs of overdose may include effects from hyponatremia such as seizure, altered mental status, cardiac arrhythmias, and worsening edema. Other signs of overdose may include oliguria and rapid weight gain due to fluid retention (see Warnings and Precautions). In case of overdose, NOCTIVA should be discontinued immediately, serum sodium should be assessed, and appropriate medical treatment initiated.

**PATIENT COUNSELING INFORMATION**

Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Hyponatremia: Inform patients that NOCTIVA can cause hyponatremia, which may be life-threatening. Inform patients to moderate fluid intake in the evening and nighttime hours, to monitor for symptoms of hyponatremia (such as headache, nausea or vomiting, restlessness, fatigue, drowsiness, dizziness, muscle cramping, or altered mental status), to undergo appropriate medical treatment initiated.

NOCTIVA can be resumed when these conditions resolve. NOCTIVA should be discontinued immediately, serum sodium should be assessed, and appropriate medical treatment initiated.

In case of overdosage, NOCTIVA should be discontinued immediately, serum sodium should be assessed, and appropriate medical treatment initiated.

**DRUG INTERACTIONS**

No specific pharmacokinetic studies were conducted to evaluate potential drug-drug interactions between NOCTIVA and other medications.

Drugs That May Cause Severe Hyponatremia: Concomitant use of NOCTIVA and loop diuretics or systemic or intranasal glucocorticoids is contraindicated because of the risk of severe hyponatremia (see Boxed Warning, Contraindications, and Warnings and Precautions). NOCTIVA can be started or resumed 3 days or 5 half-lives after the glucocorticoid is discontinued, whichever is longer.

Drugs That May Cause Water Retention: Monitor serum sodium more frequently in patients taking NOCTIVA concomitantly with medications that may cause water retention and increase the risk for hyponatremia (e.g., tricyclic antidepressants, selective serotonin reuptake inhibitors, chlorpromazine, opioid analgesics, NSAIDs, lamotrigine, and carbamazepine) (see Warnings and Precautions).

Drugs Administered Intranasally: The drug interaction potential between NOCTIVA and other intranasally administered drugs has not been studied. NOCTIVA is not recommended for use in patients who require treatment with other drugs via the nasal route.
We love what we do, but it shouldn’t be this hard

Although most are satisfied with their career choice in medicine and even more as a urologist, this year’s survey reflects the deep dissatisfaction most have for the direction medical care has taken.

Only 12% of urologists indicate they are very familiar with Merit-based Incentive Payment System or Advanced Alternative Payment Models, the new and future methods of reimbursement. Only 20% participate in AQUA, the AUA’s registry designed to assist reporting. In fact, 90% consider the new emphasis on quality measures to be irrelevant.

Although most are satisfied with their career choice in medicine and even more as a urologist, this year’s survey reflects the deep dissatisfaction most have for the direction medical care has taken. In view of this, most are seeking to diminish their direct participation by joining larger employers or leaving the system altogether. We still love what we do, but it shouldn’t be so hard.
Study: Many post-op ER visits preventable

Patient education efforts do not significantly reduce return visits

Laird Harrison
UT Correspondent

SAN FRANCISCO—About half of postoperative visits to emergency rooms following urologic surgery could be prevented, but simply improving patient education may not significantly reduce the number of these visits, researchers say.

“What we may think is common sense would have prevented a lot of emergency department visits,” Hari Sawkar, MD, chief urology resident at the University of Southern California (USC) in Los Angeles told Urology Times. He presented the research at the AUA annual meeting in San Francisco.

“...about half of postoperative visits to emergency rooms following urologic surgery could be prevented, but simply improving patient education may not significantly reduce the number of these visits, researchers say. “What we may think is common sense would have prevented a lot of emergency department visits,” Hari Sawkar, MD, chief urology resident at the University of Southern California (USC) in Los Angeles told Urology Times. He presented the research at the AUA annual meeting in San Francisco.

“What we may think is common sense would have prevented a lot of emergency department visits.”

HARI SAWKAR, MD

Few studies describe emergency department visits following urologic surgery, he said. Most of these are after stone surgery, and study designs vary substantially, with researchers reporting rates of emergency department visits from 7% to 15%.

To characterize emergency department utilization and readmissions, the authors used data from the USC Los Angeles County + USC Medical Center. Located in East Los Angeles, the 600-bed facility has 40,000 discharges and handles 150,000 emergency department visits per year. The patient population is ethnically and linguistically diverse, with many economically disadvantaged.

Dr. Sawkar and his colleagues identified cases of patients returning to the emergency room within 90 days of urologic surgery. They reviewed medical records to determine clinical causes and whether the emergency room visits were preventable. They then designed interventions in an attempt to reduce the number of preventable emergency department visits.

At baseline (July to September 2015), the medical center did 53 urologic procedures per month, of which 20.8% resulted in emergency department visits, with 50.9% of those visits deemed preventable. The mean number of days from surgery to an emergency department visit was 13.9.

The most common reason for an emergency room visit, accounting for 25.8% of the visits, was a question about a wound. Another 16.4% stemmed from a non-wound infection, and 16.1% were for surgical site pain. Drain and catheter issues accounted for another 15.8%, and hematuria for 13.3%.

Based on their analysis of these causes, the authors found two common problems leading to a preventable emergency department visit. First, the patients couldn’t get access to urology providers to ask questions. Second, they had unclear expectations about recovery from the surgery.

To see if they could address these problems, the authors devised handouts specific to the most common urologic procedures and provided them to patients in English and Spanish. Patients received preoperative calls from nurse practitioners and postoperative calls by operating residents.

The handouts include a description of the procedure. They tell patients how to prepare—for example, by avoiding medications that can increase bleeding. They explain what to expect after surgery, such as pain and hematuria with transurethral resection of a bladder tumor (TURBT).

The handouts also list symptoms that justify a trip to the emergency room or a 911 call. In the case of TURBT, symptoms listed are: severe pain, uncontrolled vomiting, high fevers, significant bleeding, chest pain, shortness of breath, severe headache, or loss of consciousness.

In the 24 months after introducing the handouts, the authors recorded 1,333 urologic procedures leading to 204 emergency department visits (15.3%), of which 99 (48.53%) were preventable, and 51 readmissions (3.83%). The mean time from the operating room to the emergency department was 12.6 days.

The most common reasons for the emergency department visits after the introduction of the handouts were pain and clogged, leaking, or dislodged Foley catheter, drain, or percutaneous nephrostomy tubes. Both of these accounted for 18%. Another 11% each were for infectious complications and hematuria.

The change in the rate of preventable emergency department visits was not statistically significant, said Dr. Sawkar, who worked on the research with Jeffrey Loh-Doyle, MD, and colleagues. “Even though our intervention didn’t work, we can try new things,” Dr. Sawkar said.

Since collecting these statistics, the medical center has launched a website with procedure-specific information, a comprehensive urology phone tree to reduce the number of calls fielded by frontline staff, and opportunities for patients to contact residents on call after the clinic is closed. The authors have not yet determined the results of these new efforts.

In Brief
For up-to-date news, visit urologytimes.com

AUA ISSUES POSITION STATEMENT ON OPIOID USE
The AUA recently released a position statement regarding opioid use. The statement includes sections regarding opioid duration and amount, storage and disposal of opioids, and more.

“The [AUA] strongly believes urologists have a responsibility to minimize their patients’ pain while addressing overprescribing of opioids,” the AUA said in the statement.

To read the full statement, see bit.ly/AUAA opioids.

CLINICAL UPDATES
8 • prostate cancer
10 • bladder cancer
12 • infertility
19 • stone disease
Clinical Updates

**PROSTATE CANCER / Findings bolster case for personalized screening strategies**

**Midlife PSA strongly predicts PCa in African-Americans**

Andrew Bowser
UT Correspondent

A single baseline PSA measurement taken during midlife strongly predicted the subsequent diagnosis of aggressive prostate cancer up to 12 years later among African-American men in the United States, according to researchers.

Findings of the case-control study corroborate results of two earlier studies in the United States and Sweden suggesting midlife PSA had predictive value for prostate cancer in largely Caucasian populations.

**Findings help fill research gap**
The findings also help fill a research gap by providing new data on the potential role of midlife PSA measurement in African-American men, who suffer a higher burden of disease versus Caucasian men, said authors of the study published in *European Urology* (Sept. 17, 2018 [Epub ahead of print]).

“Taken together, the findings of the three studies to date provide ‘strong support’ for using a midlife PSA level to determine a personalized screening strategy, according to lead author Mark A. Preston, MD, MPH, assistant professor of surgery at Harvard Medical School, Boston, and his co-authors. “There’s a solid body of evidence now that a midlife PSA is very predictive of aggressive prostate cancer, and risk-stratified screening, or smarter screening, is where we should be headed,” Dr. Preston said in an interview with *Urology Times*.

This latest study provides promising evidence that midlife PSA measurement could indeed improve on standard PSA screening, although more research is needed, according to the authors of an editorial commenting on the results *(Eur Urol* Sept. 26, 2018 [Epub ahead of print]).

“The extent to which any personalized screening program would reduce overdiagnosis and overtreatment remains unclear,” authors Rebecca E. Graff, PhD, Linda Kachuri, PhD, and John S. Witte, PhD, of the University of California, San Francisco, wrote in their editorial.

That said, the present study highlights the association between midlife PSA levels and aggressive disease, since aggressive disease is the most clinically relevant and less likely to be over-diagnosed, Dr. Preston and colleagues said in their report.

Their nested, case-control study included African-American men from the southeastern United States participating in the Southern Community Cohort Study. Total PSA was measured in blood collected and stored at the time the men were recruited into the study at community health centers between 2002 and 2009.

Dr. Preston focused the analysis on a total of 197 incident prostate cancer patients aged 40-64 years when they entered the study, of whom 91 had aggressive disease, and 569 controls who were matched by age, blood draw date, and enrollment site.

Median PSA increased with age—0.72 ng/mL for the 40-49 age group versus 1.03 ng/mL for the 60-64 age group—with a median follow-up of 9 years.

**Substantially increased risk seen for men with PSA above median**
Investigators found that men with PSA level above the median, compared to men with PSA at or below the median, were at substantially increased risk of prostate cancer. Looking specifically at aggressive prostate cancer, they reported odds ratios of 49.6 and 18.7 for men aged 40-54 years and 55-64 years, respectively.

When they analyzed the men with PSA in the 90th percentile or higher versus those at or below median, the odds ratios increased to 174 for the 40- to 54-year-olds and 51.8 for the 55- to 64-year-olds, Dr. Preston and colleagues reported.

The study had a number of limitations, the authors acknowledged, including the fact that they used a composite endpoint of aggressive prostate cancer based on stage, grade, and mortality.

Nevertheless, the findings to date argue strongly for using midlife PSA to risk-stratify those men who, on one hand, may have lower risk and may need less screening in the future, and on the other, those who may need more frequent screening so that intervention, if needed, can be done in a timely fashion, Dr. Preston said.

“There’s a solid body of evidence now that a midlife PSA is very predictive of aggressive prostate cancer, and risk-stratified screening, or smarter screening, is where we should be headed.”

MARK A. PRESTON, MD, MPH

**YTUBE VIDEOS ULTRASONIC PROPULSION OF STONES**

“Ytube” is a video resource for urologists and other physicians who focus on men’s health. Videos cover surgical aspects of a variety of men’s health issues, with the goal of providing clinicians a current reference. *James M. Hotaling, MD, MS | Section Editor urologytimes.com/YTUBE*

University of Washington researchers have developed a noninvasive, surgical stone management system that uses a handheld ultrasound device to target, detach, break, and expel stones and stone fragments from the urinary space to facilitate natural clearance. This video shows how the ultrasound system is used to image, target, and reposition stones or fragments to facilitate passage or relieve an obstruction.

| MATHEW D. SORENSEN, MD, MS | PATRICK SAMSON, MD | MICHAEL R. BAILEY, PhD | JONATHAN D. HARPER, MD |

8 | Urology Times | DECEMBER 2018
No link observed between androgen deprivation therapy, dementia

Future studies should examine effects of novel oral agents, expert says

John Schieszer
UT Correspondent

A new study suggests there is no link between the use of androgen deprivation therapy (ADT) and dementia in men with non-metastatic prostate cancer who received definitive radiotherapy.

This finding, published in *JAMA Oncology* (2018; 4:1616-7), contradicts other studies on the topic.

Previous research has found a strong, statistically significant association between ADT use and both dementia and Alzheimer’s disease in men with prostate cancer. However, these investigations included men with localized and metastatic disease who received a variety of different treatments.

“The more important question is whether long term (>3 year[s]) of ADT use/continuous long-term use is associated with dementia,” said Dr. Moul, who was not involved with the study.

Dr. Moul said that future studies should examine whether ADT combined with long-term novel oral agents, such as abiraterone (ZYTIMA) and enzalutamide (XTANDI), is associated with brain dysfunction in advanced prostate cancer.

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**SBRT SHOWS LONG-TERM EFFICACY FOR PCA**

A recent study of stereotactic body radiation therapy (SBRT) for low- and intermediate-risk prostate cancer shows that both the long-term efficacy and safety of SBRT compare favorably with the profiles of other established radiotherapy modalities.

For more, see [www.urologytimes.com/SBRT-PCA](http://www.urologytimes.com/SBRT-PCA).
Clinical Updates

BLADDER CANCER / Difference in incidence not seen for rectal cancer

Neoadjuvant immunotherapy found efficacious in MIBC

Dave Levitan
UT Correspondent

Neoadjuvant pembrolizumab (Keytruda) was safe to administer and resulted in a significant proportion of patients with muscle-invasive bladder cancer (MIBC) presenting at radical cystectomy with pT0 disease, according to a new study.

The benefit was mostly seen in patients with programmed death ligand 1 (PD-L1)-positive tumors, or those with high tumor mutation burden.

Recommended treatment for MIBC includes neoadjuvant pembrolizumab (94%).

Among 35 patients deemed to be PD-L1 positive, pT0 was achieved in 19 patients (54.3%), compared with only 13.3% of those who were PD-L1 negative (p=.011).

The benefit was mostly seen in patients with programmed death ligand 1 (PD-L1)-positive tumors, or those with high tumor mutation burden.

Recommended treatment for MIBC includes neoadjuvant pembrolizumab (94%).

EBRT for prostate cancer raises risk of developing bladder Ca

Dave Levitan
UT Correspondent

A retrospective study found that treatment for prostate cancer with external beam radiotherapy (EBRT) is associated with an increased risk for development of bladder cancer when compared with treatment with radical prostatectomy.

The finding is limited by potential biases in this type of analysis, however.

“Therapy of a first tumor might influence risk of harboring a second tumor, and identifying such a factor would improve selection of patients among those who are at an increased risk of developing a potentially deadly second primary tumor,” wrote study authors led by Marco Moschini, MD, PhD, of the Luzerner Kantonsspital in Lucerne, Switzerland.

The new study used the Surveillance, Epidemiology, and End Results database to investigate the influence of radical prostatectomy and EBRT on the risk of developing a secondary malignancy, specifically bladder cancer or rectal cancer.

The study included a total of 84,397 individuals, of whom 33,252 (39%) were treated with radical prostatectomy and 51,145 (61%) were treated with EBRT. Patients were followed for a median of 69 months, and the results were published in European Urology (Oct. 4, 2018 [Epub ahead of print]).

There were some important differences between the two groups of patients with regard to baseline characteristics. The radical prostatectomy patients had a median age of 69 years, compared with 74 years in those undergoing EBRT (p<.001). More radical prostatectomy patients were Caucasian and more were married (82% vs. 71%, p<.001), and more EBRT patients were smokers (32% vs. 31%, p<.001). There were also differences with regard to Gleason scores and clinical disease stage.

5-, 10-year incidence reported

The cumulative incidence of bladder cancer was 1.06% in the full cohort; for rectal cancer, this rate was 0.37%. The 5-year cumulative bladder cancer incidence in those undergoing radical prostatectomy was 0.75%, compared with 1.26% for those undergoing EBRT; at 10 years, those rates were 1.63% and 2.34% (p<.001). There were no differences in incidence between the treatment groups for rectal cancer.

A multivariate analysis found that patients treated with EBRT were more likely to develop bladder cancer, with a hazard ratio of 1.35 (95% CI: 1.18–1.53; p<.001). No such difference was seen with regard to rectal cancer.

The authors noted that a lack of information on the dose of radiotherapy is a limiting factor, and that improvements in EBRT technique in recent years may mean the risks have changed. Also, the retrospective nature of the study means that selection bias and other limitations cannot be ignored.

L. Michael Glodé, MD, a professor emeritus at the University of Colorado Cancer Center, Denver, who was not involved in the study, highlighted those limitations.

“Although the concern regarding radiotherapy-induced pelvic cancers remains, the challenges of seeking comparable groups of patients in a retrospective study are significant,” he said, noting that the patients with higher bladder cancer rates were also older, less healthy, and more likely to be smokers. “As with many surgery-versus-radiotherapy prostate cancer studies, the absence of prospectively randomized studies continues to plague our field.”

The PURE-01 study included 50 patients with MIBC, regardless of cisplatin eligibility. They received three cycles of the immune checkpoint inhibitor pembrolizumab every 3 weeks prior to RC. The results were published in the Journal of Clinical Oncology (Oct. 20, 2018 [Epub ahead of print]).

The median age in the study was 66 years, and 82% of the patients were male. A majority of patients had a clinical T stage of T3N0 (54%), followed by T2N0 (32%) and T2-3N1 (4%). Most patients received three cycles of pembrolizumab (94%).

42% rate of pT0 stage ‘unprecedented’

All patients underwent RC. Of those, 21 patients (42%) achieved a pT0 stage, which the authors described as “unprecedented.” Six patients had residual pTa (three patients), pTis (two patients), or pT1 tumors (one patient); this resulted in a total of 27 patients (54%) being downstaged to nonmuscle-invasive tumors. Ten patients had
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†Data on file (2013 internal study), Teleflex Incorporated, Report #D001591. Testing conducted on porcine carotids, sample size = 33, p≤ 0.05. Clinical performance cannot be extrapolated from the data. Testing pressures range beyond physiological pressures.

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High paternal age may raise PCa rate

John Schieszer
UT Correspondent

SAN FRANCISCO—The public health impact of increasing paternal age requires further investigation, and clinicians should discuss with their patients the potential impact older fathers may have on their children, according to researchers at Stanford University School of Medicine, Stanford, CA.

They reported that paternal age is on the rise. This is concerning because the prevalence rates of certain cancers, congenital disorders, and psychiatric illnesses have been shown to directly correlate with advancing paternal age.

The authors reported that the mean paternal age in the U.S. increased from 27.4 years in 1972 to 30.9 years in 2015. It is theorized that some cancers, congenital disorders, and other illnesses may be on the rise because of de novo mutations occurring during after conception.

For this investigation, the authors categorized births into ranges of paternal age, and all rates were adjusted for maternal age. The number of births affected by each disease was calculated for each year based on the incidence rate of disease for a given paternal age group (cases per 4 million annual births).

% of fathers age >40 years more than doubled
The authors found that the percentage of fathers with age greater than 40 years more than doubled over the study period (4.1% to 8.5%). They also found that the increase in paternal age in 2015 may have contributed to an estimated 34,031 additional cases of prostate cancer in their offspring compared to 1972 per 4 million annual births. Achondroplasia due to increasing paternal age was also estimated to increase by 51% (610 cases in 1972 to 923 cases in 2015). The authors estimate there was a 21.6% increase in the incidence of autism and a 39.5% increase in bipolar disease expected in births occurring in 2015 compared to 1972.

