ONCOLOGY REPORT 2018

UROLOGICAL CANCER

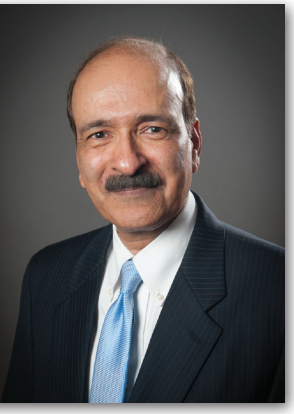
Bon Secours

Our Lady of Bellefonte Hospital

The Difference a Decade Makes

by Kirti Jain, M.D.

A report from the Cancer Committee Chairman



Kirti Jain, M.D.
Medical Oncologist-
Hematologist

Cancer, for a long time, was one of the most confounding medical problems for physicians and one of the most devastating health problems for patients. We knew little about its cause, and even less about its treatment. Most treatments were discovered empirically or even accidentally. Oncology lagged behind most other disciplines in medicine.

What a difference a single decade can make!

Advances in molecular biology and genetics quickly changed all that. It allowed us to develop precision drugs based on solid scientific principles. The pace of new drug discovery picked up. More oncological drugs are now approved yearly than the total number of drugs available when I became an oncologist in the 1980s! Ever-expanding indications for immune checkpoint inhibitors and targeted drugs are leading to better survival, better tolerance to treatment, or both. Last year marked a milestone in the history of precision cancer medicine when the FDA approved the first tissue-agnostic treatment, which means it was approved for use solely on the basis of the genetic make-up of a person's cancer, rather than the histological type of cancer or its location in the body. CAR T-cell therapies — a type of cancer immunotherapy that uses a patient's own engineered immune cells to attack and kill cancer cells is producing long term remissions in some extremely resistant cancers. Cloud computing has become a boon to cancer research by allowing real-time scientific collaboration across the world at an unprecedented scale. As we try to find new connections between genes and tumor types, enormous storage and analytical computing power is needed—as much as a terabyte per patient—something only possible with cloud computing.

A number of technological and treatment planning innovations have made radiation therapy safer, easier and more convenient for patients. An example worth mentioning is external beam radiation therapy which confers outcomes similar to radical prostatectomy. The standard treatment lasts eight to nine weeks but we have learned hypofractionation, meaning a higher dose per treatment allows it to be completed in four to five weeks with similar efficacy. Further, ultra-hypofractionated stereotactic ablative radiation therapy (SART) can be completed in as few as five treatments. I am happy to say these technologies are available on the OLBH campus.

Robotic cancer surgery has become routine, allowing much smaller incisions, reduced pain and quicker recovery. The extremely flexible robotic arm and magnifying lenses allow surgery in areas where it would be impossible for a human arm to reach. Evolution and innovations in robotic surgery are pushing imaginative frontiers like automated guidance systems for intricate surgeries such as those on the brain or spine. Use of virtual incision miniature robots is being explored.

Path-breaking research is taking place in the field of early detection of cancer. The dream all of us have that a blood test could detect cancer anywhere is the body may indeed come true in the near future.

I could go on.....suffice to say that cancer research in all fields of oncology is rapidly changing how we approach a patient with cancer. The practice of oncology is more fun today than it has ever been—with a vast increase in our armamentarium, rapidly evolving science behind oncology, and above all the growing hope cancer deaths could one day be history!

On a more personal note, I have been very fortunate to have presided over a wonderful OLBH Cancer Committee for several years. Committee members have contributed a lot toward developing a quality cancer program at OLBH. Some of these amazingly dedicated and gifted colleagues should take the lead now. Therefore, this will likely be my last chairman's letter, but I look forward to remaining actively engaged in the next fun-filled decade of oncology.

Kirti Jain, M.D.
Chairman, Cancer Committee

Treatment Advances in the Fight Against Prostate Cancer

by Anshu Kumar Jain, M.D.

Anshu Kumar Jain, M.D.
Radiation Oncologist

Prostate cancer remains the most common cancer diagnosed in men and the second leading cause of cancer-related death in men. Nearly 175,000 cases were diagnosed last year, and it is estimated that one in nine men will be diagnosed with prostate cancer in their lifetime. However, early diagnosis and detection combined with advances in treatment have made curing most patients a realistic option. Even in advanced stage patients in whom a cure may not be possible, the cancer can be controlled for several years and in some cases decades.