The percentage of children born in 2015 expected to suffer from substance abuse increased by 14.2%, and a similar trend was found with failing grades (increase of 13.4%) and low education attainment (2.8%) compared to 1972 due to effects associated with increasing paternal age, according to the authors.

Paul Turek, MD, a men’s reproductive health specialist in San Francisco, said the study findings are somewhat alarming.

“The impact of paternal age on children’s health could conceivably be the first real ‘genetic epidemic’ to hit humanity in the era of genomic medicine,” Dr. Turek told Urology Times. However, he said that these findings must be viewed with caution.

“Realize that their estimates of diseases and their incidences in offspring is still a murky science, with lots of loose ends and unknowns,” Dr. Turek said.

“While we were expecting the number of births with cancer and neurocognitive deficits to increase, we were certainly surprised by the sheer number of births that were estimated to have been affected in 2015 compared to 1972.”

YASH KHANDWALA, MD

IMMUNOTHERAPY
continued from page 10

pathologic lymph node involvement, and five had treatment failure. (Four had lack of a radiologic response, and one discontinued pembrolizumab due to transaminitis.)

Among 35 patients deemed to be PD-L1 positive, pT0 was achieved in 19 patients (54.3%), compared with only 13.3% of those who were PD-L1 negative (p=0.01). A significant association was also seen between pT0 response and tumor mutation burden, and authors wrote that a meaningful cutoff would correspond to the 80th percentile for mutation burden.

The most frequent all-grade adverse event was thyroid dysfunction, in nine patients (18%). Three patients (6%) had grade 3 adverse events, only one of which led to discontinuation of the therapy. Postsurgical complications were similar to those seen in previous reports of RC.

“These results will encourage the clinical development of new neoadjuvant therapies and allow for more patients with MIBC to receive multimodality therapy,” the authors concluded. “Pending the results of the next randomized studies, pembrolizumab may now be considered an option for cisplatin-ineligible patients with a PD-L1-expressing or high tumor mutation burden tumor.”

Paul Mathew, MD, associate professor at Tufts Medical Center in Boston, who was not involved in the research, praised the “remarkably high” response rates seen with this therapy, and noted that those ongoing and future studies will still help in defining the role of biomarkers, including PD-L1 and others.

“The fact that this therapy appears both effective and well tolerated without significant impact on surgical eligibility will likely translate into a far higher adoption rate of neoadjuvant therapy in muscle-invasive urothelial carcinoma compared with the historically dismal rates with chemotherapy,” Dr. Mathew said.

“Paternal age should be considered a meaningful factor in determining the risk of adverse events. The impact of paternal age on children’s health could conceivably be the first real ‘genetic epidemic’ to hit humanity in the era of genomic medicine,” Dr. Turek told Urology Times.

However, he said that these findings must be viewed with caution.

“Realize that their estimates of diseases and their incidences in offspring is still a murky science, with lots of loose ends and unknowns,” Dr. Turek said.

“While we were expecting the number of births with cancer and neurocognitive deficits to increase, we were certainly surprised by the sheer number of births that were estimated to have been affected in 2015 compared to 1972.”

YASH KHANDWALA, MD
A new study is suggesting a significant number of men were using finasteride at the AUA annual meeting in San Francisco that investigators from the University of Toronto reported for male infertility are overlooked in men. Inves- tigators found that many potentially reversible causes the men are not being fully investigated.

“You would think most men would be off testosterone by the time they actually make it to us, but in fact we found 5% were taking testosterone.”

KEITH JARVI, MD

Many men undergo ART procedures without full workup

John Schieszer
UT Correspondent

SAN FRANCISCO—a new study is suggesting that many couples with male factor infertility are being treated with intrauterine insemination (IUI) or in vitro fertilization (IVF) even though the men are not being fully investigated.

The large, broad North American patient survey found that many potentially reversible causes for male infertility are overlooked in men. Investigators from the University of Toronto reported at the AUA annual meeting in San Francisco that a significant number of men were using finasteride (Propecia) and taking testosterone even though these agents are known to harm fertility.

“We got information on how frequently men were using testosterone, and testosterone is known to cause infertility in men. So, you would think most men would be off testosterone by the time they actually make it to us, but in fact we found 5% were taking testosterone,” said study first author Keith Jarvi, MD, professor of surgery at the University of Toronto. “It was incredibly surprising. It is shocking that it is happening still. People should know.”

Dr. Jarvi and his co-authors looked at men in The Andrology Research Consortium, which includes men presenting for infertility investigation at 24 North American subspecialty male infertility centers. A total of 4,335 men completed a standardized male infertility questionnaire between May 2015 and September 2017. Mean age of the men was 37 years, and their female partners’ mean age was 34 years. In this cohort, 74% had not been previously assessed by a male fertility specialist.

Dr. Jarvi and his colleagues turned up some rather interesting findings. They discovered that IUI and IVF had been used to treat some of the couples even though they had never had a male factor infertility investigation. There were several potentially reversible causes for the male infertility, including a previous vasectomy and medication and lifestyle factors.

The survey showed that cigarettes were used by 11% and marijuana was used by 9.5% of the men. Limited alcohol consumption (two or fewer drinks/day) was common and only 6.4% reported they had more than two drinks daily. Cocaine use was reported by 2% of the men.

Finasteride finding surprising

Dr. Jarvi, who presented the study findings at the meeting, said it was surprising how many men were on finasteride for baldness.

“Propecia is used to prevent hair loss and we know Propecia may also cause infertility and almost 4.5% of these guys were on Propecia,” Dr. Jarvi said in an interview with Urology Times. “They are coming to our offices. So, they were on it and they should have been off it.”

The survey showed that the testosterone had been prescribed by urologists, endocrinologists, and primary care physicians in almost equal numbers to manage low energy (31%), diminished libido (20%), improved athletics and strength (15%), and other reasons.

Ablative RT may be alternative for solitary-kidney RCC

Excellent local oncologic control observed in treated patients

Cheryl Guttman Krader
UT Contributing Editor

Stereotactic ablative body radiotherapy (SABR) for renal cell carcinoma (RCC) in patients with a solitary kidney provides excellent local oncologic control with acceptable impact on renal function, according to findings from an individual-patient pooled analysis from the International Radiosurgery Oncology Consortium for Kidney (IROCK).

The research was reported by Rohann Correa, MD, PhD, at the American Society for Radiation Oncology annual meeting in San Antonio.

“We believe that referral for kidney SABR is worthy of consideration in patients with solitary-kidney RCC who are faced with limited and risky management options.”

ROHANN CORREA, MD, PhD

RCC, particularly in the high-risk setting of solitary kidney disease, and particularly for patients who are poor candidates for operative or interventional management for reasons of medical comorbidity or tumor size and/or location. We believe that referral for kidney SABR is worthy of consideration in patients with solitary-kidney RCC who are faced with limited and risky management options.”

To investigate SABR as a definitive treatment option in patients with solitary-kidney RCC, Dr. Correa and colleagues conducted a pooled analysis from the Inter-Radiosurgery Oncology Resident at London Health Sciences Center, London, ON, working with Alexander Louie, MD, PhD, and colleagues.

“Our encouraging data support further study of SABR as an alternative treatment modality for...
**Indication and Important Safety Information**

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

**Important Safety Information**

**Warnings and Precautions**

**Seizure** occurred in 0.4% of patients receiving XTANDI in clinical studies. In a study of patients with predisposing factors for seizure, 2.2% of XTANDI-treated patients experienced a seizure. Patients in the study had one or more of the following pre-disposing factors: use of medications that may lower the seizure threshold; history of traumatic brain or head injury, cerebrovascular accident or transient ischemic attack, Alzheimer’s disease, meningioma, or leptomeningeal disease from prostate cancer, unexplained loss of consciousness within the last 12 months, history of seizure, presence of a space occupying lesion of the brain, history of arteriovenous malformation, or history of brain infection. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Advise patients of the risk of developing a seizure while taking XTANDI and of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

**Posterior Reversible Encephalopathy Syndrome (PRES)**
In post approval use, there have been reports of PRES in patients receiving XTANDI. PRES is a neurological disorder which can present with rapidly evolving symptoms including seizure, headache, lethargy, confusion, blindness, and other visual and neurological disturbances, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably MRI. Discontinue XTANDI in patients who develop PRES.

**Hypersensitivity** reactions, including edema of the face (0.5%), tongue (0.1%), or lip (0.1%) have been observed with XTANDI in clinical trials. Pharyngeal edema has been reported in post-marketing cases. Advise patients who experience any symptoms of hypersensitivity to temporarily discontinue XTANDI and promptly seek medical care. Permanently discontinue XTANDI for serious hypersensitivity reactions.

**Ischemic Heart Disease** In the placebo-controlled clinical studies, ischemic heart disease occurred more commonly in patients on the XTANDI arm compared to patients on the placebo arm (2.7% vs 1.2%). Grade 3-4 ischemic events occurred in 1.2% of patients on XTANDI versus 0.5% on placebo. Ischemic events led to death in 0.4% of patients on XTANDI compared to 0.1% on placebo. Monitor for signs and symptoms of ischemic heart disease. Optimize management of cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Discontinue XTANDI for Grade 3-4 ischemic heart disease.

**Falls and Fractures** In the placebo-controlled clinical studies, falls occurred in 10% of patients treated with XTANDI compared to 4% of patients treated with placebo. Fractures occurred in 8% of patients treated with XTANDI and in 3% of patients treated with placebo. Evaluate patients for fracture and fall risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

**Embryo-Fetal Toxicity** Safety and efficacy of XTANDI have not been established in females. XTANDI can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment with XTANDI and for 3 months after the last dose of XTANDI. XTANDI should not be handled by females who are or may become pregnant.

**Adverse Reactions**
The most common adverse reactions (≥ 10%) that occurred more frequently (≥ 2% over placebo) in the XTANDI patients from the randomized placebo-controlled trials were asthenia/fatigue, decreased appetite, hot flush, arthralgia, dizziness/vertigo, hypertension, headache and weight decreased. In the bicalutamide-controlled study, the most common adverse reactions (≥ 10%) reported in XTANDI patients were asthenia/fatigue, decreased appetite, hot flush, arthralgia, dizziness/vertigo, hypertension, headache and weight decreased.
XTANDI significantly prolonged metastasis-free survival in patients with nonmetastatic CRPC and significantly extended overall survival and radiographic progression-free survival in patients with metastatic CRPC.

**Nonmetastatic CRPC:** Median metastasis-free survival was 3 years (36.6 months [95% CI, 33.1-36.6]) with XTANDI + LHRH therapy vs 14.7 months (95% CI, 14.2-15.0) with placebo + LHRH therapy (HR = 0.29 [95% CI, 0.24-0.35]; P < 0.0001).†

- As seen in the PROSPER trial: a multinational, randomized, double-blind phase 3 trial that enrolled 1401 patients with nonmetastatic CRPC who progressed on LHRH therapy. Eligibility criteria included PSA doubling time ≤ 10 months and no prior chemotherapy.

**Metastatic CRPC:** 23% reduction in the risk of death with XTANDI + LHRH therapy vs placebo + LHRH therapy (HR = 0.77 [95% CI, 0.67-0.88]) and 83% reduction in the risk of radiographic progression or death vs placebo + LHRH therapy (HR = 0.17 [95% CI, 0.14-0.21]; P < 0.0001).‡

- As seen in the PREVAIL trial: a multinational, randomized, double-blind phase 3 trial that enrolled 1717 patients with metastatic CRPC who progressed on LHRH therapy. Eligibility criteria included no prior chemotherapy.

### Drug Interactions

**Effect of Other Drugs on XTANDI**

Avoid strong CYP2C8 inhibitors, as they can increase the plasma exposure to XTANDI. If co-administration is necessary, reduce the dose of XTANDI.

Avoid strong CYP3A4 inducers as they can decrease the plasma exposure to XTANDI. If co-administration is necessary, increase the dose of XTANDI.

**Effect of XTANDI on Other Drugs**

Avoid CYP3A4, CYP2C9, and CYP2C19 substrates with a narrow therapeutic index, as XTANDI may decrease the plasma exposures of these drugs. If XTANDI is co-administered with warfarin (CYP2C9 substrate), conduct additional INR monitoring.

**Please see adjacent pages for Brief Summary of Full Prescribing Information.**

**References:**

2. Pfizer. XTANDI. Data on File.
XTANDI® (enzalutamide) capsules for oral use

BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

INDICATIONS AND USAGE

XTANDI is an androgen receptor inhibitor indicated for the treatment of patients with castration-resistant prostate cancer.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Seizure

Seizure occurred in 0.4% of patients receiving XTANDI in clinical studies. In these trials, patients with predisposing factors for seizure were generally excluded. Seizures occurred from 13 to 604 days after initiation of XTANDI. Patients experiencing seizure were permanently discontinued from therapy and all seizure events resolved.

In a single-arm trial designed to assess the risk of seizure in patients with pre-disposing factors for seizure, 8 of 366 (2.2%) XTANDI-treated patients experienced a seizure. Three of the 8 patients experienced a second seizure during continued treatment with XTANDI after their first seizure resolved. It is unknown whether anti-epileptic medications will prevent seizures with XTANDI. Patients in the study had one or more of the following pre-disposing factors: the use of medications that may lower the seizure threshold (~ 54%), history of traumatic brain or head injury (~ 28%), history of cerebrovascular accident or transient ischemic attack (~ 24%), and Alzheimer’s disease, meningioma, or leptomeningeal disease from prostate cancer, unexplained loss of consciousness within the last 12 months, past history of seizure, presence of a space occupying lesion of the brain, history of arteriovenous malformation, or history of brain infection (all < 5%). Approximately 17% of patients had more than one risk factor.

Advise patients of the risk of developing a seizure while receiving XTANDI and of engaging in any activity where sudden loss of consciousness could cause serious harm to themselves or others. Permanently discontinue XTANDI in patients who develop a seizure during treatment.

Posterior Reversible Encephalopathy Syndrome (PRES)

There have been reports of posterior reversible encephalopathy syndrome (PRES) in patients receiving XTANDI. PRES is a neurological disorder which can present with rapidly evolving symptoms including seizure, headache, lethargy, confusion, blindness, and other visual and neurological disturbances, with or without associated hypertension. A diagnosis of PRES requires confirmation by brain imaging, preferably magnetic resonance imaging (MRI). Discontinue XTANDI in patients who develop PRES.

Hypersensitivities

Hypersensitivity reactions, including edema of the face (0.5%), tongue (0.1%), or lip (0.1%) have been observed with enzalutamide in four randomized clinical trials. Pharyngeal edema has been reported in post-marketing cases. Advise patients who experience any symptoms of hypersensitivity to temporarily discontinue XTANDI and promptly seek medical care.

Permanently discontinue XTANDI for serious hypersensitivity reactions.

Ischemic Heart Disease

In the combined data of three randomized, placebo-controlled clinical studies, ischemic heart disease occurred more commonly in patients on the XTANDI arm compared to patients on the placebo arm (2.7% vs 1.2%). Grade 3-4 ischemic events occurred in 1.2% of patients in the XTANDI arm compared to 0.5% in the placebo arm. Ischemic events led to death in 0.4% of patients in the XTANDI arm compared to 0.1% in the placebo arm.

Monitor for signs and symptoms of ischemic heart disease. Optimize cardiovascular risk factors, such as hypertension, diabetes, or dyslipidemia. Discontinue XTANDI for Grade 3-4 ischemic heart disease.

Falls and Fractures

Falls and fractures occurred in patients receiving XTANDI. Evaluate patients for fracture and fall risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents.

In the combined data of three randomized, placebo-controlled clinical studies, falls occurred in 10% of patients treated with XTANDI compared to 4% of patients treated with placebo. Falls were not associated with loss of consciousness or seizure. Fractures occurred in 8% of patients treated with XTANDI and in 3% of patients treated with placebo. Grade 3-4 fractures occurred in 2% of patients treated with XTANDI and in < 1% of patients treated with placebo. The median time to onset of fracture was 337 days (range: 2 to 996 days) for patients treated with XTANDI. Routine bone density assessment and treatment of osteoporosis with bone-targeted agents were not performed in the studies.

Embryo-Fetal Toxicity

The safety and efficacy of XTANDI have not been established in females. Based on animal reproductive studies and mechanism of action, XTANDI can cause fetal harm and loss of pregnancy when administered to a pregnant female. Advise males with female partners of reproductive potential to use effective contraception during treatment with XTANDI. Men should not handle female contraceptives if semen contamination is possible. Discontinue XTANDI 7 days before planned conception and for 3 months after the last dose of XTANDI. XTANDI should not be handled by females who are or may become pregnant.

ADVERSE REACTIONS

Clinical Trial Experience

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

The safety and efficacy of XTANDI were assessed in 189 patients in a single-arm trial designed to assess the risk of fracture and falls in patients with metastatic hormone-sensitive prostate cancer. Patients were treated with XTANDI from 13 to 604 days after initiation of treatment. The safety and efficacy of XTANDI were evaluated in 1199 patients with metastatic prostate cancer in three randomized, placebo-controlled clinical trials. Pharyngeal edema has been observed in practice. Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Table 1. Adverse Reactions in AFFIRM

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo (N=389)</th>
<th>Grade 1-2 (%)</th>
<th>Grade 3-4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anaphylactic Conditions1</td>
<td>51</td>
<td>9.0</td>
<td>44</td>
</tr>
<tr>
<td>PerIPHERAL EDEMA</td>
<td>15</td>
<td>1.0</td>
<td>13</td>
</tr>
<tr>
<td>Musculoskeletal and Connective Tissue Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back Pain</td>
<td>26</td>
<td>5.3</td>
<td>24</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>21</td>
<td>2.5</td>
<td>17</td>
</tr>
<tr>
<td>Musculo-skeletal Pain</td>
<td>15</td>
<td>1.3</td>
<td>12</td>
</tr>
<tr>
<td>Muscular Weakness</td>
<td>9.8</td>
<td>1.5</td>
<td>6.8</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>2.6</td>
<td>0.3</td>
<td>3.0</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>22</td>
<td>2.1</td>
<td>18</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot flush</td>
<td>20</td>
<td>0.0</td>
<td>10</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6.4</td>
<td>2.1</td>
<td>2.8</td>
</tr>
<tr>
<td>Neurovascular System Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>12</td>
<td>0.9</td>
<td>5.5</td>
</tr>
<tr>
<td>Dizziness2</td>
<td>9.5</td>
<td>0.5</td>
<td>7.5</td>
</tr>
<tr>
<td>Spinal Cord Compression and Cauda Equina Syndrome</td>
<td>7.4</td>
<td>6.6</td>
<td>4.5</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>6.6</td>
<td>0.0</td>
<td>4.5</td>
</tr>
<tr>
<td>Vestibular Impairment Disorders3</td>
<td>4.3</td>
<td>0.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>4.0</td>
<td>0.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection4</td>
<td>11</td>
<td>0.0</td>
<td>6.5</td>
</tr>
<tr>
<td>Lower Respiratory Tract and Lung Infection</td>
<td>8.5</td>
<td>2.4</td>
<td>4.8</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>8.8</td>
<td>0.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6.5</td>
<td>0.3</td>
<td>4.0</td>
</tr>
<tr>
<td>Renal and Urinary Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematuria</td>
<td>6.9</td>
<td>1.8</td>
<td>4.5</td>
</tr>
<tr>
<td>Pollakiuria</td>
<td>4.8</td>
<td>0.0</td>
<td>2.5</td>
</tr>
<tr>
<td>Injury, Poisoning and Procedural Complications</td>
<td>4.6</td>
<td>0.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Skin and Subcutaneous Tissue Disorders</td>
<td>3.8</td>
<td>0.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Pruritus</td>
<td>3.8</td>
<td>0.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Dry Skin</td>
<td>3.5</td>
<td>0.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Respiratory Disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epistaxis</td>
<td>3.3</td>
<td>0.1</td>
<td>1.3</td>
</tr>
</tbody>
</table>

1. CTCAE v4
2. Includes asthma and fatigue.
3. Includes dizziness and vertigo.
4. Includes amnesia, memory impairment, cognitive disorder, and disturbance in attention.
5. Includes nasopharyngitis, upper respiratory tract infection, sinusitis, rhinitis, pharyngitis, and laryngitis.
6. Includes pneumonia, lower respiratory tract infection, bronchitis, and lung infection.
PREVAIL (NCT01219991): XTANDI versus Placebo in Chemotherapy-naive Metastatic CRPC
PREVAIL enrolled 1717 patients with metastatic CRPC who had not received prior cytotoxic chemotherapy, of whom 1715 received at least one dose of study drug. The median duration of treatment was 17.5 months with XTANDI and 4.6 months with placebo. Grade 3-4 adverse reactions were reported in 44% of XTANDI-treated patients and 37% of placebo-treated patients. Discontinuations due to adverse events were reported for 6% of XTANDI-treated patients and 6% of placebo-treated patients. The most common adverse reaction leading to treatment discontinuation was fatigue/asthenia, which occurred in 1% of patients on each treatment arm. Table 2 includes adverse reactions reported in PREVAIL that occurred at a ≥ 2% higher frequency in the XTANDI arm compared to the placebo arm.

<table>
<thead>
<tr>
<th>Table 2. Adverse Reactions in PREVAIL</th>
<th>XTANDI N = 871</th>
<th>Placebo N = 844</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grades</strong></td>
<td><strong>Grade 1 (%)</strong></td>
<td><strong>Grade 2 (%)</strong></td>
</tr>
<tr>
<td>General Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthenic Conditions&lt;sup&gt;1&lt;/sup&gt;</td>
<td>47</td>
<td>3.4</td>
</tr>
<tr>
<td>Peripheral Edema</td>
<td>12</td>
<td>0.2</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>23</td>
<td>0.7</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>17</td>
<td>0.3</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot Flush</td>
<td>18</td>
<td>0.1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14</td>
<td>7.2</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>11</td>
<td>0.3</td>
</tr>
<tr>
<td>Headache</td>
<td>11</td>
<td>0.2</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>7.6</td>
<td>0.1</td>
</tr>
<tr>
<td>Mental Impairment Disorders</td>
<td>5.7</td>
<td>0.0</td>
</tr>
<tr>
<td>Restless Legs Syndrome</td>
<td>2.1</td>
<td>0.1</td>
</tr>
<tr>
<td>Respiratory Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dyspnea&lt;sup&gt;1&lt;/sup&gt;</td>
<td>11</td>
<td>0.6</td>
</tr>
<tr>
<td>Infections and Infestations</td>
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<td></td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection&lt;sup&gt;1&lt;/sup&gt;</td>
<td>16</td>
<td>0.0</td>
</tr>
<tr>
<td>Lower Respiratory Tract and Lung Infection&lt;sup&gt;1&lt;/sup&gt;</td>
<td>7.9</td>
<td>1.5</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td>8.2</td>
<td>0.1</td>
</tr>
<tr>
<td>Renal and Urinary Disorders</td>
<td>8.8</td>
<td>1.3</td>
</tr>
<tr>
<td>Injury, Poisoning and Procedural Complications</td>
<td>13</td>
<td>1.6</td>
</tr>
<tr>
<td>Non-Pathological Fracture</td>
<td>8.8</td>
<td>2.1</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>19</td>
<td>0.3</td>
</tr>
<tr>
<td>Weight Decreased</td>
<td>12</td>
<td>0.8</td>
</tr>
<tr>
<td>Reproductive System and Breast Disorders</td>
<td>3.4</td>
<td>0.0</td>
</tr>
</tbody>
</table>

**Table 3. Adverse Reactions in TERRAIN (≥ 10%) in XTANDI-treated patients.**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>XTANDI N = 189</th>
<th>Bicalutamide N = 189</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grades</strong></td>
<td>Grade 1 (%)</td>
<td>Grade 2 (%)</td>
</tr>
<tr>
<td>Overall</td>
<td>94</td>
<td>39</td>
</tr>
<tr>
<td>General Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthenic Conditions&lt;sup&gt;2&lt;/sup&gt;</td>
<td>32</td>
<td>1.6</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot Flush</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14</td>
<td>7.1</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Constipation</td>
<td>13</td>
<td>1.1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection&lt;sup&gt;1&lt;/sup&gt;</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Lower Respiratory Tract and Lung Infection&lt;sup&gt;1&lt;/sup&gt;</td>
<td>7.9</td>
<td>1.5</td>
</tr>
</tbody>
</table>

**Table 4. Adverse Reactions in PROSPER**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>XTANDI N = 183</th>
<th>Bicalutamide N = 189</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grades</strong></td>
<td>Grade 1 (%)</td>
<td>Grade 2 (%)</td>
</tr>
<tr>
<td>Overall</td>
<td>94</td>
<td>39</td>
</tr>
<tr>
<td>General Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthenic Conditions&lt;sup&gt;2&lt;/sup&gt;</td>
<td>32</td>
<td>1.6</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot Flush</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Hypertension</td>
<td>14</td>
<td>7.1</td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Constipation</td>
<td>13</td>
<td>1.1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Infections and Infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection&lt;sup&gt;1&lt;/sup&gt;</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Lower Respiratory Tract and Lung Infection&lt;sup&gt;1&lt;/sup&gt;</td>
<td>7.9</td>
<td>1.5</td>
</tr>
</tbody>
</table>

**Laboratory Abnormalities**

In the AFFIRM and PREVAIL studies in metastatic CRPC, Grade 1-4 neutropenia occurred in 15% of patients receiving XTANDI (1% Grade 3-4) and in 6% of patients receiving placebo (0.5% Grade 3-4). Table 5 shows laboratory abnormalities that occurred in > 5% of patients, and more frequently (≥ 2%) in the XTANDI arm compared to placebo in the PROSPER study.

**Table 5. Laboratory Abnormalities in PROSPER**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>XTANDI N = 930</th>
<th>Placebo N = 465</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grades</strong></td>
<td>Grade 1 (%)</td>
<td>Grade 2 (%)</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>9.6</td>
<td>3.9</td>
</tr>
<tr>
<td>Weight Decreased</td>
<td>5.9</td>
<td>1.5</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>2.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>

**Table 4. Adverse Reactions in PROSPER**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>XTANDI N = 930</th>
<th>Placebo N = 465</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grades</strong></td>
<td>Grade 1 (%)</td>
<td>Grade 2 (%)</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>9.6</td>
<td>3.9</td>
</tr>
<tr>
<td>Weight Decreased</td>
<td>5.9</td>
<td>1.5</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>2.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>

**Laboratory Abnormalities**

In the AFFIRM and PREVAIL studies in metastatic CRPC, Grade 1-4 neutropenia occurred in 15% of patients receiving XTANDI (1% Grade 3-4) and in 6% of patients receiving placebo (0.5% Grade 3-4). Table 5 shows laboratory abnormalities that occurred in > 5% of patients, and more frequently (≥ 2%) in the XTANDI arm compared to placebo in the PROSPER study.

**Table 5. Laboratory Abnormalities in PROSPER**

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>XTANDI N = 930</th>
<th>Placebo N = 465</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grades</strong></td>
<td>Grade 1 (%)</td>
<td>Grade 2 (%)</td>
</tr>
<tr>
<td>Metabolism and Nutrition Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased Appetite</td>
<td>9.6</td>
<td>3.9</td>
</tr>
<tr>
<td>Weight Decreased</td>
<td>5.9</td>
<td>1.5</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety</td>
<td>2.8</td>
<td>0.4</td>
</tr>
</tbody>
</table>
Hypertension
In the AFFIRM and PREVAIL studies in metastatic CRPC, hypertension was reported in 11% of patients receiving XTANDI and 4% of patients receiving placebo. Medical history of hypertension was balanced between arms. Hypertension led to study discontinuation in 1% of patients in each arm in the PROSPER study in non-metastatic CRPC. Hypertension was reported in 12% of patients receiving XTANDI and 3% of patients receiving placebo.

Post-Marketing Experience
The following additional adverse reactions have been identified during post-approval use of XTANDI. Because these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency with which they occur or establish a causal relationship to drug exposure.

Body as a Whole: hypersensitivity (edema of the face, tongue, lip, or pharynx)

Gastrointestinal Disorders: vomiting

Neurological Disorders: posterior reversible encephalopathy syndrome (PRES)

Drug INTERACTIONS
Drugs that Inhibit CYP2C8
Co-administration of a strong CYP2C8 inhibitor (gemfibrozil) increased the composite area under the curve (AUC) of enzalutamide plus N-desmethyl enzalutamide by 2.2-fold. Co-administration of XTANDI with strong CYP2C8 inhibitors should be avoided if possible. If co-administration of XTANDI with a strong CYP2C8 inhibitor cannot be avoided, reduce the dose of XTANDI.

Drugs that Induce CYP3A4
Co-administration of rifampin (strong CYP3A4 inducer and moderate CYP2C8 inducer) decreased the composite AUC of enzalutamide plus N-desmethyl enzalutamide by 37%. Co-administration of strong CYP3A4 inducers (e.g., carbamazepine, phenobarbital, phenytoin, rifabutin, rifapentine) with XTANDI should be avoided if possible. St John’s wort may decrease enzalutamide exposure and should be avoided. If co-administration of a strong CYP3A4 inducer with XTANDI cannot be avoided, increase the dose of XTANDI.

Effect of XTANDI on Drug Metabolizing Enzymes
Enzalutamide is a strong CYP2A4 inducer and a moderate CYP2C9 and CYP2C19 inducer in humans. At steady-state, XTANDI reduced the plasma exposure to midazolam (CYP3A4 substrate), warfarin (CYP2C9 substrate), and omeprazole (CYP2C19 substrate). Concomitant use of XTANDI with narrow therapeutic index drugs that are metabolized by CYP3A4 (e.g., alfentanil, cyclosporine, diltiazem, erythromycin, fentanyl, indinavir, itraconazole, ketoconazole, metoprolol, omeprazole, pimozide, propoxyphene, rifampin, ritonavir, and temafibrate) should be avoided as enzalutamide may decrease their plasma exposure. Concomitant administration with CYP2C9 or CYP2C19 inducers should be avoided, as enzalutamide may decrease exposure and should be avoided. If co-administration of a strong CYP3A4 inducer with XTANDI cannot be avoided, increase the dose of XTANDI.

USE IN SPECIFIC POPULATIONS
Pregnancy
Risk Summary
The safety and efficacy of XTANDI have not been established in females. Based on animal reproductive studies and mechanism of action, XTANDI can cause fetal harm and loss of pregnancy. There are no human data on the use of XTANDI in pregnant females. In animal reproduction studies, oral administration of enzalutamide in pregnant mice during organogenesis caused adverse developmental effects at doses lower than the maximum recommended human dose (see Data). XTANDI should not be handled by females who are or may become pregnant.

Animal Data
In an embry-fetal developmental toxicity study in mice, enzalutamide caused developmental toxicity when administered at oral doses of 10 or 30 mg/kg/day throughout the period of organogenesis (gestational days 6-15). Findings included embryo-fetal lethality (increased post-implantation loss and resorptions) and decreased anogenital distance at ≥ 10 mg/kg/day, and cleft palate and absent palatine bone at 30 mg/kg/day. Doses of 30 mg/kg/day caused maternal toxicity. The doses tested in mice (1, 10, and 30 mg/kg/day) resulted in systemic exposures (AUC) approximately 0.04, 0.4 and 1.1 times, respectively, the exposures in patients. Enzalutamide did not cause developmental toxicity in rabbits when administered throughout the period of organogenesis (gestational days 6-18) at doses levels up to 10 mg/kg/day (approximately 0.4 times the exposures in patients based on AUC).

In a pharmacokinetic study in pregnant rats with a single oral 30 mg/kg enzalutamide administration on gestation day 14, enzalutamide and/or its metabolites were present in the fetuses at a Cmax that was approximately 0.3 times the concentration found in maternal plasma and occurred 4 hours after administration.

Lactation
Risk Summary
The safety and efficacy of XTANDI have not been established in females. There is no information available on the presence of XTANDI in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on the mother of nursing infants. Enzalutamide and/or its metabolites were present in milk of lactating rats (see Data).

Data
Following a single oral administration in lactating rats on postnatal day 14, enzalutamide and/or its metabolites were present in milk at a Cmax that was 4 times higher than concentrations in the plasma and occurred 4 hours after administration.

Females and Males of Reproductive Potential
Contraception
Males
Based on findings in animal reproduction studies, advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of XTANDI.

Infertility
Males
Based on animal studies, XTANDI may impair fertility in males of reproductive potential.

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

Geriatric Use
Of 2784 patients who received XTANDI in four randomized controlled clinical trials, 79% were 65 and over, while 38% were 75 and over. No overall differences in safety or effectiveness were observed between these patients and younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Patients with Renal Impairment
A dedicated renal impairment trial for XTANDI has not been conducted. Based on the population pharmacokinetic analysis using data from clinical trials in patients with metastatic CRPC and healthy volunteers, no significant difference in enzalutamide clearance was observed in patients with pre-existing mild to moderate renal impairment (30 mL/min ≤ creatinine clearance [CrCl] < 60 mL/min) compared to patients and volunteers with baseline normal renal function (CrCl ≥ 90 mL/min). No initial dosage adjustment is necessary for patients with mild to moderate renal impairment. Severe renal impairment (CrCl < 30 mL/min) and end-stage renal disease have not been assessed.

Patients with Hepatic Impairment
Dedicated hepatic impairment trials compared the composite systemic exposure of enzalutamide plus N-desmethyl enzalutamide in volunteers with baseline mild, moderate, or severe hepatic impairment (Child-Pugh Class A, B, or C, respectively) versus healthy controls with normal hepatic function. The composite AUC of enzalutamide plus N-desmethyl enzalutamide was similar in volunteers with mild, moderate, or severe baseline hepatic impairment compared to volunteers with normal hepatic function. No initial dosage adjustment is necessary for patients with baseline mild, moderate, or severe hepatic impairment.

OVERDOSAGE
In the event of an overdose, stop treatment with XTANDI and institute general supportive measures taking into consideration the half-life of 5.8 days. In a dose escalation study, no seizures were reported at ≤ 240 mg daily, whereas 3 seizures were reported, 1 each at 360 mg, 480 mg, and 600 mg daily. Patients may be at increased risk of seizure following an overdose.

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Administration of enzalutamide to male and female rasH2 transgenic mice by oral gavage daily for 26 weeks did not result in increased incidence of neoplasms at doses up to 20 mg/kg/day.

Enzalutamide did not induce mutations in the bacterial reverse mutation (Ames) assay and was not genotoxic in either the in vitro mouse lymphoma thymidine kinase (TK) gene mutation assay or the in vivo mouse micronucleus assay.

Based on nonclinical findings in repeat-dose toxicology studies, which were consistent with the pharmacological activity of enzalutamide, male fertility may be impaired by treatment with XTANDI. In a 26-week study in rats, atrophy of the prostate and seminal vesicles was observed at ≥ 30 mg/kg/day (equal to the human exposure based on AUC). In 4-, 13-, and 39-week studies in dogs, hypospermato genesis and atrophy of the prostate and epididymides were observed at ≥ 4 mg/kg/day (0.3 times the human exposure based on AUC).

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Kidney stone surgery: Should outcome target change?

Cheryl Guttmann Krader
UT Contributing Editor

Results of a study evaluating health-related quality of life (HRQoL) in patients surgically treated for kidney stones suggest a need to rethink the outcome target and focus on patient counseling to set appropriate expectations.

The research was presented at the World Congress of Endourology and SWL in Paris. It included data from 282 adults who underwent single-fraction SABR, although multi-fraction treatments were also utilized (range, 1-10) with a median fractional dose of 25 Gy (range, 6-26 Gy).

The subset of remaining patients who had bilateral functioning kidneys were slightly older on average, had slightly lower mean eGFR and larger tumors, and included a lower percentage of patients with good performance status, but received a similar radiation dose, Dr. Correa noted.

They found that in a univariable logistic regression analysis conducted to identify factors predicting a decrease in eGFR ≥15 mL/min, tumor diameter ≥4.0 cm was the only associated predictor (81.5% vs. 82.4%; p = .356). There was no significant difference between the solitary and bilateral subgroups.

“Health-related quality of life is being increasingly recognized as an important outcome measure, but to our knowledge, there has not been previous research comparing HRQoL in patients with residual fragments after surgical treatment for stone disease to those who are stone-free,” said Dr. Streeper.

Better patient counseling needed
“The findings of our study suggest that perhaps we are overtreating patients and performing unnecessary procedures to get them stone-free,” she said. “In addition, it supports the value of proper counseling. Information should be discussed with patients preoperatively so that they understand the possibility of having residual fragments and reasons for needing a secondary procedure. To mitigate frustration for patients with asymptomatic, non-obstructing residual stone fragments, postoperative counseling is needed to reassure them that observation may be an acceptable management strategy.”

Aside from Penn State, patients included in the study were treated at the University of Wisconsin, Madison, Dartmouth Hitchcock Medical Center, Lebanon, NH, and the University of British Columbia, Vancouver, BC. Data on surgical outcome for patients included in the study was identified retrospectively through review of postoperative imaging. The study cohort included 134 patients who were determined to be stone-free and 148 patients with residual stones.

The two groups were similar with respect to mean age and gender distribution. Stone-free patients had a significantly higher median body mass index than the residual fragment group (30.5 vs. 28.0 kg/m²) and had significantly fewer stone events (median of two vs. four).

Please see STONE SURGERY, on page 20

ABLATIVE RT
continued from page 13

Dr. Correa reported that in a univariable logistic regression analysis conducted to identify factors predicting a decrease in eGFR ≥15 mL/min, tumor diameter ≥4.0 cm was the only associated variable (OR: 4.21, 95% CI: 1.16-15.31, p = .029).

“Given this finding, caution is indicated when treating larger tumors in this setting,” Dr. Correa said.

Data on oncologic outcomes showed local recurrence occurred in a single patient in the solitary kidney subgroup and in two patients in the bilateral group. Cancer-specific survival was excellent in both groups, but the rate was significantly higher in the solitary subgroup than in patients with two functioning kidneys (98.2% vs. 94.3%; p = .047). There was no significant difference in the overall survival rate between the solitary and bilateral subgroups (81.5% vs. 82.4%; p = .356).

Going forward, Dr. Correa and colleagues are exploring comparative effectiveness research that will compare SABR with other available modalities for RCC (ie, surgery or thermal ablation). UT
8% of stone surgery patients use opioids long term

Substance/alcohol abuse among predictors of prolonged use, data indicate

Cheryl Guttman Krader
UT Contributing Editor

A sizable proportion of opioid-naïve patients who undergo stone surgery become chronic opioid users, according to a study conducted by urologists from Emory University, Atlanta.

The research also identified risk factors for prolonged opioid use, and therefore suggests targets for prevention, said Mohammed A. Said, MD, at the World Congress of Endourology and SWL in Paris.