Most patients are found to have prostate cancer after a blood test shows elevated levels of prostate specific antigen (PSA). The diagnosis is typically made after a prostate biopsy is performed, and in most cases the prostate cancer is limited to the prostate itself and has not spread to other parts of the body including the lymph nodes or the bones. In cases where the prostate cancer has not spread anywhere else, many patients receive treatment for their prostate cancer based on first assessing the risk of their prostate cancer. This is performed by evaluating a patient's PSA level, physical examination, and Gleason score (a pathology laboratory assessment of the cancer). Based on these factors, patients' cancers can be considered low-risk, intermediate-risk, or high-risk. Treatment options often include active surveillance, having the prostate surgically removed, or undergoing radiation therapy to the prostate. Surgery and radiation therapy are both excellent options for the treatment of prostate cancer and have their own unique risks and benefits. No one option will be right for every patient.

Radiation therapy has been used for many years with high rates of success in curing prostate cancer, especially in patients with low-risk and intermediate-risk prostate cancer. Traditionally, radiation therapy involves a daily dose of radiation treatment given five days a week typically for courses as long as 44 or 45 treatments over approximately nine weeks. Delivering treatments over the course of eight to nine weeks has resulted in safe and effective treatment of prostate cancer, but understandably can be physically and mentally taxing on patients, many of whom may be elderly and with other medical problems as well as appointments and treatments they need to undertake. Additionally, traveling daily for treatment for so many weeks can be a significant logistical and financial burden for patients and their families, many of whom are on limited or fixed incomes.

New biological insights into prostate radiation therapy have resulted in several important clinical studies investigating whether radiation therapy can be performed in a shorter period of time by giving slightly more radiation per treatment. With many of those studies complete, the American Society of Radiation Oncology (ASTRO), in combination with the American Society of Clinical Oncology (ASCO) and the American Urological Association (AUA), recently revealed a groundbreaking and practice-changing consensus statement outlining that most patients with prostate cancer can achieve the same effectiveness of traditional radiation treatment for prostate cancer, but in a much shorter period of time....only five to six weeks of treatment.

This represents a nearly 45 percent reduction in the overall course length of prostate cancer treatment using radiation therapy, but with similarly effective treatment of prostate cancer as the much longer course of

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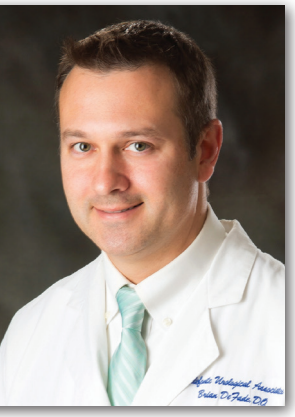
treatment. Importantly, most of the studies did not show a significantly increased risk of long-term side effects. Taken together, what this means is most future patients who undergo radiation therapy for prostate cancer can get similarly excellent treatment using radiation therapy but in a shorter amount of time, reducing cost, inconvenience, and improving quality of life for our patients.

Importantly, delivering such radiation therapy requires knowledgeable and experienced radiation oncologists as well as access to and utilization of advanced radiation therapy techniques such as intensity modulated radiation therapy (IMRT), image guided radiation therapy (IGRT), and volumetric arc therapy (VMAT). Fortunately, all of these services are available at OLBH and Ashland Bellefonte Cancer Center. The cancer center is currently installing a brand new radiation therapy machine called the Versa HD which will be capable of the most advanced techniques for prostate radiation therapy and more. By bringing HD radiation to our community, we continue in our journey and goal to provide the most advanced and compassionate cancer care in the region.

For more information about HD radiation therapy for prostate cancer, please contact **Ashland Bellefonte Cancer Center** at **(606) 836-0202.**

Treatment of **Metastatic Hormone Sensitive** Prostate Cancer

by Brian DeFade, D.O.



Brian DeFade, D.O.
Urologist

Metastatic prostate cancer remains a disease that despite androgen deprivation therapy and improved treatment options progression will occur. The median overall survival of men with metastatic hormone sensitive prostate cancer (mHSPC) after starting androgen deprivation therapy (ADT) was approximately 45 months in a few large randomized trials (1). Several new trials have shifted the treatment paradigm for mHSPC to include CHAARTED, STAMPEDE, GETUG-AFU-15, and LATTITUDE. We will review some of these trials and the current NCCN Guidelines for castrate sensitive prostate cancer (2).