Dr. Said and colleagues evaluated the incidence and predictors of prolonged opioid use in a population of 50,249 “opioid-naïve” adults (ages 18 to 64 years) undergoing shock wave lithotripsy, ureteroscopy, or percutaneous nephrolithotomy. Patients included in the study had filled a prescription for an opioid within 7 days before or after their stone procedure and had 180 days of postoperative follow-up.

Of this large cohort of patients, 8.1% became prolonged opioid users, defined as having filled another prescription for an opioid medication between 90 and 180 days after surgery. Multivariable logistic regression analysis identified substance or alcohol abuse, a history of mental health or pain disorders, and greater total oral morphine equivalent dosage at initial prescription as the strongest independent predictors of prolonged opioid use. Risk did not vary by type of stone surgery.

“The United States is in the midst of an opioid epidemic. The findings of our study indicate that urologists are wrong if they think that prescribing opiates to patients undergoing stone surgery is not contributing to this issue.”

MOHAMMED A. SAID, MD

The mean total score was 112.9 for the group with residual stone fragments and 117.3 for the stone-free group (p=.17). Mean frustration scores were 3.73 for the residual stone fragment group and 4.08 for stone-free patients (p=.03).

Dr. Streep acknowledged that the study has limitations because of its retrospective design.

“The onus is on us to find ways to prevent prolonged opiate use in this patient population. Our study supports the need to prescribe opioid alternatives and to raise awareness among prescribers for which patients are at highest risk for long-term use.”

The study was conducted by extracting information from the Truven MarketScan insurance claims database for the years 2009 through 2015. Patients were considered opioid-naïve and included in the analysis if they had not filled a prescription for an opioid within 1 week to 12 months prior to their stone surgery. Patients who received anesthesia 1 to 6 months after their stone surgery were excluded.

Additional variables associated with prolonged opioid use included female sex, multiple procedures, higher Charlson comorbidity index, and Southern region.

TABLE HEALTH-RELATED QUALITY OF LIFE SCORE BY STONE-FREE STATUS

<table>
<thead>
<tr>
<th>Patients with residual fragments</th>
<th>Stone-free patients</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean total Wisconsin Stone Quality of Life score</td>
<td>112.9</td>
<td>117.3</td>
</tr>
<tr>
<td>Mean frustration score</td>
<td>3.73</td>
<td>4.08</td>
</tr>
</tbody>
</table>

Source: Nicole M. Streeper, MD

These included variation in the interval between surgery and completion of the WISQOL, which ranged from 2 months to 2 years. In addition, the methods of imaging used at the four institutions varied and included x-ray, ultrasound, and computed tomography scan, and it is possible that some patients were misclassified.
Active surveillance (AS) for prostate cancer is included in virtually all the guidelines, and its use has been increasing steadily over the last decade. AS, requiring follow-up testing, has become the current standard of care for men with low-risk prostate cancer. According to Ginsburg et al, many men on AS are lost to follow-up and thus at potentially increased risk for disease progression and poor outcomes (Eur Urol 2018; 74:704-7).

The authors analyzed data in the Michigan Urologic Surgery Improvement Collaborative (MUSIC) registry, which includes patients with prostate cancer from 44 academic and community urology practices. For this study, they included those patients whose managing physician had recorded AS as the initial management strategy in the medical records.

Over a 6-year period from 2011 to 2017, there were 2,211 patients who were initially identified as being managed with AS. The median surveillance period was 32.1 months. The median age was 66.2 years, and other clinical and demographic characteristics were in line with other published reports. Lost to follow-up (LTFU) status was defined as a period of at least 18 months without any surveillance testing such as PSA, imaging, or prostate biopsy entered into the registry or medical record.

10% of patients lost to follow-up

The authors identified 217 patients (10%) as LTFU during a median follow-up of 32.1 months. African-American men and those with higher Charlson comorbidity index were associated with increased risk of LTFU. Most of the LTFU cases (126/217, 58%) occurred soon after or in the first 6 months after being identified as AS candidates in the registry. Also, there was wide variability in LTFU-free probability among different practices ranging from 52% to 99%.

AS protocols in use today are designed with variable intervals for PSA testing and prostate biopsy (and magnetic resonance imaging) to capture any progression in the grade/stage of cancer in a timely fashion. This study does not provide information on the recommended frequency of monitoring tests, but it’s safe to assume that heterogeneity existed across various study practice sites.

Further, almost 20% of patients in this AS cohort had Gleason score 7-10 prostate cancer. Some of these patients were likely poor candidates for early treatment due to comorbidities and may have been on a watchful waiting approach instead of a rigorous AS protocol. Also, it’s possible that some men sought care at a practice that is not part of MUSIC.

It’s important to remember that missing some monitoring tests over a relatively short period of time does not necessarily result in metastases or death from these cancers with a long natural history. Still, there is some concern based on published reports that a few men who are initially managed with AS may experience disease progression and lose the window of curability.

The data presented here in regards to LTFU do not question the safety or feasibility of AS, but this study highlights the need for each practice to perform a self-audit of its AS protocol and take all necessary measures to ensure that patients are not lost during the monitoring period.
Program (QPP), which rewards value and outcomes under the Merit-based Incentive Payment System (MIPS) and Advanced Alternative Payment Models (APMs), the survey found nearly 60% currently participate in MIPS and about 20% in APMs.

The State of the Specialty survey, launched in 2006, looks at the practice trends, attitudes, future plans, and often troubling concerns of practicing urologists. This year’s installment included new questions about MIPS and APM participation. Most respondents fall in the 45 to 59 (36%) or 60 to 65 age group (27%). Also see, “How the survey was conducted,” page 24.

Retirement and other plans

The pressures and frustrations facing many physicians appear to hit urologists particularly hard, and the survey findings suggest that these factors may lead to early retirement. When asked about their retirement plans, 28% said they are actively considering retirement within 2 years, and 29% have made some non-specific plans to retire in 5 to 10 years. One-fourth had no plans to retire, and 8% are already retired.

The common factors influencing respondents’ decision on when to retire are declining reimbursement (67%), burnout (64%), government influence in medicine (59%), and loss of interest/enjoyment (41%). Other factors were doctors’ workload (32%), not wanting to take the recertification/maintenance of certification exam (32%), and personal health/ability (31%).

“Physicians are the least cared for members of the health care delivery system. Our time sacrifice is the least respected and least valued,” said one urologist in a fill-in response. “Actively searching for a way out of medicine,” another said. Said another: “Can’t wait to get out! [in] 2 months because this is killing me.”

Some urologists have more immediate retirement plans. In a question about their plans for 2019, 16% said they will retire from the practice of urology, and another 18% plan to reduce their workload (partially retire). Other plans include looking for a medical job in a non-clinical setting (13%), adding another urologist to their practice, and working locum tenens (both 12%).

Participation in MIPS, APMs

Still in its infancy, the Centers for Medicare & Medicaid Services’ QPP essentially shifts physician reimbursement from fee for service to a system that rewards value of care. Fifty-eight percent of urologists say they participate in MIPS, one of two new avenues to reimburse the program. Only 19% participate in the second path, APMs, according to the survey.

Most urologists lack a clear understanding of their choices regarding MIPS and APMs, with 46% reporting they understand the choices somewhat, 12% very well, and 42% not very well at all. CMS has approved the AUA Quality Registry (AQUA Registry) as a Qualified Clinical Data Registry (QCDR), meaning it can be used by urologists to satisfy reporting requirements in MIPS. Just over one-third (37%) of urologists report current participation in the AQUA Registry or another QCDR, and 7% said they plan to participate in the AQUA Registry or another QCDR within the next year. Thirty-nine percent were not sure if they would do so.

The most common method used by urology practices for reporting MIPS measures is to report directly to CMS via electronic health record software (61%). Less common methods are a third-party vendor (21%) and the AQUA Registry or other QCDR (18%). Twenty percent of practices have had to appeal their MIPS score at least once, and of those, 18% were successful.

Of note, the survey was developed prior to the AUA’s announcement that it now offers a MIPS Manual Entry Webtool, a reporting option for providers who are unable to report electronically through the AQUA Registry. The webtool allows providers to report on both QPP and non-QPP urology-specific measures, which are most relevant to urologic providers, according to the AUA. For more information, visit bit.ly/AUAWebtool.

Responses to survey questions about the time and money urologists spend tracking and reporting MIPS measures were not usable due to a low response rate. However, fill-in responses indicate that providers are spending considerable time
What factors influence your decision on when to retire?

- **Declining reimbursement** 67%
- **Burnout** 64%
- **Government influence in medicine** 59%
- **Loss of interest/enjoyment** 41%
- **Workload** 32%
- **Do not want to take recertification/MOC exam** 32%

What are your plans for 2019?

- **Reduce workload (partially retire)** 18%
- **Retire from the practice of urology** 16%
- **Seek a medical job in a non-clinical setting** 13%
- **Add another urologist to practice** 12%
- **Work locum tenens** 12%
- **Seek a job/business in a non-medical field** 6%
- **Become a hospital-employed urologist** 6%
- **Merge with other urology group(s)** 3%

What is your attitude toward value-based care?

- **It’s a good idea in theory but much harder to execute in practice** 29%
- **It’s a bad idea that will not succeed** 7%
- **I don’t know enough to make an opinion** 7%
- **It’s good for the health care system and good for my patients** 54%

To what extent do these factors contribute to your feeling burned out?

- **Use of electronic health records** 68%
- **Falling revenue and rising overhead** 65%
- **Prior authorization requirements** 51%
- **Workload** 50%
- **Unappreciative/unreasonable patients** 44%
- **Quality metrics/reporting requirements** 38%
- **Increasing government regulations** 37%
- **Increasing overhead/overhead management** 37%
- **Pressure to keep up with patient load** 37%
- **“Working for large company”** 33%
- **“Major decisions being made in health care delivery without physician input”** 33%
- **“Too much premium dollars going to pharmaceutical companies and others profiting inappropriately”** 33%

**Source:** All graphics based on Urology Times State of the Specialty survey results
How well do you understand your choices regarding MIPS and APMs?

- Very well: 12%
- Somewhat: 46%
- Not very well at all: 42%

What method does your practice use for MIPS reporting?

- AQUA Registry or other QCDR: 18%
- Third-party vendor: 21%
- Report directly to CMS via EHR software: 61%

Have you found MIPS reporting to be clinically relevant/meaningful?

- Yes: 0%
- Not sure: 10%
- No: 90%

Does your practice currently participate in the AQUA Registry or another QCDR?

- Yes: 37%
- No: 63%

Does your practice plan to participate in the AQUA Registry or another QCDR within the next year?

- Yes: 7%
- Not sure: 39%
- No: 54%

 reporting measures. One respondent described the number of hours spent on reporting as “endless,” and a second said it was “too much.”

Asked if they found MIPS reporting to be clinically relevant or meaningful, 90% of urologists said no and 10% were unsure. None said yes.

Satisfaction and burnout

Urologists tend are lukewarm about their choice of a career in medicine (half said they would make this career choice if they were starting out today), but high satisfaction with their choice of specialty (86% would choose to practice urology if starting out). A total of 88% agree or strongly agree with the statement, “I used to enjoy being a physician more, but it’s less lucrative/more stressful now.”

Given a list of possible concerns, urologists’ rankings indicate that it is the business and administrative aspects of practice, rather than patient care, that they find most burdensome. As in past surveys, their most pressing concerns are increasing government regulations (94%), declining reimbursement (93%), prior authorization requirements (92%), and increasing overhead/overhead management (89%).

One-third report being burned out, and another 30% say they’re not currently burned out but are heading in that direction. Use of electronic health records was the leading factor leading to feelings of burnout (68% said it “very much” contributes to burnout), followed by falling revenue and/or rising overhead (65%), prior authorizations (51%), workload (50%), and unappreciative/unreasonable patients (44%).

Asked for other contributors to burnout, one urologist cited “Major decisions being made in health care delivery without physician input.” Another responded: “Too much premium dollars going to pharmaceutical companies and others profiting inappropriately.”

How the survey was conducted

The 2018 Urology Times State of the Specialty survey was conducted via email in early October 2018. All survey recipients were subscribers to Urology Times, and all were required to report they were a urologist or urology resident before responding to the survey. A total of 158 responses were received. The majority of respondents were age 45 to 59 (36%) or 60 to 65 (27%), and 58% were in private practice. Those who responded were eligible to enter a drawing to win one of three $100 Visa gift cards.
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How artificial intelligence may reshape urologic practice

AI is poised to revolutionize use of medical data, but challenges remain

Over the past several years, there has been an explosion in investment and application of artificial intelligence (AI) in health care. Leveraging a combination of large volumes of digital medical data available after the advent of electronic medical records, increasing sophistication in medical testing, and computing power, AI is projected to revolutionize our use of medical data. Health care AI investment is booming, totaling $2.14 billion in 2016, according to a 2017 CB Insights research report.

When it comes to health care applications, AI is a topic that remains clouded in mystery. The Oxford Dictionary defines AI as “the theory and development of computer systems able to perform tasks that normally require human intelligence.” In health care, AI is not specifically defined but is generally thought of as using machine learning algorithms to complete tasks such as drug discovery, virtually assisting patients, and automating complex medical tasks such as analysis of diagnostic tests.

AI is already being applied to urologic practice in three general areas: radiologic and pathologic diagnosis, patient monitoring and telemedicine, and automating repetitive tasks. It is being tested in two other areas: data analytics and precision medicine, and surgical training and quality improvement (table 1). This article examines current and potential future uses of AI as well as its benefits and shortcomings.

Current applications in urology

Radiologic and pathologic diagnoses are some of the more publicized and prolific applications of AI. There has even been a term coined for it in radiology—radiomics—which uses data algorithms to analyze large volumes of quantitative features from medical images. Lu et al in a recent study designed a machine learning algorithm to identify potentially metastatic pelvic lymph nodes and compared the AI results to those of radiologists. Their machine learning model was comparable to radiologist reads with an area under the curve of 0.912, indicating a high level of concordance while doing so in 20 seconds per case versus the radiologist average of 600 seconds (Cancer Res 2018; 78:5135-43).

Among more urology-specific examples (table 2), Sun et al used a machine learning algorithm to predict intra-prostatic tumor location from multiparametric prostate MRI with 70%-87% accuracy (Australas Phys Eng Sci Med 2017; 40:39-49). Donovan et al developed and validated an AI-based test that automated Gleason grade scoring and combined this with biomarkers to accurately predict post-op prostate cancer progression. They were able to predict clinical failure of treatment with a C-Index of 0.82, which is better than conventional nomograms (Prostate Cancer Prostatic Dis Aug. 7, 2018 [Epub ahead of print]). AI has the potential to increase speed of radiologic and pathologic reads, reduce costs, and uncover subtle disease characteristics that might otherwise go unnoticed by humans in the diagnosis of urologic disease.

Patient monitoring and telemedicine. Wearable technology has been growing annually, with estimates that approximately 18% of Americans use such devices at least once a month, according to research by eMarketer. The large volume of recorded data that inherently comes with this technology is beyond human ability to analyze and sift through unaided. Currently, we are able to monitor blood glucose, electrolytes, activity levels, arrhythmias, and oxygen saturation, all of which can cloud to electronic health systems and providers.

While each data point may not be overly necessary to analyze individually, as these sensors multiply, they outgrow our ability to integrate them all without AI assistance. AI is being applied to augment this task and may make the promise of telemedicine, often touted but not fully realized, more practical by adding a layer of security/monitoring and pulling in greater objective information.

Increased AI-guided telemedicine has also taken the form of “remote-presence” mobile robots like the Vita by InTouch Health (figure). Telemedicine robots provide video remote access to patients. The existing shortage of U.S. urologists will only deepen in the coming years, and greater use of telemedicine may blunt this shortage by allowing us to reach patients in clinic or on the wards in areas without urologists, see consultations from afar, and even round on post-op patients.

Automated repetitive tasks. Another growing use of AI is in automation and completion of complex but repetitive

<table>
<thead>
<tr>
<th>TABLE 1. HOW AI MAY IMPACT UROLOGIC CARE</th>
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<tbody>
<tr>
<td>Facilitate faster and more accurate radiologic and pathologic diagnoses</td>
</tr>
<tr>
<td>Expand patient monitoring and telemedicine</td>
</tr>
<tr>
<td>Automate repetitive tasks</td>
</tr>
<tr>
<td>Increase individualized medicine through complex data analytics and algorithms</td>
</tr>
<tr>
<td>Improve surgical training and quality</td>
</tr>
</tbody>
</table>

Source: Daniel Au, MD, and J. Brantley Thrasher, MD
Tasks normally performed by humans. Robots are already completing complex tasks in hospitals in several capacities. TUG is an autonomous robot commercially available from Aethon and has been in use in hospitals around the world including at UCSF Benioff Children’s Hospital and some VA medical centers. TUGs can use elevators, open doors, and use a camera and laser-based system to guide themselves without a set track to intelligently deliver supplies, drugs, and food, and remove waste around the hospital.

AI supply chain computers are also coming into use that can automatically order supplies when low and change order amounts based on usage patterns so surgical materials are there when you need them.

Xenex has designed robots to sterilize ORs and other areas of the hospital using high-intensity UV light, causing cellular damage to bacteria, viruses, and spores already in use at Mayo Clinic and Ochsner Health System.

The machines described above can help urologists increase nursing and OR staff efficiency, decrease OR turnover times, and help ensure that needed supplies are in stock and where they need to be.

Future applications

Data analytics and precision medicine. Precision or individualized medicine is a hot topic in medicine today. IBM has recently partnered Watson, its AI system, with Memorial Sloan Kettering Cancer Center as well as Quest Diagnostics to study ways to identify and diagnose cancers earlier, conduct faster genomic analyses, and even guide cancer treatment. Personalized medicine requires complex integration of a vast array of data points that is inherently labor intensive. AI has the potential to bring “super nomograms” to the fore of medicine by merging diverse data such as imaging features, genomics, molecular markers, and clinical data into one integrated analysis.

Patel et al compared a Watson-based model to a traditional molecular tumor board model to identify oncologic genomic events. In 32% of the 1,018 study patients, the Watson-based model identified genomic events that were not identified via the standard molecular tumor board model, the majority of which were actionable by qualifying patients for previously unconsidered biomarker-based clinical trials. The study authors concluded that AI could rapidly decrease the time needed for genetic sequencing-guided cancer care as well as aid physicians in identifying clinical trial eligibility (Oncologist 2018; 23:179-85).

Surgical training and quality improvement. AI is also being used to improve innate human performance. Hung et al used AI to track and analyze instrument motion tracking and camera manipulation on a da Vinci Surgical System during radical retropubic prostatectomy to predict clinical outcomes, including prolonged length of stay, with 87% accuracy. Additionally, they found some of the metrics measured by their AI model also helped predict patients’ ultimate length of Foley catheter duration (JAMA Surg 2018; 153:770-1).

In the future, this type of AI system could give instant feedback to surgeons regarding case performance and objective insights into surgical technique.

Challenges and benefits

While AI technology presents many opportunities, its application has been rocky to date, particularly for radiologists and pathologists. However, the potential benefits of AI in urology are significant, including increased speed of radiologic and pathologic reads, reduced costs, and uncovering subtle disease characteristics that might otherwise go unnoticed by humans in the diagnosis of urologic disease.

**TABLE 2.** SELECTED PEER-REVIEWED STUDIES OF AI USE IN UROLOGY

<table>
<thead>
<tr>
<th>Topic</th>
<th>Author</th>
<th>Design</th>
<th>Key finding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate MRI</td>
<td>Sun Y et al</td>
<td>Feasibility</td>
<td>Machine learning algorithm predicted intra-prostatic tumor location from multi-parametric prostate MRI with 70%-87% accuracy</td>
</tr>
<tr>
<td>Prostate cancer pathology</td>
<td>Donovan et al</td>
<td>Prospectively designed retrospective study</td>
<td>AI-based test that automated Gleason grade scoring was combined with biomarkers to accurately predict post-op prostate cancer progression</td>
</tr>
<tr>
<td>Robotic prostatectomy training and quality</td>
<td>Hung et al</td>
<td>Pilot</td>
<td>Used AI to track and analyze instrument motion tracking, camera manipulation, and other performance metrics on a da Vinci Surgical System during prostatectomy to predict clinical outcomes, including prolonged length of stay, with 87% accuracy</td>
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Source: Daniel Au, MD, and J. Brantley Thrasher, MD
AI IN UROLOGY
continued from page 27

ticularly in the areas of data mining and clinical decision support. Despite some successes, IBM’s Watson division has also been beset by shortcomings and failures. MD Anderson ended an oncology clinical decision support system powered in part by Watson in 2017 after investing $62 million from 2013 to 2017. Numerous reported problems were found in an audit, including inaccurate treatment advice and problems integrating and extracting data from different electronic health records, according to a March 8, 2017 article in Becker’s Hospital Review.

After other setbacks, the Watson health care division underwent a large round of layoffs in June of 2018. In spite of the challenges, it is worth noting that MD Anderson has not completely abandoned AI efforts and is considering new partners. Other hospital systems such as Cleveland Clinic and Memorial Sloan Kettering have continued to invest in Watson.

AI expansion in health care raises other concerns, including the gradual replacement of human jobs and issues with data security and HIPAA compliance. AI expansion in health care raises other concerns, including the gradual replacement of human jobs and issues with data security and HIPAA compliance. AI also presents new trust and liability issues; ie, who is responsible when things go wrong? In other endeavors, such as automated driving vehicles, which have led to fatalities, developers and legal experts are already being forced to confront this scenario.

The potential benefits of AI likely mean that it is here to stay, however. With increasing pressure to reduce health care costs nationally, the promise of cost and efficiency savings with AI-assisted health care will likely continue to drive investment. There is increasing peer-reviewed data demonstrating AI’s ability to factor in hundreds or thousands of data points quickly, well beyond human abilities. Analysis of large volumes of difficult to integrate data streams is likely exactly what is needed for individualized medicine to move forward.

Lastly, there is a hope that AI may improve providers’ satisfaction and quality of life by automating some tasks, allowing physicians to spend more time with patients.

Moving forward
The future of AI in health care is bright and we should expect to see continued investment in the technology, leading to more peer-reviewed studies and eventually more commercially available applications. AI could make urologists’ lives easier by improving diagnosis, individualizing medicine, expanding telemedicine, automating tasks, augmenting surgical training, and extending our reach in an era of increasing workforce shortages.
Testis Ca screening: Why USPSTF ‘D’ grade is misguided

No evidence currently exists to suggest screening is either harmful or beneficial

The U.S. Preventive Services Task Force (USPSTF) recommendations are based on a rigorous review of existing peer-reviewed evidence and are intended to help primary care clinicians and patients decide together whether a preventive service is right for a patient’s needs. Each year, the USPSTF makes a report to Congress that identifies critical evidence gaps in research related to clinical preventive services and recommends priority areas that deserve further examination.

Recommendations made by the USPSTF are independent of the U.S. government and should not be construed as an official position of any government body. However, in 2010, the Patient Protection and Affordable Care Act (ACA) created a link between USPSTF recommendations and various coverage requirements. Duly, some advocacy groups and others have frequently misinterpreted the ACA linkage as licensing the Task Force to explicitly recommend for or against coverage. Needless to say, the increasing influence of USPSTF recommendations in our health care system is clear and obvious.

Regarding testicular cancer screening, the USPSTF currently suggests that there is a lack of available evidence demonstrating that routine testicular cancer (TCa) screening (including both testicular self-examination [TSE] and clinician examination) has greater yield and/or accuracy for detecting TCa at more curable stages than chance discovery (Ann Intern Med 2011; 154:483–6). The Task Force also claims that, generally, TCa is >90% curable and that TCa screening is unlikely to offer meaningful health benefits.

One adverse outcome readily offered as evidence that TCa screening should not be recommended is the potential onset of anxiety associated with a false-positive result. Essentially, according to the USPSTF, among others (eg, Lin and Sharangpani, Ann Intern Med 2010; 153:396–9), TSE and clinician examinations have limited value; thus the reason for a “D” recommendation.

There are no RCTs to assess testicular cancer screening benefits or harms to make a conclusive recommendation.

In 1996, the Task Force indicated that it found little evidence to suggest a recommendation for or against routine screening of the testes for cancer as the evidence base was insufficient. TCa screening was granted a “C” recommendation, essentially stating that the Task Force doesn’t know if TCa screening is beneficial or detrimental. Fair enough. Interestingly, the Task Force included some language suggesting that those males deemed “high risk” could possibly be consulted about performing routine screening for the disease to reduce the risk of late-stage discovery.

When it comes to empirical evidence, the Task Force aims to analyze randomized controlled trials (RCTs) for forming the foundation of its recommendations. Pertainingly specific to TCa screening, two glaring issues come about regarding this standard:

First, it’s nearly impossible to conduct a TCa screening RCT that is methodologically rigorous enough to produce the kind of evidence necessary to make a conclusive decision on TCa screening effectiveness. Second, there are no RCTs currently that assess TCa screening, which is mostly due to the previous point as well as a dearth of available funds to conduct such work.

Nevertheless, in 2004, the Task Force reevaluated its “C” recommendation for TCa screening and came to the conclusion that there was “fair” evidence that TCa screening harms outweigh the benefits. One of the main arguments for this change from a “C” to a “D” recommendation (ie, unsupportive of the behavior) was that no studies were produced that demonstrated a reduced mortality of TCa from routine screening. What is also evident is that no evidence emerged demonstrating harms of TCa screening either. It was a wash, just like in 1996.

However, instead of upholding the “C” recommendation, the recommendation was switched to a “D.” Even though the USPSTF changed the rules for what constitutes a “C” recommendation in which it recommends that the select service should be offered to select individuals due to their particular risk of the disease in question, the evidence still doesn’t support the switch from a “C” to a “D.”

In fact, that new definition further supports the Task Force’s previous stance in which TCa screening should be discussed with high-risk individuals. This position is also currently shared by the AUA, 2014 (“Men’s Health Checklist”); Society for Adolescent Health and Medicine, 2012 (“A Adolesc Health” 2012; 50:424-5); and American Cancer Society, 2015 (“Signs and Symptoms of Testicular Cancer” (table). If anything, the recommendation should be an “I,” whereby there is no conclusive evidence demonstrating harm or benefit for an informed decision to be made regarding TCa screening. It certainly should not be a “D” according to the Task Force’s own methodology and operational definitions of the recommendation system.

In 2008, the Task Force called for a new review of TCa screening. In 2010, Lin and Sharangpani responded to the
**TCA SCREENING**  
continued from page 29

call and rubber-stamped the Task Force’s “D” recommendation (Ann Intern Med 2010; 153:396-9). However, the authors were hardly unique in their conclusions; that is, there is no new evidence showcasing benefits nor harms from TCA screening.

The USPSTF ‘D’ recommendation is not grounded in empirical evidence.

The problem with Lin and Sharangpani’s piece, and, in fact, the entirety of the Task Force’s “D” recommendation, can be reduced to two primary points:

First, there are no RCTs to assess TCA screening benefits or harms to make a conclusive recommendation. The evidence used in determining such recommendations simply doesn’t exist. However, the Task Force does recognize the difficulty in producing RCTs for most topics and does accept non-RCT designs to inform the recommendation process. Even with this more liberal standard of evidence, in the case of TCA screening, no studies match up to the needed designs testing asymptomatic males. Again, the evidence doesn’t exist.

Second, the Task Force indicates that “fair” evidence exists suggesting the harms of screening outweigh the benefits. Fair evidence is generally defined by the Task Force when existing evidence is sufficient enough to determine the effect upon health outcomes. However, the Task Force fails to define what “sufficient” means. It is left to the discretion of the reviewer, which is probably a primary causal factor to the current issue. What sufficient means for one person may mean something different to another person. But this relates back to the first point, which is that there is no evidence. How can evidence be fair and/or sufficient if it doesn’t exist?

The USPSTF “D” recommendation is not grounded in empirical evidence. Simply, according to the Task Force’s methodology, the evidence does not exist to recommend anything. The recommendation, therefore, should be an “I.” We would advocate for the recommendation to be changed back to a “C,” but to be fair, there is no smoking gun evidence to suggest that TCA screening is beneficial either.

There are studies currently underway that are trying to build a body of evidence demonstrating TCA screening’s benefit. Further, there is an emerging body of evidence suggesting TCA screening is beneficial beyond detecting cancer and may also be helpful in detecting hydroceles, varicoceles, possible hernias, and any type of scrotal skin issue including some sexually transmitted infections, among other concerns (Am J Mens Health 2015; 9:506-18). Not only can males detect these issues, but they can become more familiar with their bodies, which is an all-around positive outcome to achieve.

**Conclusion**

We suggest the following actions in order to assuage this issue:

- Encourage the Task Force to reopen its review of TCA screening.
- Encourage more funding opportunities to produce the kind of evidence needed to make a recommendation.
- In lieu of a new review, the current “D” recommendation should be changed to an “I” (insufficient evidence) recommendation, as there is no evidence to suggest either way TCA screening is harmful or beneficial.
- The Task Force review board should consist of content-specific experts to inform the decision-making process regarding the recommendation for TCA screening. Is it a truly informed decision if not one content expert is sitting on the review panel?

As a reference, a critique of this entire review process is provided for by Rovito et al (Prev Med Rep 2016; 3:361-6).

**TABLE. LEADING GROUPS’ POSITIONS ON TESTIS CANCER SCREENING**

<table>
<thead>
<tr>
<th>Professional group</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. Preventive Services Task Force</td>
<td>• Do not screen (“D” grade)</td>
</tr>
<tr>
<td></td>
<td>• Inadequate evidence that screening has higher yield or greater accuracy for detecting testicular cancer at earlier (and more curable) stages</td>
</tr>
<tr>
<td></td>
<td>• Adequate evidence that benefits of screening are small to none</td>
</tr>
<tr>
<td></td>
<td>• Potential harms of screening include false-positive results, anxiety, and harms from diagnostic tests or procedures</td>
</tr>
<tr>
<td>American Urological Association</td>
<td>• Testicular self-exam recommended in men aged 18+ years (level of evidence insufficient/poor [USPSTF] but may be indicated with symptoms and/or higher risk cases)</td>
</tr>
<tr>
<td>Society for Adolescent Health and Medicine</td>
<td>• Complete examination of male genitals should be performed annually as part of a comprehensive physical exam</td>
</tr>
<tr>
<td></td>
<td>• Complete genital exam should be performed as part of diagnostic assessment when a male presents with genitalic symptoms</td>
</tr>
<tr>
<td></td>
<td>• Clinicians should use the male genital exam as an opportunity to promote young men’s sexual/reproductive health (SRH) and educate about male anatomy, function, and SRH matters</td>
</tr>
<tr>
<td>American Cancer Society</td>
<td>• Men should be aware of testicular cancer and be advised to see a doctor if they find a lump in a testicle</td>
</tr>
<tr>
<td></td>
<td>• Men with certain risk factors for developing testicular cancer should consider monthly self-exams and talk about it with their doctor</td>
</tr>
<tr>
<td></td>
<td>• No recommendation on regular testicular self-exams for all men because self-exams have not been studied enough to know if they reduce deaths from this cancer</td>
</tr>
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**Tx FOR TUMORS WITH NTRK GENE FUSION APPROVED**

The FDA has granted accelerated approval to larotrectinib (VITRAKVI) for adult and pediatric patients with solid tumors that have a neurotrophic receptor tyrosine kinase gene fusion without a known acquired resistance mutation, that are either metastatic or where surgical resection is likely to result in severe morbidity, and who have no satisfactory alternative treatments or whose cancer has progressed following treatment.

This is the second tissue-agnostic FDA approval for the treatment of cancer. Approval was based on data from three multicenter, open-label, single-arm clinical trials: LOXO-TRK-14001 (NCT02122913), SCOUT (NCT02637687), and NAVIGATE (NCT02576431).
The Medicare Physician Fee Schedule final rule is out. Medicare has not adopted all of the proposed changes for 2019 that were discussed in our August column ("Medicare proposed rule outlines significant changes," page 26). However, the final rule does include a timeline that will implement many of the changes recommended by 2021 with some revisions. Below, we will address a few of the most notable inclusions in the final rule for 2019 and touch on preparation that will need to be undertaken for 2021. (To view the rule in its entirety, go to bit.ly/2019finalrule.)

Evaluation/management

The Centers for Medicare & Medicaid Services (CMS) has delayed the proposed major changes to E/M documentation and payment until 2021, which we will discuss later in this article. Here, we will focus on relevant CMS changes for E/M coding for 2019 and 2020.

First, CMS has removed the requirement that justification of a home visit in lieu of an office-based visit is documented in the medical record.

### CMS has removed the requirement that justification of a home visit in lieu of an office-based visit is documented in the medical record.

Justification of a home visit in lieu of an office-based visit is documented in the medical record. Second, CMS has finalized a policy to simplify history and exam for established patients. For 2019 and 2020, 1995 and 1997 guidelines remain as the framework for documentation of all E/M visits. The changes pertain to how these requirements are met.

It appears that although CMS lists exam as part of the simplification as a general rule for the established patient, this simplification seems to indicate that the provider will not have to reenter any exam entered by staff, and document that the information was reviewed for the visit.

The requirements remain as listed in the 1995 and 1997 guidelines. With regard to documentation of history, we note the following from the final rule:

- “We proposed to expand this policy to further simplify the documentation of history and exam for established patients such that, for both of these key components, when relevant information is already contained in the medical record, practitioners may choose to focus their documentation on what has changed since the last visit, or on pertinent items that have not changed, and need not record the defined list of required elements if there is evidence that the practitioner reviewed the previous information and updated it as needed. Practitioners should still review prior data, update as necessary, and indicate in the medical record that they have done so.”
- “For new and established patients for E/M office/outpatient visits, practitioners need not re-enter in the medical record information on the patient’s chief complaint and history that has already been entered by ancillary staff or the beneficiary. The practitioner may simply indicate in the medical record that he or she reviewed and verified this information.”
- “We note that this policy to simplify and reduce redundancy in documentation is optional for practitioners, and they may choose to continue the current process of entering, re-entering and bringing forward information.”

In summary, the changes to outpatient E/M documentation in the office for 2019 and 2020 are:

- History of Present Illness (HPI) can be documented by patient or staff and reviewed by provider. Specifically stating that physicians do not have to personally document the HPI will be very beneficial. There has been some confusion on this issue, with some compliance departments requiring that the billing provider must document the entire HPI, while others suggested that staff could collect HPI but the provider must finalize and “own” the HPI.
- Review of Systems (ROS) and Past Family and Social History (PFSH) have previously been documented in the chart can be reviewed and updated without re-documenting all elements.
- Reviewing and updating previously collected ROS and PFSH has been allowed with the 1995 and ’97 guidelines.
- However, of interest is that they did not mention having to document the date of the previous documentation, as required in the previous guidelines. This will simplify the documentation process.
- Physical exam that has been documented in the medical record can be reviewed by the physician.

The ability of the physician to review PE for established patient information will be limited for urologists as PE is rarely a limiting factor for established patients. Remember: Only two
out of three key components are required for established patient visits.

We note that CMS reiterated that focus on new or relevant existing information that is medically relevant should be confirmed or further documented by the physician.

In short, the focus of the reviews under these revised rules will continue to be on medical necessity of the information documented and the services rendered for each visit. As we have taught in the past, medical necessity must be the driver of appropriate E/M level selection and appropriate documentation protocols. Simple copy and paste without review and documentation of a medically appropriate update will likely remain a target of any chart reviews.

**Telemedicine codes**

**Virtual check-in code.** CMS is adding a new code and coverage for a virtual check-in. This service would be billable when a physician or other qualified health care professional has a brief nonface-to-face check-in with a patient via communication technology, to assess whether the patient’s condition necessitates an office visit. Unlike other services Medicare pays for under telehealth rules, the virtual check-in visit can be provided via phone only or via audio and visual technology.

G2012 (Brief communication technology-based service, e.g. virtual check-in, by a physician or other qualified health care professional who can report evaluation and management services, provided to an established patient, not originating from a related E/M service provided within the previous 7 days nor leading to an E/M service or procedure within the next 24 hours or soonest available appointment; 5-10 minutes of medical discussion) can only be reported if the service is provided by a physician or advanced practice provider.

As noted in the description, this service can only be provided to established patients. Medicare has elected not to include any frequency limitations at this time, but as with all Medicare services, the virtual check-in visit must be medically necessary. As the description indicates, if the virtual check-in visit is within 7 days of an E/M visit or the virtual check-in leads to an E/M visit in the near future, the virtual check-in visit will be considered bundled into the E/M visit before or after the virtual check-in visit.

Finally, as the patient will be responsible for co-payment with the visit, the patient must consent to the service. Consent can be verbal or written. We recommend that written forms be obtained from the patient when in the office and included in the medical record. This form could be a blanket form that informs patients that the check-in service is available and covered but will have an associated co-payment. However, Medicare is expecting that the patient will initiate the majority of these visits and in lieu of a signed consent for a virtual visit, inclusion of the verbal approval in the patient record as proof of verbal agreement will be acceptable.

**As we have taught in the past, medical necessity must be the driver of appropriate E/M level selection and appropriate documentation protocols.**

We can see a number of applications for this code in urology. CMS is seeking comment on appropriate parameters to prevent overuse and abuse of this service and will be closely monitoring the utilization of this code.

**Remote evaluation of video or images from patient.** Medicare has added code G2010 (Remote evaluation of recorded video and/or images submitted by an established patient [e.g., store and forward], including interpretation with follow-up with the patient within 24 business hours, not originating from a related E/M service provided within the previous 7 days nor leading to an E/M service or procedure within the next 24 hours or soonest available appointment).

Similar to the virtual check-in code above, the service is limited to established patients and cannot be preceded by an E/M visit in the last 7 days or lead to an E/M visit in the near future. Also, as with check-in visits, the service must be medically necessary and written or verbal consent must be documented as the patient will have partial responsibility for payment.

Medicare has expanded the response method for code G2010 to include not only telephone and audio-visual follow-up for received image and/or video but will also allow follow-up through HIPAA-compliant texting, email, and/or patient portal communication. Medicare will be carefully monitoring utilization of this new code.

**Global period data**

CMS will be reminding physicians in Florida, Kentucky, Louisiana, Nevada, New Jersey, North Dakota, Ohio, Oregon, and Rhode Island in practices with 10 or more physicians that they are to report post-operative visits for 209 different procedures. Urology has not participated very well in this program. Remember that failing to report post-op visits as requested may result in lower payments for these services in the long run.

**Impact of relative value unit changes on urology**

There were a number of changes to RVUs for 2019, both positive and negative. The impact of all the changes is projected to be favorable for urology, with a positive 4% impact on the overall income for urologists. We encourage you to review your fee schedules for 2019, as some of these changes may impact your contracted rates in addition to your Medicare fees.