In 2013 SWOG 9346 concluded that continuous ADT remained the standard of care for mHSPC. (3). SWOG 9346 assessed 1134 patient undergoing treatment with intermittent versus continuous ADT for 8 months. (4) These patients were then risk stratified into low, intermediate, and high-risk categories based on PSA levels. Low-risk patients had a PSA of 0.2 or less with a median survival of 75 months, intermediate-risk patients had a PSA up to four with a median survival of 44 months, and high-risk patients had a PSA greater than four with a median survival of 13 months. (4) For this reason further consideration should be given before the addition of docetaxel and/or abiraterone due to comorbidities, and treatment related toxicities that could affect quality of life and overall survival.

Chaarted:

A total of 790 patients were randomized into ADT plus docetaxel or ADT alone. After a median follow-up of 28.9 months, the median overall survival was 13.6 month longer with ADT plus docetaxel (combination group) than with ADT alone (57.6 months vs. 44 months). (5) It is important to note that patients with high volume metastatic disease, as defined by the presence of visceral metastasis and/or four bone metastasis, had a significantly better improvement in overall survival with the addition of docetaxel. (4.5) This subgroup of patients had a median OS of 17 months longer in the combination group than in ADT alone (49.2 months vs. 32.3 months. (Sweeney). This survival improvement was not seen in patients with low volume disease. A meta-analysis of patients with low volume disease in the CHAARTED and GETUG-AFU-15 studies suggested the same outcome with no OS (overall survival) benefit for the addition of docetaxel or abiraterone. (4). Another smaller subset of GETUG-AFU-15 with docetaxel and ADT confirmed a survival advantage for patients with high volume disease.

Stampede:

A total of 1,917 patient were randomized into a 1:1 ratio to receive ADT alone or ADT plus abiraterone acetate (1000 mg) and prednisilone (5 mg daily) (combination therapy). (6) The primary outcome measure was OS and the intermediate primary outcome was failure-free survival. The three-year survival of the combination group was 83 percent versus 76 precent in the ADT alone group. (6). The three year failure-free survival was 75 percent for the combination group with a mean failure free survival of 43.9 months, and 45 percent three-year failure free survival for the ADT alone group with a mean failure free survival of 30 months. (6) This study showed that ADT plus abiraterone and prednisolone as compared to ADT alone was associated with a 71 percent relative improvement to time to treatment failure, which translated into a 37 percent difference in overall survival. (6)

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Lattitude:

In this double-blind, placebo controlled, phase III trial, 1,199 patients were randomly assigned to receive ADT plus abiraterone (1000 mg, given daily as four 250 mg tablets) plus prednisone (5 mg daily) (abiraterone group) or ADT plus dual placebos (the placebo group) with the two primary end points of the study being OS and radiographic progression. (7). At the first interim analysis of this trial at 30.4 months, median OS was longer in the abiraterone group than in the placebo group (not reached vs. 34.7 months) with a relative risk of death 38 percent lower in the abiraterone group. (7) The median length to radiographic progression-free survival was 33 months in the abiraterone group and 14.8 months in the placebo group. (7). Furthermore, all secondary endpoints had better outcomes including time to pain progression, next subsequent therapy, initiation of chemotherapy, psa (prostate specific antigen) progression, and next skeletal event. (7)

Conclusion:

These studies have shown that a combination of ADT plus docetaxel, ADT plus abiraterone and prednisone are important consideration in MHSPC, and that using these combinations before castrate resistance is reached in the appropriate patient groups can significantly improve OS and quality of life in these patient, and are becoming the new standard of care. It is interesting to note that in these trials patient with large volume metastatic disease tended to fair better than those with low volume disease and these findings are reflected in the current NCCN guidelines. NCCN version 4.2018 recommendations for systemic therapy for MO disease are orchietomy, or LHRH agonist +/- anti-androgen, or LHRH agonist or observation; for M1 disease they recommend: ADT and docetaxel 75mg/m2 for 6 cycles, or ADT and abiraterone with prednisone, or orchiectomy, or LHRH agonist +/- anti-androgen for > 7 days to prevent testosterone flare, or LHRH agonist + anti-androgen, or LHRH antagonist, or ADT and abiraterone with methylprednisolone. (2)

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Immunotherapy in Bladder Cancer

by Venu Konala, M.D.