Unfortunately, we do not have room in this article to list all changes. AUAcodingtoday.com and Medicare fee schedule look-up tools will be updated prior to Jan. 1, 2019 to allow offices to review and adjust fees and expected reimbursements.

**Looking ahead to 2021**

There were some significant modifications to the proposed rules and the adopted rules to be implemented in 2021. The most important change was the decision not to reduce payment when E/M office/outpatient visits are furnished on the same day as procedures. CMS left the door open for additional comments and changes to be adopted later.

The major changes for 2021 E/M codes are as follows:

- paying a single rate for E/M office/outpatient visit levels 2, 3, and 4 with a minimum documentation requirement meeting a level 2 visit
- E/M office/outpatient levels 1 and 5 visits will continue to have unique payment levels
- adoption of new add-on codes that describe the additional resources inherent in visits for primary care and particular kinds of specialized medical care (includes urology) for use with levels 2-4 only
- adoption of a new “extended-visit” add-on code for use only with E/M office/outpatient level 2 through 4 visits
- flexibility in how visit levels are documented, specifically a choice to use the current “level 2” framework (as discussed above), medical decision-making only, or time
- elimination of the requirement for counseling or coordinating care to charge based on time.

Stay tuned; 2021 is barely over 2 years away.
ANTI-PDL1 CANCER IMMUNOTHERAPY

Results for first-line, cisplatin-ineligible patients

<table>
<thead>
<tr>
<th></th>
<th>ORR</th>
<th>CR</th>
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<tbody>
<tr>
<td>6.7% CR</td>
<td>23.5%</td>
<td>0.9%</td>
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<tr>
<td>(n=28/199; 95% CI, 16.2, 32.2)</td>
<td>16.8%</td>
<td>0.3%</td>
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</table>

MEDIAN DOR NOT REACHED (range: 3.7, 16.6+)

TECENTRIQ delivered durable responses (median follow-up: 14.4 months)

- 33% ORR in patients with disease progression at least 12 months following neoadjuvant or adjuvant therapy (n=8/24*; 95% CI, 16, 55)

IMvigor210 was a pivotal Phase II, multicenter, open-label, 2-cohort trial that included a cohort of 119 patients with locally advanced or metastatic urothelial carcinoma who were ineligible for cisplatin-containing chemotherapy and were either previously untreated or had disease progression at least 12 months after neoadjuvant or adjuvant chemotherapy. Patients received TECENTRIQ 2000 mg IV q3w. Major efficacy endpoints included ORR assessed by IRF using RECIST V1.1 and DoR. Patients were considered cisplatin-ineligible if they met any one of the following criteria: impaired renal function (CrCl of 30 to 59 mL/min), ECOG PS of 2, hearing loss of ≥25 dB at 2 continuous frequencies, or grade 2-4 peripheral neuropathy. CI-confidence interval; CR-complete response; DoR-duration of response; ECOG-Eastern Cooperative Oncology Group; IRF-independent review facility; V1.1-intraobserver; V1.1+interobserver; V1.1+overall response rate; PDI-programmed death ligand-1 PR=partial response; PS=performance status; q3w=every 3 weeks; RECIST=Response Evaluation Criteria in Solid Tumors.

- *Number of RF assessed confirmed responders

**Important Safety Information**

**Indication**

TECENTRIQ is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:

- Are not eligible for cisplatin-containing chemotherapy, and whose tumors express PD-L1 (PD-L1-stained tumor-infiltrating immune cells ≥50% of the tumor area), as determined by an FDA-approved test, or
- Are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status, or
- Have disease progression during or following any platinum-containing chemotherapy, or within 12 months of neoadjuvant or adjuvant chemotherapy.

This indication is approved under accelerated approval based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

**Serious Adverse Reactions**

Please refer to the full Prescribing Information for important dose management information specific to adverse reactions.

**Immune-Mediated Pneumonitis**

- Immune-mediated pneumonitis or interstitial lung disease, including fatal cases, have occurred with TECENTRIQ treatment.
- Across clinical trials, 2.5% of patients developed pneumonitis, including Grade 3 (0.6%), Grade 4 (0.2%), and Grade 5 (0.0%) events.
- Monitor patients for signs and symptoms of pneumonitis. Evaluate patients with suspected pneumonitis with radiographic imaging. Administer corticosteroids followed by a taper. Withhold TECENTRIQ for Grade 2 and permanently discontinue for Grade 3 or 4 pneumonitis.

**Immune-Mediated Hepatitis**

- Liver test abnormalities and immune-mediated hepatitis, including fatal cases, have occurred with TECENTRIQ treatment.
- Across clinical trials, hepatitis occurred in 9% of patients, including Grade 3 (2.9%), Grade 4 (0.4%), and Grade 5 (0.0%) events.
- Monitor patients for signs and symptoms of hepatitis, during and after discontinuation of TECENTRIQ, including clinical chemistry monitoring. Administer corticosteroids followed by a taper for immune-mediated hepatitis. Withhold TECENTRIQ for AST or ALT elevations more than 3 and up to 8 times the upper limit of normal or total bilirubin more than 15 and up to 3 times the upper limit of normal. Permanently discontinue TECENTRIQ for AST or ALT elevations more than 8 times the upper limit of normal or total bilirubin more than 3 times the upper limit of normal.

**Immune-Mediated Colitis**

- Immune-mediated colitis or diarrhea have occurred in 20% of patients, including Grade 3 (0.4%) events.
- Across clinical trials, diarrhea or colitis occurred in 20% of patients, including Grade 3 (0.4%) events.
- Monitor patients for signs and symptoms of diarrhea or colitis. Withhold TECENTRIQ for Grade 2 and permanently discontinue for Grade 4 diarrhea or colitis.

**Immune-Mediated Endocrinopathies**

- TECENTRIQ can cause immune-mediated endocrinopathies, including thyroid disorders, adrenal insufficiency, and type 1 diabetes mellitus, including diabetic ketoacidosis, and hypophysitis/hypopituitarism.
- Withhold TECENTRIQ for Grade 2 to 4 endocrinopathies.
- Thyroid Disorders:
  - Across clinical studies, hypothyroidism occurred in 4.6% of patients and hyperthyroidism occurred in 1.6% of patients.
  - Monitor thyroid function prior to and during treatment with TECENTRIQ. Initiate hormone replacement therapy or medical management of hyperthyroidism as clinically indicated.
- Adrenal Insufficiency:
  - Across clinical studies, adrenal insufficiency occurred in 0.4% of patients, including Grade 3 (0.0%) events.
  - Monitor patients for clinical signs and symptoms of adrenal insufficiency. For Grade 2 to 4 adrenal insufficiency, initiate corticosteroids and hormone replacement therapy as clinically indicated.
- Type 1 Diabetes Mellitus:
  - Across clinical studies, type 1 diabetes mellitus occurred in <0.1% of patients.
  - Monitor patients for hyperglycemia or other signs and symptoms of diabetes. Initiate treatment with insulin as clinically indicated.

**Other Immune-Mediated Adverse Reactions**

- TECENTRIQ can cause immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system.
- Across clinical trials, cardiac, dermatologic, gastrointestinal, general, hematomalous, musculoskeletal, neurological, ophthalmological, renal, and vascular immune-mediated adverse reactions occurred at an incidence of <1% in patients who received TECENTRIQ or were reported for other products in this class of therapy.
- For suspected Grade 2 immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated. For severe (Grade 3 or 4) immune-mediated adverse reactions, withhold TECENTRIQ and administer corticosteroids. Permanently discontinue TECENTRIQ for Grade 4 immune-mediated adverse reactions involving a major organ.

**Infections**

- TECENTRIQ can cause severe infections including fatal cases.
- Across clinical trials, infections occurred in 42% of patients, including Grade 3 (8.7%), Grade 4 (5.9%), and Grade 5 (0.0%) events.
- Monitor patients for signs and symptoms of infection. For Grade 3 or 4 infections, withhold TECENTRIQ and resume oncology therapy.

**Infusion-Related Reactions**

- TECENTRIQ can cause severe or life-threatening infusion-related reactions.
- Across clinical trials, infusion-related reactions occurred in 13.9% of patients, including Grade 3 (1.0%) events.
- Monitor for signs and symptoms of infusion-related reactions. Interrupt or slow the rate of infusion in patients with Grade 3 or 2 infusion-related reactions. Permanently discontinue TECENTRIQ in patients with Grade 3 or 4 infusion-related reactions.

**Embryo-Fetal Toxicity**

- Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a pregnant woman. Verify pregnancy status of females of reproductive potential prior to initiating TECENTRIQ. Advise females of reproductive potential to use effective contraception during treatment with TECENTRIQ and for at least 5 months after the last dose.

**Nursing Mothers/Fertility**

- Because of the potential for serious adverse reactions in breastfed infants from TECENTRIQ, advise female patients not to breastfeed while taking TECENTRIQ and for at least 5 months after the last dose.

- Based on animal studies, TECENTRIQ may impair fertility in females of reproductive potential.

**Most Common Adverse Reactions**

The most common adverse reactions in cisplatin-ineligible UC (rate ≥20%) were fatigue (52%), decreased appetite (24%), diarrhea (24%), and nausea (22%). The most common adverse reactions in previously treated UC (rate ≥20%) were fatigue (52%), decreased appetite (26%), nausea (25%), urinary tract infection (22%), pyrexia (21%), and constipation (21%). You may report side effects to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at 1-888-635-2555.

- Please see Brief Summary of Prescribing Information on adjacent pages.

TECENTRIQ® [atezolizumab]

Initial U.S. Approval: 2016

This is a brief summary of information about TECENTRIQ. Before prescribing, please see full Prescribing Information.

1 INDICATIONS AND USAGE

1.1 Locally Advanced or Metastatic Urothelial Carcinoma

TECENTRIQ is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who:

• are not eligible for any platinum-containing chemotherapy regardless of PD-L1 status, or

• are not eligible for cisplatin-containing chemotherapy, and whose tumors express PD-L1 (PD-L1 ≥ 1% of tumor area).

For suspected Grade 2 immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated. For severe (Grade 3 or 4) adverse reactions, administer corticosteroids, prednisone 1 to 2 mg/kg/day or equivalents, followed by a taper. Interrupt or permanently discontinue TECENTRIQ based on the severity of the reaction (see Dosage and Administration (2.3) and Adverse Reactions (6.1)).

In patients with locally advanced or metastatic urothelial carcinoma who were previously treated with platinum-containing chemotherapy, TECENTRIQ was administered at a dose of 1200 mg intravenously every 3 weeks until unacceptable toxicity or disease progression.

Cisplatin-Ineligible Patients with Locally Advanced or Metastatic Urothelial Carcinoma

In a single arm study (PCD4989g) which enrolled 524 patients with metastatic urothelial carcinoma, TECENTRIQ was administered at a dose of 1200 mg intravenously every 3 weeks until unacceptable toxicity or disease progression of at least 12 months after neoadjuvant or adjuvant chemotherapy (see Clinical Studies (14.3)).

5.5 Other Immune-Mediated Adverse Reactions

TECENTRIQ can cause severe and fatal immune-mediated adverse reactions. These immune-mediated reactions may involve any organ system. While immune-mediated reactions usually manifest during treatment with TECENTRIQ, immune-mediated adverse reactions can also manifest after discontinuation of TECENTRIQ.

For suspected Grade 2 immune-mediated adverse reactions, exclude other causes and initiate corticosteroids as clinically indicated. For severe (Grade 3 or 4) adverse reactions, administer corticosteroids, prednisone 1 to 2 mg/kg/day or equivalents, followed by a taper. Interrupt or permanently discontinue TECENTRIQ based on the severity of the reaction (see Dosage and Administration (2.3) and Adverse Reactions (6.1)).

In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ, Grade 2 immune-mediated adverse reactions occurred in 17% of patients, including Grade 2 (0.7%) infections, 1.1% (0.2%) hypophysitis, and 1.0% (0.03%) hemorrhagic cysts.

In clinical studies enrolling 2616 patients who received TECENTRIQ, Grade 2 hypophysitis occurred in 0.7% of patients.

5.6 Infections

TECENTRIQ can cause severe infections including fatal infections. Monitor for signs and symptoms of infection. For Grade 3 or higher infections, TECENTRIQ should be discontinued. See Warnings and Precautions (5.6) and Adverse Reactions (6.1). In clinical studies enrolling 2616 patients who received TECENTRIQ, infections occurred in 42% of patients, including Grade 3 (9.8%), Grade 4 (1.5%), and Grade 5 (1%). In patients with urothelial carcinoma, the most common Grade 3 or higher infection was urinary tract infections, occurring in 6.5% of patients. In NSCLC, the most common Grade 3 or higher infection was pneumonia, occurring in 0.8% of patients.

5.7 Infusion-Related Reactions

TECENTRIQ can cause severe or life-threatening infusion-related reactions. Monitor for signs and symptoms of infusion-related reactions. Interrupt, slow the rate of, or permanently discontinue TECENTRIQ based on the severity (see Dosage and Administration (2.3) and Adverse Reactions (6.1)). For Grade 2 or 3 infusion-related reactions, consider using pre-medications with subsequent doses. In clinical studies enrolling 2616 patients with various cancers who received TECENTRIQ (see Clinical Trials Experience (6.7)), infusion-related reactions occurred in 1% of patients, including Grade 3 (0.2%).

5.8 Embryo-Fetal Toxicity

Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a pregnant woman. There are no available data on the use of TECENTRIQ in pregnant women. Animal studies have demonstrated that inhibition of the PD-L1/PD-1 pathway can lead to increased risk of immune-mediated fetal loss resulting in fetal death. Verify pregnancy status of females of reproductive potential prior to initiating TECENTRIQ. Advise females of reproductive potential to use effective contraception during treatment with TECENTRIQ and for at least 5 months after the last dose (see Use in Specific Populations (8.1, 8.3)).

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the label:

• Immune-Mediated Pneumonitis (see Warnings and Precautions (5.5))

• Immune-Mediated Hepatitis (see Warnings and Precautions (5.5))

• Immune-Mediated Colitis (see Warnings and Precautions (5.5))

• Immune-Mediated Endocrinopathies (see Warnings and Precautions (5.5))

• Other Immune-Mediated Adverse Reactions (see Warnings and Precautions (5.5))

• Infections (see Warnings and Precautions (5.5))

• Infusion-Related Reactions (see Warnings and Precautions (5.5))

6.1 Clinical Trials Experience

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

The data described in the Warnings and Precautions section reflect exposure to TECENTRIQ in patients in two randomized, active-controlled phase III studies (PCD4989g and PCD4989h) and one open-label single arm studies (PCD4989j, MG02015, BIRCH, FRH) which enrolled 524 patients with metastatic urothelial carcinoma, 1636 patients with metastatic non-small cell lung cancer (NSCLC), and 609 patients with metastatic NSCLC. TECENTRIQ was administered at a dose of 1200 mg intravenously every 3 weeks in all studies except PCD4989j. Among the 2616 patients, 36% were exposed for longer than 6 months and 10% were exposed for longer than 12 months.

The data described in this section were obtained from one open-label, single arm, multicohort study (MG02015) and one randomized open-label, active-controlled study (BIRCH) in which TECENTRIQ was administered to 429 patients with locally advanced and metastatic urothelial carcinoma and 609 patients with metastatic NSCLC. In these trials, TECENTRIQ was administered at a dose of 1200 mg intravenously every 3 weeks.

Cisplatin-Ineligible Patients with Locally Advanced or Metastatic Urothelial Carcinoma

The safety of TECENTRIQ was evaluated in 250 (21%) Cohort 1, a multicenter, open-label, single-arm trial that included 119 patients with locally advanced or metastatic urothelial carcinoma who were ineligible for cisplatin-containing chemotherapy. Neoadjuvant chemotherapy, defined as chemotherapy administered to 429 patients with locally advanced and metastatic urothelial carcinoma and 609 patients with metastatic NSCLC. In these trials, TECENTRIQ was administered at a dose of 1200 mg intravenously every 3 weeks.
The safety of TECENTRIQ was evaluated in IMvigor210 (Cohort 1), a multicenter, open-label, single-arm trial that included 310 patients with locally advanced or metastatic urothelial carcinoma who had disease progression during or following at least one platinum-containing chemotherapy regimen or who had disease progression within 12 months of treatment with a platinum-containing neoadjuvant or adjuvant chemotherapy regimen (see Clinical Studies (14.2)). Patients received TECENTRIQ 1200 mg intravenously every 3 weeks until unacceptable toxicity, radiographic progression, or clinical progression or docetaxel (n=578) 75 mg/m² intravenously every 3 weeks until unacceptable toxicity or disease progression. The study excluded patients with active or prior autoimmune disease or with medical conditions that required systemic corticosteroids. The study population characteristics were: median age of 63 years (50 to 85 years), 46% age 65 years or older, 62% male, 71% White, 20% Asian, 68% former smoker, 16% current smoker, and 63% had ECOG performance status of 1. The median duration of exposure was 12.3 weeks (8.1 to 48 weeks).

The most common adverse reactions (≥20%) in patients receiving TECENTRIQ were fatigue (43.5%), decreased appetite (26.2%), dyspnea (23.5%), dyspnea (22%), and cough (26.4%). The most common Grade 3−4 adverse reactions were urinary tract infection, urinary tract infection, bacterial, cystitis, and uresepsis.

Table 2 summarizes the adverse reactions that occurred in ≥10% of patients with urothelial carcinoma in IMvigor210 (Cohort 1).