Venu Konala, M.D.
Medical Oncologist-Hematologist

In the United States bladder cancer is the fifth most common cancer with estimated new cancer cases of 81,190 and estimated deaths of 17,240 in 2018[1]. New bladder cancer cases in Kentucky were estimated to be 1,200 in 2018[1]. Males have a higher incidence than females[1] and tobacco smoking is the greatest risk factor. Significant advances have been made in the treatment of bladder cancer in the last two years with the introduction of immunotherapy.

Cisplatin based chemotherapy in advanced stage IV cancer has increased overall survival, but cures are rare with limited life expectancy. Our body's own immune system is able to recognize abnormal cells that can turn cancerous and can destroy them. The type of immune cells that attack cancer cells are T-lymphocytes. However, cancer cells have developed the ability to evade immune cells from destroying them.

Significant research was conducted to understand the mechanism of how cancer cells escape the immune system. It was identified that immune cells like cytotoxic T-cells have receptors such as cytotoxic T-lymphocyte associated protein 4 (CTLA-4) and programmed cell death protein 1(PD-1). When these receptors are triggered by certain ligands such as PD-L1 on the surface of cancer cells, the cytotoxic T-cells essentially shut down and can't perform their essential function of destroying the cancer cells.

The understanding of how cancer cells evade the immune system led to the development of multiple immunotherapy bio-engineered agents, some of which block PD-1 and CTLA-4 on T-cells and others which block PDL1 on tumor cells – which led to the immune system recognizing cancer cells and destroying them.

The most significant breakthrough in cancer therapy during the last decade was the development of cancer immunotherapy. Immunotherapy is a rapidly evolving field in oncology, and multiple immunotherapeutic monoclonal antibodies have been approved for treatment in different cancers either as first-line agents alone or in combination with chemotherapy or second-line agents or further line of treatments.

Immunotherapy doesn't work in all patients, research is still going on to identify markers, which will help us to choose patients who will respond well to immunotherapy. For example, PDL1 levels, tumor proportion scores (TPS), combined positive scores (CPS), and the number of mutation identified in the tumor are being used as markers.

Immunotherapy is also approved for MSI-H (microsatellite instability-high) and mismatch repair deficient (dMMR) solid tumors after progressing on prior treatments with no satisfactory alternative treatment options[2]. Patients who respond to immunotherapy tend to have a prolonged response.

Immunotherapy is mainly approved as a second-line agent in metastatic bladder cancer. Its use as a first-line agent is only limited to patients who are ineligible for cisplatin based treatments. Five drugs are approved by the FDA including three PD-1 inhibitors [Pembrolizumab, Nivolumab, Atezolizumab] and two PD-L1 inhibitors [Durvalumab and Avelumab] for patients who have progressed during or after platinum-based therapy. However only two drugs were approved based on phase III clinical trials which included a substantial number of patients – Pembrolizumab and Atezolizumab, out of which only the KEYNOTE study done with Pembrolizumab showed overall survival difference.

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Clinical trials are summarized in the tables below.

Table 1 – Metastatic Urothelial Cancer Clinical trials – approved drugs in second line setting, cisplatin refractory

Clinical Trial	Drug	Phase	Overall Survival	Progression Free Survival	Overall Response Rate	Duration of Response
KEYNOTE-0453	Pembrolizumab	3	10.3 months	2.1 months	21%	68% at 1 year
IMvigor2114	Atezolizumab PDL1 >5%	3	11.1 months	NR	23%	15.9 months
CheckMate2755	Nivolumab	2	8.74 months	2 months	19.6%	*NR*
Javelin Solid Tumor6	Avelumab	1b	13.7 months	2.6 months	18.2%	*NR*
MEDI47367	Durvalumab	1/2	18.2 months	1.5 months	17.8%	*NR*

In cisplatin-ineligible patients, Atezolizumab and Pembrolizumab are the FDA-approved checkpoint inhibitors.

Table 2 – Clinical trials leading to approved drugs for cisplatin ineligible patient

Clinical Trial	Drug	Phase	Overall Survival	Progression Free Survival	Overall Response Rate	Duration of Response
KEYNOTE-0528,8,9	Pembrolizumab	2	11.5 months	*NR*	29%	68% at 1 year
IMvigor21110	Atezolizumab	2	15.9 months	2.7 months	23%	*NR*

NR - Not Reported

However, with the approval of several immunotherapy agents for second line therapy and a lack of clinical trials comparing one versus the other – an optimal sequence is unknown.