Table 3: Grade 3–4 Laboratory Abnormalities in ≥1% of Patients with Urothelial Carcinoma in IMvigor210 (Cohort 1)

Table 4: Adverse Reactions in ≥10% of Patients with Urothelial Carcinoma in IMvigor210 (Cohort 2)

Table 5: Grade 3–4 Laboratory Abnormalities in ≥1% of Patients with Urothelial Carcinoma in IMvigor210 (Cohort 2)

Table 6: summarizes adverse reactions that occurred in at least 10% of patients treated with TECENTRIQ.
Table 6: Adverse Reactions Occurring in ≥ 10% of Patients with NSCLC Receiving TECENTRIQ in OAK

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>TECENTRIQ (1200 mg every 3 weeks)</th>
<th>Docetaxel (75 mg/m² every 3 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades (%)</td>
<td>Grade 3–4 (%)</td>
</tr>
<tr>
<td>General</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatigue/Anorexia</td>
<td>44</td>
<td>4</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>18 (&lt;1)</td>
<td>13 (&lt;1)</td>
</tr>
<tr>
<td>Respiratory</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>26 (&lt;1)</td>
<td>21 (&lt;1)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>22</td>
<td>2.8</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>20 (&lt;1)</td>
<td>1.3</td>
</tr>
<tr>
<td>Arthritis</td>
<td>12</td>
<td>0.5</td>
</tr>
<tr>
<td>Metabolism and Nutrition</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>23 (&lt;1)</td>
<td>24</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>18 (&lt;1)</td>
<td>23 (&lt;1)</td>
</tr>
<tr>
<td>Constipation</td>
<td>18</td>
<td>11 &lt;1</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>16 (&lt;1)</td>
<td>14 &lt;1</td>
</tr>
<tr>
<td>Skin</td>
<td>12</td>
<td>17 &lt;1</td>
</tr>
<tr>
<td>Rash</td>
<td>1 (Graded p NCI CTCAE v4.0)</td>
<td>1 (&lt;1)</td>
</tr>
</tbody>
</table>

1. Graded per NCI CTCAE v4.0

1. Includes fatigue and asthenia
2. Includes cough and exertional cough
3. Includes musculoskeletal pain, musculoskeletal stiffness, musculoskeletal chest pain, myalgia
4. Includes rash, erythematous rash, generalized rash, maculopapular rash, papular rash, papular rash, pemphigoid

Table 7: Laboratory Abnormalities Worsening From Baseline Occurring in ≥ 20% of NSCLC Patients Receiving TECENTRIQ in OAK

<table>
<thead>
<tr>
<th>Laboratory Abnormality</th>
<th>TECENTRIQ (1200 mg every 3 weeks)</th>
<th>Docetaxel (75 mg/m² every 3 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All Grades (%)</td>
<td>Grade 3–4 (%)</td>
</tr>
<tr>
<td>Chemistry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypoalbuminemia</td>
<td>48</td>
<td>4</td>
</tr>
<tr>
<td>Hypoatremia</td>
<td>42</td>
<td>7</td>
</tr>
<tr>
<td>Increased Alkaline Phosphatase</td>
<td>39</td>
<td>2</td>
</tr>
<tr>
<td>Increased AST</td>
<td>31</td>
<td>3</td>
</tr>
<tr>
<td>Increased ALT</td>
<td>27</td>
<td>3</td>
</tr>
<tr>
<td>Hypophosphatemia</td>
<td>27</td>
<td>5</td>
</tr>
<tr>
<td>Hypogammaglobulin</td>
<td>26</td>
<td>1</td>
</tr>
<tr>
<td>Increased Creatinine</td>
<td>23</td>
<td>2</td>
</tr>
<tr>
<td>Hematology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anemia</td>
<td>67 (&lt;1)</td>
<td>3</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>49</td>
<td>14</td>
</tr>
</tbody>
</table>

1. Graded according to NCI CTCAE version 4.0
2. Each test incidence is based on the number of patients who had both baseline and at least one on-study laboratory measurement available: TECENTRIQ (range: 546–865); Docetaxel (range: 532–560)

6.2 Immunogenicity

As with all therapeutic proteins, there is a potential for immunogenicity. Among 855 patients with NSCLC in OAK, 30% tested positive for treatment-emergent anti-drug antibodies (ADA) at one or more post-dose time points. The median onset time to ADA formation was 3 weeks. The ability of these binding ADA to neutralize atezolizumab is unknown. Patients who tested positive for treatment-emergent ADA also had decreased systemic atezolizumab exposure (see Clinical Pharmacology [12.2]). Exploratory analyses showed that the subset of patients who were ADA positive by week 4 (21%, 119/560) appeared to have less efficacy (effect on overall survival) as compared to patients who tested negative for treatment-emergent ADA by week 4 (see Clinical Studies [12.2]). The presence of ADA did not have a clinically significant effect on the incidence or severity of adverse reactions.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concurrent medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to atezolizumab in the studies described above with the incidence of antibodies in other studies or to other products may be misleading.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on its mechanism of action (see Clinical Pharmacology [12.1]), TECENTRIQ can cause fetal harm when administered to a pregnant woman. There are no available data on the use of TECENTRIQ in pregnant women.

Animal studies have demonstrated that inhibition of the PD-L1/PD-1 pathway can lead to increased risk of immune-related rejection of the developing fetus resulting in fetal death (see Data). Advise females of reproductive potential of the potential risk to a fetus.

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal reproduction studies have not been conducted with TECENTRIQ to evaluate its effect on reproduction and fetal development. A literature-based assessment of the effects on reproduction demonstrated that a central function of the PD-L1/PD-1 pathway is to preserve pregnancy by maintaining maternal immune tolerance to a fetus. Blockade of PD-L1 signaling has been shown in murine models of pregnancy to disrupt tolerance to a fetus and to result in an increase in fetal loss; therefore, potential risks of administering TECENTRIQ during pregnancy include increased rates of abortion or stillbirth. As reported in the literature, there were no malformations related to the blockade of PD-L1/PD-1 signaling in the offspring of these animals; however, immune-mediated disorders occurred in PDL1 knockout mice. Based on these findings, potential risks of administering TECENTRIQ during pregnancy include increased risk of developing immune-mediated disorders or altering the normal immune response.

8.2 Lactation

Risk Summary

There is no information regarding the presence of atezolizumab in human milk, the effects on the breastfed infant, or the effects on milk production. As human IgG is excreted in human milk, the potential for absorption and harm to the infant is unknown. Because of the potential for serious adverse reactions in breastfed infants from TECENTRIQ, advise women not to breastfeed during treatment and for at least 5 months after the last dose.

8.3 Females and Males of Reproductive Potential

8.3.1 Pregnancy Testing

Verify pregnancy status in females of reproductive potential prior to initiating TECENTRIQ (see Use in Specific Populations [8.1]).

Contraception

Females

Based on its mechanism of action, TECENTRIQ can cause fetal harm when administered to a pregnant woman. (see Use in Specific Populations [8.1]). Advise females of reproductive potential to use effective contraception during treatment with TECENTRIQ and for at least 5 months following the last dose.

Infectivity

Females

Based on animal studies, TECENTRIQ may impair fertility in females of reproductive potential while receiving treatment (see Nonclinical Toxicology [13.1]).

8.4 Pediatric Use

The safety and effectiveness of TECENTRIQ have not been established in pediatric patients.

8.5 Geriatric Use

Of the 609 patients with NSCLC treated with TECENTRIQ in OAK, 45% were 65 years or older. No overall differences in safety or efficacy were observed between patients ≥ 65 years of age and younger patients.

Of the 310 previously-treated patients with urothelial carcinoma treated with TECENTRIQ in IMvigor210 (Cohort 2), 59% were 65 years or older. Of the 119 cisplatin-ineligible patients with urothelial carcinoma treated with TECENTRIQ in IMvigor210 (Cohort 1), 63% were 65 years or older and 41% were 75 years or older. The overall response rate in patients 65 years or older was 23%, while in patients 75 years or older was 29%. Grade 3 or 4 adverse reactions occurred in 53% of patients 65 years or older and 51% of patients 75 years or older. No overall differences in safety or efficacy were observed between patients ≥ 75 years of age and younger patients.

8.6 OVERDOSE

There is no information on overdose with TECENTRIQ.

17 PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Medication Guide). Immune-mediated adverse reactions

Inform patients of the risk of immune-mediated adverse reactions that may require corticosteroid treatment or interruption or discontinuation of TECENTRIQ, including:

- Pneumonitis: Advise patients to contact their healthcare provider immediately for any new or worsening cough, chest pain, or shortness of breath (see Warnings and Precautions [5.2]).
- Hepatitis: Advise patients to contact their healthcare provider immediately for jaundice, severe nausea or vomiting, pain in the right side of abdomen, lethargy, or easy bruising or bleeding (see Warnings and Precautions [5.3]).
- Colitis: Advise patients to contact their healthcare provider immediately for diarrhea, blood or mucus in stools, or severe abdominal pain (see Warnings and Precautions [5.3]).
- Endocrinopathies: Advise patients to contact their healthcare provider immediately for signs or symptoms of hypophysitis, hyperthyroidism, hypothyroidism, adrenal insufficiency, or type 1 diabetes mellitus, including diabetic ketoacidosis (see Warnings and Precautions [5.4]).
- Other Immune-Mediated Adverse Reactions: Advise patients to contact their healthcare provider immediately for signs or symptoms of other potential immune-mediated adverse reactions (see Warnings and Precautions [5.5]).

Infections

Advise patients to contact their healthcare provider immediately for signs or symptoms of infection (see Warnings and Precautions [5.6]).

Infusion-Related Reactions

Advise patients to contact their healthcare provider immediately for signs or symptoms of infusion-related reactions (see Warnings and Precautions [5.7]).

Enteropancreatic Tachyphylaxis

Advise females of reproductive potential that TECENTRIQ can cause harm to a fetus and to inform their healthcare provider of a known or suspected pregnancy (see Warnings and Precautions [5.8], Use in Specific Populations [8.1, 8.3]).

Advise females of reproductive potential to use effective contraception during treatment and for at least 5 months after the last dose of TECENTRIQ (see Use in Specific Populations [8.3]).

Lactation

Advise female patients not to breastfeed while taking TECENTRIQ and for at least 5 months after the last dose (see Use in Specific Populations [8.3]).
Disaster preparation: Make sure your practice is ready

Plan should address needs of patients, staff, providers, and the business

Hurricane Michael came ashore in a heavily populated area of the Florida panhandle on Oct. 10, 2018. As I wrote this article 3 weeks later, two major hospitals in the region remained closed to all but emergency room services, and many community medical practices were closed indefinitely. Others were scrambling to find temporary office space. The prognosis is guarded: A year following Hurricane Katrina, only one-fourth of physicians had returned to New Orleans to practice (Health Aff [Millwood] 2006; 25:w393–406).

Would your urology practice survive such a blow? The answer may lie in how well you have prepared to deal with a disaster—before it hits. In this article, I will review some topics in disaster preparedness from several different perspectives.

Meeting patients’ needs

The patients’ needs are the first to consider. The acute interruption of a busy urology practice will create a group of high-acuity patients with urgent needs. This group includes those scheduled for urgent or emergent surgery, those who just had a surgical procedure, and patients due for time-sensitive cancer medications (sipuleucel-T [Provenge], for example).

It is very likely that a disaster will interrupt power and land lines in your practice, and you should be prepared for electronic forms of communication with your patients—email, text, cell phone, patient portal, and website.

Natural disasters typically result in power outages and communication challenges, but you should have a plan in place to communicate with patients once it is possible. The foundation of this plan is the disciplined collection and updating of patient information during normal operations: phone, cell phone, secondary contact information, and especially email. Of course, you need access to this information, and the benefits of remote hosting or a cloud environment may become clearer during disaster recovery.

Your business phones are probably going to be down, and your practice will be tough to contact. Patients may attempt to communicate through a patient portal. Is your practice really serious about registering patients for the portal, or are you doing the bare minimum for a government program like the Merit-based Incentive Payment System?

Finally, your practice website can be a valuable tool for communication. A flashing banner with instructions and contact information may help redirect patients and enable continuity of care.

A less acute but equally important group of patients to consider and attempt to consists of those with elective surgery scheduled, those with a recent prostate biopsy, and those with upcoming appointments. If you have taken the time to configure your appointment scheduling templates, create appointment types, and enter appointment notes, it will be easy to generate reports or browse the schedule efficiently. If you have no standards, hundreds of templates, or aren’t using advanced functions in your scheduler, it will be a long and arduous process. If you keep your surgery schedule in a “notebook” instead of electronically, consider that that may be lost in a disaster.

This may be a good time to review your scheduling practices and ask if they would serve you well in an emergency. Appointment reminder systems can be leveraged in an emergency to blast messages to a controlled group of patients—again, if your collection of demographics has been thorough.

Once you are able to communicate with patients, it is inevitable that some will have been displaced or have another reason to transfer their care immediately. You should be prepared to facilitate the transfer of their medical records electronically and assume that the patient cannot “come by the office.”

If you have never tested direct messaging or other electronic forms of records transfer, now may be the time. It is possible that the number of requests may overwhelm your capacity to keep up even once normal operations are restored. There are third-party vendors that can assume some or all of this burden, and your preparation plan might include evaluating their programs’ benefits and costs.

If any of your information systems are hosted locally, you should already have an IT disaster plan that addresses power outages, battery backup, and backup/restoration of data. These plans typically anticipate a few hours or days of downtime, but a hurricane or tornado can leave a region without power for much longer.

You should have a plan that includes protecting and relocating servers and critical pieces of your infrastructure to a secure and

PRACTICE POINTERS

- Natural disasters typically result in power outages and communication challenges, but you should have a plan in place to communicate with patients once it is possible.
- Your practice website can be a valuable tool for communication. A flashing banner with instructions and contact information may help redirect patients and enable continuity of care.
- Often when disaster strikes there are federal emergency funds allocated to small businesses—know how to apply for these funds.
relocations and restorations should be done by an IT professional who knows your practice, your systems, and your infrastructure. Identifying such a person and creating such a plan should be done before it is needed, and then tested.

**Think about your staff and physician safety and needs during an emergency.** Have you identified a shelter or safe location? Do you have an evacuation plan? If you plan to stay, do you have enough water, food, and gasoline to last for more than a week? What will you do if there is no power for 2 weeks?

Your disaster plan should include a rendezvous point, time, and emergency contact number outside the disaster zone. Do you have access to all of your employees’ contact info online? If your practice is big enough, your plan may include transferring staff to other offices and filling open positions; physicians may be able to do locum tenens work in the region or elsewhere. Your plan should address retention of staff and employees, payroll, emotional support, access to benefits, and the basics of human resources.

Finally, you need a business continuity plan. Often when disaster strikes there are federal emergency funds allocated to small businesses—know how to apply for these funds. Most business insurance plans offer some sort of optional coverage for business interruption—coverage for lost revenue and expenses—including the cost of relocation. Review your insurance to see whether and how much coverage exists. While a hurricane is a rare event, it is a reminder that other forms of disaster (fire, flooding, power outage) may close your practice for an extended period of time, and you should have a plan.

Bottom line: Natural disasters serve as a reminder that most urology practices are small businesses and should have a basic plan in place for dealing with events that cause the temporary or permanent closure of the office. Your plan should address the needs of patients, staff, providers, and the business. Benjamin Franklin said, “By failing to prepare, you are preparing to fail.” While the chances are small you will face a natural disaster, preparation is your best defense.

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**8 Most Revealing Key Practice Indicators for Urology**

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days in A/R or Turn Ratio</td>
<td></td>
</tr>
<tr>
<td>Total $ per RVU</td>
<td></td>
</tr>
<tr>
<td>Average Charge per Visit</td>
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</tr>
<tr>
<td>Average Receipt per Visit</td>
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</tr>
<tr>
<td>Gross Collections</td>
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<tr>
<td>Net Collections</td>
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<tr>
<td>Denial Rate</td>
<td></td>
</tr>
<tr>
<td>% AR by aging bucket</td>
<td></td>
</tr>
</tbody>
</table>

Want to know the PRS KPI benchmarks?  
go to: prsnetwork.com/billing

**FYI:**  
PRS Provides Outsourced Billing Services  
go to PRSNetwork.com, email or call us for more info

info@prsnetwork.com  
prsnetwork.com  
(800) 972 - 9298

**Consider staff/physician safety**

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DISASTER PREP  
continued from page 37

climate-controlled environment where they can be brought back up and accessed. These

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**If any of your information systems are hosted locally, you should already have an IT disaster plan that addresses power outages, battery backup, and backup/restoration of data.**
Flexible spending vs. health savings accounts: How to choose

High-deductible health insurance coverage necessary to use HSA

**FINANCIAL TIPS**

- Health care flexible spending accounts (FSAs) and health savings accounts (HSAs) allow an individual to put money into the account on a pre-tax basis and take the money out of the account tax free as long as it is used for qualified medical expenses.
- One main difference between HSAs and FSAs is that with HSAs, once a contribution is made, the funds can be invested in mutual funds, exchange-traded funds, stocks, and other investments to potentially help grow the balance.
- A limited-purpose FSA is a health care spending account that can only be used for eligible vision and dental expenses.

**Q:** My employer offers both a health care flexible spending account and a health savings account. Can I use both and if not, which option is better?

**A:** Health care flexible spending accounts (FSAs) and health savings accounts (HSAs) are great ways to pay for medical, dental, and vision expenses. Both allow an individual to put money into the account on a pre-tax basis and take the money out of the account tax free as long as it is used for qualified medical expenses. Qualified expenses include deductibles, copays, coinsurance, and other expenses not covered by your insurance plan.

These accounts cannot be used to pay for insurance premiums, and removing the funds for non-qualified purposes results in having to pay taxes and a 10% penalty if under age 65. Both accounts can be an effective way to save for your medical expenses, but an individual cannot have both an FSA and an HSA. Determining which option is best for you requires an understanding of the nuanced differences between the two.

An FSA allows you to contribute up to $2,650 (2018) each year on a pre-tax basis. FSAs are use-it-or-lose-it accounts, meaning any balance remaining at the end of the year will be permanently forfeited. For this reason, when using an FSA, it’s important to estimate your health care costs as accurately as possible. Some FSAs allow you to roll over $500 to the following year, but anything above $500 is forfeited. Other FSAs will extend the deadline to use the funds by 2½ months, but then any carry-over balance still remaining by mid-March is forfeited.

Unlike an HSA, you do not need to be covered by a high-deductible health insurance plan to be eligible to use an

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**Flexible spending accounts are use-it-or-lose-it accounts, meaning any balance remaining at the end of the year will be permanently forfeited.**

FSA. If you are currently using an FSA, be sure to check your current balance and, if necessary, determine how to use those funds before they are at risk of being forfeited.

HSAs are like FSAs, but with some added features. First, you must have a high-deductible health plan (HDHP) to be eligible to use an HSA. The U.S. government currently defines an HDHP as one with a deductible of $1,350 or greater ($2,700 if the plan is used by the whole family) and an out-of-pocket maximum equal to or greater than $6,650 ($13,300 for family).

If eligible, an individual can contribute up to $3,450 ($3,500 in 2019) on a pre-tax basis into the account or, if the entire family is on the plan, $6,900 pre-tax ($7,000 in 2019). One main difference between HSAs and FSAs is that with HSAs, once a contribution is made, the funds can be invested in mutual funds, exchange-traded funds, stocks, and other investments to potentially help grow the balance. HSAs are one of the only accounts that provide tax benefits in the accumulation, growth, and distribution stage. The investments grow tax free, and as long as the money comes out of the account for a qualified purpose, no taxes are due on the investment gain.

Another difference between HSAs and FSAs is that any remaining balance in an HSA can be rolled over each year. If you don't use all the funds, you can continue to invest year to year, so you never have to worry about forfeiting your contributions. Some individuals continue rolling over their balance all the way into retirement.

HSAs can be used to pay for Medicare Parts A, B, and D premiums and Medicare HMO premiums. However, premiums for a Medicare supplemental policy, such as Medigap, are not eligible expenses. Some use their HSA as a supplemental retirement account earmarked specifically for medical expenses in retirement.

Overall, FSAs and HSAs are useful tools for saving and paying for medical expenses. Each option has advantages and disadvantages. We recommend speaking with your financial adviser to determine which option is best for you.

**Q:** My HSA does not cover all vision and dental expenses. Is there an option to save for those expenses in a tax-advantaged way?

**A:** A limited-purpose FSA (LPFSA) is a health care spending account that can only be used for eligible vision and dental expenses. Unlike a health care FSA, however, an LPFSA can be held at the same time as an HSA. When coordinated with an HSA, the LPFSA can further reduce your taxes while allowing you to allocate HSA funds to other purposes—including retirement. Funding dental vision expenses from an LPFSA may allow you to keep more savings in your HSA. Over time, those additional savings can help your retirement nest egg grow larger.
How concerned are you about patients taking counterfeit meds?

It’s a slight concern—a little bit less now that Viagra is generic—but, typically, a lot of patients, when they’re trying to save money, order stuff online and can’t necessarily be sure where it’s coming from or whether it’s real.

I warn my patients to get their medications at a pharmacy here in the U.S., but there’s not a whole lot I can do once they have the prescription in hand.

A lot of this is avoided with EHR because we send a prescription directly to the pharmacy. But sometimes I have a patient who requests the paper script, and I can’t do anything once I give them the prescription except warn them.

Nobody actually has ever told me they’ve gotten something bad, but every once in a while patients ask if I can tell whether what they have is real or not, and I tell them, ‘No, I’m not a chemist; there’s no way I can tell.’