Immunotherapy is better tolerated than chemotherapy with common side-effects of pruritus, fatigue, nausea, diarrhea, decreased appetite and asthenia. We need to be watchful of auto-immune side effects, where the immune system can attack any organ, often the thyroid, though serious toxicities are uncommon [3-7].

There are ongoing clinical trials using a combination of immunotherapy and chemotherapy in a first line setting for metastatic urothelial cancer and also to determine the duration of treatment. Additionally, there are various clinical trials studying immunotherapy alone or in combination with chemotherapy in the neoadjuvant (before surgery) and adjuvant (after surgery) settings to increase the chances of a cure. We also need better biomarkers to identify who will respond well to immunotherapy.

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Staging in Bladder Cancer

Bladder cancer is the most common malignancy involving the urinary tract. A majority of the bladder cancers are urothelial carcinomas. After establishing a diagnosis of bladder cancer, staging plays an important role for further management. Most of the solid tumors are staged using TNM staging. A primary tumor is categorized into T1, T2, T3, T4 depending upon the extent of the tumor invasion – as there is no significant difference between AJCC seventh and eighth editions. Regional lymph node metastasis - any lymph nodal involvement constitutes stage IV disease in seventh addition[2], whereas in eighth edition - lymph nodal involvement in true pelvis in combination with T1-T4a constitutes stage III disease. However, if there is a T4b primary tumor regardless of the lymph nodes status or disease beyond common iliac nodes - patients are classified as having stage IVA disease. They are classified as 4B disease, if there is involvement of organs be on para-aortic lymph nodes.

Bladder cancer TNM staging AJCC UICC 2017[1]

Primary tumor (T)

T Category	T Criteria
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Ta	Noninvasive papillary carcinoma
Tis	Urothelial carcinoma in situ: Flat tumor
T1	Tumor invades lamina propria (subepithelial connective tissue)
T2	Tumor invades muscularis propria
T2a	Tumor invades superficial muscularis propria (inner half)
T2b	Tumor invades deep muscularis propria (outer half)
T3	Tumor invades perivesical soft tissue
T3a	Microscopically
T3b	Macroscopically (extravesical mass)
T4	Extravesical tumor directly invades any of the following: Prostatic stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall
T4a	Extravesical tumor invades directly into prostatic stroma, seminal vesicles, uterus, vagina
T4b	Extravesical tumor invades pelvic wall, abdominal wall

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Regional lymph nodes (N)

N category	N criteria
NX	Lymph nodes cannot be assessed
N0	No lymph node metastasis
N1	Single regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node)
N2	Multiple regional lymph node metastasis in the true pelvis (perivesical, obturator, internal and external iliac, or sacral lymph node metastasis)
N3	Lymph node metastasis to the common iliac lymph nodes

Distant metastasis (M)

M category	M criteria
M0	No distant metastasis
M1	Distant metastasis
M1a	Distant metastasis limited to lymph nodes beyond the common iliacs
M1b	Non-lymph-node distant metastases

Prognostic stage groups

T	N	M	Stage
Ta	N0	M0	0a
Tis	N0	M0	0is
T1	N0	M0	I
T2a	N0	M0	II
T2b	N0	M0	II
T3a, T3b, T4a	N0	M0	IIIA
T1-T4a	N1	M0	IIIA
T1-T4a	N2, N3	M0	IIIB
T4b	Any N	M0	IVA
Any T	Any N	M1a	IVA
Any T	Any N	M1b	IVB

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Intravesical Gemcitabine:

A better alternative for treatment of non-muscle invasive bladder cancer?

by Jeremy Bonzo, M.D.

Jeremy Bonzo, M.D.
Urologist

Recent evidence may change the way we treat Stage I, non-muscle invasive bladder cancer. The frequent follow up, imaging, cystoscopy, and urinary studies required for treatment of non-muscle invasive bladder cancer makes it one of the most expensive cancers to treat over a patient's lifetime. Of the 80,000 patients diagnosed with bladder cancer in 2017, 75 percent were diagnosed with non-muscle invasive cancer and most of these were low grade. Low grade non-muscle invasive tumors infrequently progress to muscle invasive bladder cancer and have different biochemical and genetic properties that make them less aggressive. However, they tend to recur at a high rate and effort has been made to decrease recurrence of these tumors to decrease the morbidity and cost of patient treatment.