Sophia Ford-Grant, MD / St. Louis

Patients certainly can end up with counterfeit medications because of radio/TV advertising that they are available outside the country, so I am concerned. Most of those are going to be erectile dysfunction medications, but the likelihood of anybody being hurt by those medications is pretty slim.

I have some patients who try medicines through health stores to boost their testosterone, and most don’t even know what their testosterone levels are. They just start taking them, not knowing what’s in them. I guess they could be dangerous because of the effects they can have on the liver. With prescription ED meds, counterfeits might not be effective, but patients won’t be hurt by them.

I put most of my people on the generic ED drugs; they’re getting very inexpensive. They vary from $2-$4 a pill for the generic sildenafil instead of $40-$75 a pill for the brand names. That should solve most of the problems of people ordering things online that might not be real.

I’m not concerned about counterfeit pain medication because I don’t prescribe it unless someone has acute stones; then they get about 3 days’ worth.

Charles Welliver, MD / Albany, NY

A study showed that up to 50% of mail-order Viagra did not come in as advertised.

That’s a concern.

Now that sildenafil has gone generic, it’s less of a problem, but still people tell me they’ll import their medicines from Canada and other countries, and I’m not even sure that’s legal.

I’m as concerned about non-FDA-approved supplements containing ingredients that can be dangerous.

Saw palmetto is used for BPH around the world; the AUA helped sponsor studies that show it doesn’t work any better than a placebo. But some companies put finasteride in, which shrinks the prostate. So people take a drug that works and don’t realize it’s actually something else which can potentially be dangerous. If you take finasteride and don’t know it, and your PSA is low, you might hide an elevated PSA. We urge our patients to use FDA-approved drugs and pharmacies that are regulated.

Charles Keoleian, MD / Manistee, MI

Dr. Welliver

Charles Keoleian

DR. WELLIVER

DR. KEOLEIAN

It’s probably much more common than we think. I have patients who tell me they bought something on the Internet that didn’t work. Certainly there are safety concerns, but it’s kind of an equal concern about the safety of the medication and whether it actually works.

Patients tell me they bought “Canadian pharmacy Viagra” and it didn’t work. A study a couple years ago looked to see if there was any actual medication in those pills, and something like only one out of 20 had Viagra in it. I’d be more concerned if it were dangerous, but that really doesn’t seem to occur.

Usually I tell my patients the stuff is not FDA regulated, the safety is not understood, and that the study showed how infrequently the medication even contains what they think they’re getting.

That dissuades most men, especially in the sexual medication world now that there is generic Viagra and Cialis. Now, I can offer them a less expensive actual medication as opposed to counterfeit baloney. Now that the generic has come in, I hope we’ll see less counterfeiting.

Charles Welliver, MD / Albany, NY

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The Department of Surgery at the University of Vermont College of Medicine is seeking a Clinical Practice Physician in the Division of Urology to join the Champlain Valley Physicians Hospital (CVPH) in Plattsburgh, New York. CVPH is a progressive medical center with nine state-of-the-art OR’s and Ambulatory Surgery Center. This position offers the unique opportunity to work in a community setting while having an active affiliation with Vermont’s only Academic Medical Center; the only ACS verified Level 1 trauma center in the state providing tertiary care to patients from Vermont and Northern NY. Serving the patients from Upstate New York for decades, the local urologic surgery practice recently joined the faculty at the University of Vermont and are now seeking an additional colleague to join the dynamic Urology faculty that span the network hospitals. Specifically, the Division seeks applications from individuals seeking a community Urology practice employment opportunity with a collegial and collaborative setting with University support.

Applicants must be board certified or board eligible and eligible for medical licensure in the state of New York. This is a full-time, 12 month, salaried position.

Plattsburgh is located on the shores of Lake Champlain, near the Adirondack Mountains, Olympic-Lake Placid region, Montreal and Burlington, VT.

The University is especially interested in candidates who can contribute to the diversity and excellence of the academic community through their research, teaching, and/or service. Applicants are requested to include in their cover letter information about how they will further this goal.

The University of Vermont is an Equal Opportunity/Affirmative Action Employer. All qualified applicants will receive consideration for employment without regard to race, color, religion, sex, sexual orientation, gender identity, national origin, disability, protected veteran status, or any other category legally protected by federal or state law. The University encourages applications from all individuals who will contribute to the diversity and excellence of the institution.

Interested individuals should apply online at https://www.uvmjobs.com/postings/31529 (position number 00024781).

Inquiries may be directed to Mark Plante, MD, FRCS(C), FACS, Division Chief, via Kathryn Raymond Kathryn.Raymond@uvmhealth.org.
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The Tallwood Institute is comprised of a world-class Urology and Kidney care team of local and national leaders in their fields. Many of our physicians have advanced sub-specialty training and are backed by a full team of interdisciplinary medical and surgical specialists. The institute is structured around six interdisciplinary disease management teams including urologic oncology, pelvic health and urinary incontinence, stones, men’s health, chronic kidney disease and general urology. The teams meet regularly with the mission of establishing care pathways based on evidence-based medicine, providing education and improving process and quality. As a member of the Tallwood Urology and Kidney Institute, you will be able to participate in any of these teams.

Hartford HealthCare is Connecticut’s most comprehensive healthcare network. Our fully integrated health system includes a tertiary-care teaching hospital, five community hospitals, the most extensive behavioral health services network in Connecticut, a large primary care physician practice group, a regional home care system, an array of senior care services, and a large physical therapy rehabilitation network.

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Send CV and letter of interest to:
Clayton Tebbetts at Clayton.Tebbetts@hhchealth.org
St. Luke’s University Health Network, the region’s largest, most established health system, a major teaching hospital, and one of the nation’s 100 Top Hospitals is seeking a board eligible/ board certified Urologist to join our dynamic, rapidly growing Urology practice. St Luke’s Center for Urology is a hospital-employed practice within the St Luke’s University Health Network. At present we comprise 14 urologists and 7 Advanced Practitioners with continued growth expected over the next few years. We are expanding to cover growth as the Network now includes 10 hospitals. We are looking for our next urologist to work primarily on our Warren Hospital Campus in Phillipsburg, New Jersey. Our next partner will also work in Pennsylvania and in conjunction with colleagues throughout the St. Luke’s University Health Network (SLUHN) system.

Our urology program boasts the latest office and endourologic equipment. Extremely well-regarded robotics program in place since 2003, currently utilizing the newest Davinci Xi system. We enjoy strong support from our Interventional Radiology and Radiation Oncology colleagues.

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• Teaching, research, quality improvement and strategic development opportunities

About St. Luke’s University Health Network
Founded in 1872, St. Luke’s University Health Network (SLUHN) is a fully integrated, regional, non-profit network of 14,000 employees providing services at 10 hospitals and over 300 outpatient sites. With annual net revenue of $1.9 billion, the Network’s service area includes 10 counties: Lehigh, Northampton, Berks, Bucks, Carbon, Montgomery, Monroe and Schuylkill counties in Pennsylvania and Warren and Hunterdon counties in New Jersey.

About the Lehigh Valley
Set amid gentle hills and charming country sides, Lehigh Valley, PA is home to Allentown, Bethlehem, and Easton, as well as dozens of small towns and picturesque boroughs, parks, trails, and waterways. Steeped in pre-Colonial, Early American, and industrial history, the region’s storied past became its uplifting present, bestowing visitors anything from crayons and craft beer to Martin Guitars and museums, covered bridges, and nationally-recognized events like Musikfest and Christkindlmarkt.

The Lehigh Valley is in close proximity to NYC, Philly, and DC. Outstanding higher education facilities include Lehigh University and Moravian College. Cost of living is low and coupled with minimal congestion; choose among a variety of charming urban, semi-urban and rural communities your family will enjoy calling home. There is easy access to outdoor activities like skiing, snowboarding, white water rafting, and zip lining. The Lehigh Valley encompasses three unique cities in one suburban area. For more information please visit www.discoverlehighvalley.com.

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If you are interested in learning more about the opportunity, please contact: Christine Figler, Physician Recruiter, St. Luke’s University Health Network, Christine.Figler@sluhn.org
**PEDIATRIC UROLOGIST**

The Department of Surgery at the University of Vermont College of Medicine and its affiliated medical centers, the University of Vermont Medical Center and Vermont Children’s Hospital, is seeking a Pediatric Urologic Surgeon. The University of Vermont Medical Center and Vermont Children’s Hospital, along with the university, offers a full spectrum of pediatric medical and surgical specialties. The institution has a Level III NICU, a fully staffed PICU, and serves as the regional adult and pediatric regional trauma center. The Division of Urology holds a long-standing reputation as a premier urologic surgery practice for the surrounding communities’ pediatric and adult patients with urologic care needs and enjoys an excellent relationship with the Department of Pediatrics. With a highly respected residency training program with a robust compliment of dynamic faculty across the network hospitals, the Division seeks applications from individuals seeking an academic career in a collegial and collaborative setting.

Applicants must be BE/BC in Urology and Pediatric Urology, eligible for licensure in the State of Vermont, and eligible to work in the United States. They must have experience in the teaching of medical students and surgical residents, and the clinical and research activities of an academic division of Pediatric Surgery.

This is a full-time, 12-month salaried faculty appointment in the Clinical Scholar Pathway at the rank of Assistant or Associate Professor and carries with it attending staff privileges at University of Vermont Medical Center, a level 1 trauma center that serves as a tertiary care facility serving Vermont and northern New York State. Salary is competitive and commensurate with ability and experience.

Burlington, is located on the eastern shore of Lake Champlain between the Adirondack and Green Mountains, is consistently ranked one of the top places to live and work. Numerous recreational and cultural opportunities across four seasons are available, with Vermont considered to be an outstanding environment to practice medicine.

The University is especially interested in candidates who can contribute to the diversity and excellence of the academic community through their research, teaching, and/or service. Applicants are requested to include in their cover letter information about how they will further this goal.

The University of Vermont is an Equal Opportunity/Affirmative Action Employer. Applications from women, veterans, individuals with disabilities and people from diverse racial, ethnic, and cultural backgrounds are encouraged.

Interested individuals should apply online at [https://www.uvmjobs.com/postings/30302](https://www.uvmjobs.com/postings/30302) (position number 00024730).

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ignificant Medicare regulatory changes finalized in November will end legal incentives that have enabled hospitals to leverage Medicare payment policy to generate profits allowing them to acquire physician practices and gain competitive advantages in the health care marketplace.

Contained in the Medicare Outpatient Prospective Payment System (OPPS) final rule for 2019, the changes were hailed by Deepak A. Kapoor, MD, chairman of health policy at LUGPA, and were met with vehement opposition by the American Hospital Association (AHA).

**Payments to be leveled for outpatient visits**

The changes state that:

- Over a 2-year period, the Centers for Medicare & Medicaid Services will level payments for outpatient office visits regardless of site of service. For the first time, all physicians practicing medicine away from a hospital campus will be paid the same amount for doing the same work.
- CMS is closing a loophole that had permitted acquired off-campus physician offices to benefit from cost advantages in the 340B drug program.
- Ambulatory Service Center (ASC) payment updates will no longer be under the hospital market basket pricing schedule rather than the Consumer Price Index (CPI), eliminating the payment discrepancy between hospital-owned and free-standing ambulatory facilities.
- Under the new rule, hospitals will be paid 70% of the OPPS rate in calendar year 2019, a figure that will drop to 40% in 2020 and beyond. This is estimated to reduce Medicare costs by $380 million in 2019, CMS said, adding that it would support more patient choice in care access.

“Today’s rule advances competition by creating a level playing field for providers so they can compete for patients on the basis of quality of care. The final policies remove unnecessary and inefficient payment differences, so patients can have more affordable choices and options,” said CMS Administrator Seema Verma.

However, Tom Nickels, executive vice president of government relations and public policy for the AHA, said the OPPS rule would be harmful to hospitals and that the AHA is going to court.

**FAST FACTS**

The Medicare Outpatient Prospective Payment System final rule:

- will level payments for outpatient office visits regardless of site of service
- closes a loophole that had permitted acquired off-campus physician offices to benefit from cost advantages in the 340B drug program
- was praised by LUGPA and sharply criticized by the American Hospital Association

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**CMS has clearly stated that patients should not pay more for the same service on different sites.**

DEEPAK A. KAPOOR, MD

“Today’s misguided final rule will have negative consequences for the patients we serve,” he said. “This rule, which phases in over 2 years payment cuts to hospital outpatient clinic visits, is based on unsupported analyses and erroneous policy rationales. These ill-advised cuts will hit patients in rural and vulnerable communities especially hard. Congress recognized the crucial role of hospital outpatient departments in the communities they serve and, in 2015, specifically protected existing facilities from unwarranted payment reductions.

“Today’s final rule could stifle hospitals’ ability to modernize care and meet the needs of their patients and communities.”

Nickels said the rule exceeds the administration’s legal authority and that the AHA, other hospital organizations, the Association of American Medical Colleges and member hospitals “intends to promptly bring a court challenge” to the site-neutral provisions.

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**340B program has been a ‘piggybank’**

However, LUGPA’s Dr. Kapoor, in an exclusive interview with Urology Times, charged that many hospital corporations have been using the 340B pricing program for years as a “piggybank” to fatten their bottom lines in instances where they operate clinics in both low-income and high-income areas.

“They’ve been buying drugs for the indigent population at lower rates for those facilities and selling them to suburban clinics where there are no indigent patients at all,” he said. “They’ve been using those drugs to supply non-safety net offices that they had purchased.”

Dr. Kapoor cited a study which the authors said they found that hospital-affiliated clinics that registered for the 340B program in 2004 or later served communities that were wealthier and had higher rates of health insurance compared to communities served by hospitals and clinics that registered prior to 2004 (Health Aff [Millwood] 2014; 33:1786-92).

Making matters even worse, contended Dr. Kapoor, is that those profits often are used to purchase more physician practices and control market share. And, he said, “It is all being done on the backs of consumers.”

CMS’s new rule, he said, “will severely curtail the ability of hospitals to control market share dollars.”

By closing a loophole that had permitted acquired off-campus physician offices to benefit from cost advantages in the 340B drug program, Dr. Kapoor said hospitals no longer will be able to charge more for exactly the same service that had been provided in the past by that office.

That is especially important with respect to evaluation and management services, he said.

“Medicare now says that if you see a doctor in an off-campus facility, you will pay the prevailing rate. We actually have had situations where two doctors in the same building would provide the same service, but one would get 50% more for doing the same work just because that practice had been acquired by a hospital,” Dr. Kapoor said.

“CMS has clearly stated that patients should not pay more for the same service on different sites,” he said.

Regarding the ASC payment decision, Dr. Kapoor said that by basing payments on the facility payment schedule rather than the CPI, hospital payment increases will be lower than if the CPI was still used. That, he explained, would further limit hospitals’ ability to purchase physician practices and reduce competition.
A 49-year-old male patient presented to his urologist for right flank pain and was diagnosed with probable kidney stones. The urologist recommended extracorporeal shock wave lithotripsy. That procedure was ultimately successful and the kidney stones resolved.

As part of his pre-procedure workup, the patient submitted to a computed tomography scan on a Friday afternoon, which revealed findings suspicious for colon cancer. The second page of the radiology report, faxed to the urologist the same day, stated: “soft tissue mass involving the descending sigmoid colon suspicious for colonic neoplasm... further evaluation with a colonoscopy is recommended.” However, the urologist failed to read the second page. As a result, no further workup was done.

Seventeen months later, the patient was turned down for life insurance due to elevated carcinoembryonic antigen levels in his blood, indicating a probable cancer. That test led to a workup that diagnosed colon cancer 2 months later.

Suit brought against urologist, radiologist, hospital

The patient brought suit against his urologist, the radiologist, and the hospital. He claimed the radiologist was negligent in failing to personally convey the unexpected and significant finding regarding the mass to the urologist, and that the urologist was negligent for failing to read the second page of the radiology report. He claimed the hospital was vicariously liable for the radiologist’s negligence. The patient claimed that had the cancer been properly diagnosed 19 months earlier, he would have had a 50% to 80% chance of 5-year survival, yet because the cancer had metastasized he was essentially left with a 0% 5-year chance of survival.

The patient further contended that although he would have required surgery and an initial course of chemotherapy even if the cancer had been timely diagnosed, he would not have needed the extensive second abdominal surgery, as well as the second, experimental course of chemotherapy, which he continues to take.

During pre-trial discovery depositions, the radiologist testified that immediately after he interpreted the patient’s CT scan, he telephoned the urologist to advise of the results. However, the radiologist testified that he could not reach the urologist, and instead left his name and the name of the patient about whom he was calling, but did not leave any substantive information about the scan. Instead, he faxed the report to the urologist.

In accordance with hospital protocol, the radiologist testified at his deposition that he filed a “ticket” with the hospital’s radiology computer system, which resulted in the radiology department secretary calling the urologist’s office Monday morning, the next business day. Hospital records indicated that the secretary confirmed that the faxed radiology report had been received.

The urologist testified at his deposition that he had read the radiology report, but did not see the critical statement as to the finding of the mass on the second page. The urologist testified that when he read the first page, it appeared to show everything he needed to know regarding prepping for the lithotripsy, and he never noticed there was a second page.

The patient’s expert testified in his pre-trial deposition that the radiologist breached the standard of care by failing to personally convey the unexpected and suspicious findings to the urologist. He was critical of the radiologist for failing to document his telephone call to the urologist, and further critical that if such a phone call had been made, the standard of care requires a personal follow-up by the radiologist to the urologist to address the critical and suspicious findings on the CT scan.

In response, the defendant radiologist’s expert testified in pre-trial deposition that the radiologist met the standard of care by faxing the report to the urologist’s office, and then confirming that the office had received the report the following business day.

In pretrial discovery discovery, the patient’s expert oncologist opined that had the colon cancer diagnosis been made in a timely fashion, the cancer was then likely only Stage IB or at worst, IIA, and testified that the 5-year survival rate for Stage IB colon cancer is approximately 75% to 80%. He testified also that the prognosis for early Stage III has a 50% to 75% 5-year survival rate.

Expert weighs in on earlier Dx

However, the plaintiff’s expert oncologist testified that when the cancer was finally diagnosed, it was at least late Stage IIIB and probably Stage IV, and the 5-year survival rate was essentially 0%. The patient’s expert oncologist also opined that had the cancer been diagnosed when it should have been, any metastasis would have been far less widespread and the patient would not have been required to undergo the second surgery, nor the subsequent experimental round of chemotherapy.

In the face of such grim facts and circumstances, the case settled prior to trial for $4,500,000, with $2,300,000 from the defendant urologist and $2,200,000 from the co-defendants radiologist and hospital.

LEGAL PERSPECTIVE: Going forward, this urologist will never fail to read any radiology report in its entirety, and this radiologist will most certainly follow up and document each and every attempt to communicate suspicious findings. What began as a routine and successful lithotripsy ended in a delayed diagnosis, lost chance of survival, and scores of extensive surgeries and continued chemotherapy treatment. Given the fact that all involved agreed that the mass was indicative of colon cancer, and the dramatic impact of the diagnosis delay to this middle-aged man, this case presented challenging circumstances for all involved. If the case proceeded to trial, it could have likely returned a daring verdict, perhaps even above the settlement amount, in the hands of a jury.
Most common adverse events reported include hematuria, dysuria, micturition urgency, pelvic pain, and urge incontinence. Most symptoms were mild to moderate in severity and resolved within two to four weeks after the procedure.

1. No instances of new, sustained erectile or ejaculatory dysfunction. McVary, J Sex Med 2014
Supine Positioning for PCNL on a Patient with a Horseshoe Kidney

Fabio Vicentini, MD

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