Courses of weekly intravesical instillations of chemotherapy or immunotherapy are used to reduce the likelihood of recurrence in patients with frequently recurring, multifocal, or large low-grade or any high-grade non-muscle-invasive urothelial cancer. A single dose of intravesical chemotherapy within 24 hours of transurethral resection of bladder tumor (TURBT) is recommended in the absence of bladder perforation because it decreases the cancer recurrent rate by 13 percent. Mitomycin C, a DNA alkylating agent, is the most commonly used intravesical chemotherapy agent. However, it is costly, often in short supply, and has side effects including contact dermatitis and irritative voiding symptoms.

Gemcitabine (2',2'-difluorodeoxycytidine) is a chemotherapeutic agent that inhibits DNA synthesis and is used systemically to treat more advanced bladder cancers. Recent evidence has suggested, however, that it is safe and maybe as effective as standard of care (mitomycin) for use as intravesical chemotherapy to prevent cancer recurrence. This was studied in the SWOG S0337 randomized clinical trial. In this study, published in JAMA in May 2018, intravesical gemcitabine administered as a single dose after resection of bladder tumor reduced the risk of cancer recurrence by nearly 20 percent and significantly reduced the risk of recurrence during a median of four years.

Although no head-to-head comparison of gemcitabine has been done to current standard (mitomycin C) it appears to be a more appealing option in the clinical setting for many reasons. One, it is readily available, whereas there are often shortages of mitomycin. Secondly, it is well tolerated, with mitomycin having a greater toxicity when instilled intravesically than gemcitabine. Third, and one of the most important in the age of cost-consciousness in health care, is that compared with mitomycin, gemcitabine is considerably less expensive (two grams of gemcitabine is $55.70 while 40 mg of mitomycin is $1,062.72).

The research published in the SWOG trial may be the beginning of a shift away from mitomycin intravesical chemotherapy and towards use of cheaper but equally and maybe even more efficacious treatments. However, prior to adopting the use of agents such as gemcitabine as standard of care, head-to- head comparisons need to be performed. In the meantime, intravesical gemcitabine poses an effective option for use after bladder tumor resection to prevent recurrences and has a low cost to the hospital and low side effect profile for the patient.

Collaboration: OLBH a Member of Markey Cancer Center Affiliate Network

Bon Secours Kentucky Health System's Cancer Care at Bellefonte program is a member of the University of Kentucky Markey Cancer Center Affiliate Network (MCCAN). The MCCAN is a group of community hospitals in the Commonwealth of Kentucky that provide high-quality cancer services and programs in their communities with the support of the University of Kentucky's Markey Cancer Center.

The MCCAN extends the Markey Cancer Center's reach so patients across the Commonwealth can receive the same high-quality cancer care close to their homes, including patients of OLBH. The affiliation gives cancer patients in the Tri-State area access to additional specialty and subspecialty physicians and care, including clinical trials and advanced technology, while allowing them to visit OLBH for most treatment. OLBH is one of 19 hospitals in the MCCAN.

For more information about the MCCAN, visit **ukhealthcare.uky.edu/markey-cancer-center/refer-patient/affiliate-network.**

Support Services *For Cancer Patients & Families*

Support Groups

Breast Cancer Support Group: Each month at OLBH's Breast Cancer Support Group a new topic is presented to those whose lives have been affected by a diagnosis of breast cancer.

Man to Man: Man to Man offers monthly support meetings for those whose lives have been affected by a diagnosis of prostate cancer.

Smoking Cessation: OLBH offers a free, eight-week smoking cessation support group that utlizes Freshstart, the American Cancer Society's quit smoking program.

To learn more concerning OLBH's free cancer-related support groups, call the OLBH ***CareLine*** at **(606) 833-CARE (2273)**.

Cancer Rehabilitation

OLBH's Cancer Rehabilitation is a comprehensive multidisciplinary program designed to offer outpatient rehabilitation services to patients and survivors. Customized programs are created to address rehabilitation needs for a variety of conditions including, but not limited to:

- Fatigue
- Numbness in feet/hands
- Weakness
- Scar tissue formation
- Poor endurance
- Lymphedema
- Decline in balance
- Difficulty swallowing
- Postural changes
- Cognitive/communication problems
- Pain
- Energy conservation
- Difficulty walking

Those experiencing problems that were not present prior to a cancer diagnosis, especially those that affect daily function and quality of life, might be candidates for cancer rehabilitation. For more information concerning OLBH's Cancer Rehabilitation program, call the Human Motion Vitality Center at **(606) 833-3517.**

Table 3 – American Joint Committee on Cancer (AJCC)
TNM Staging System for Renal Pelvis and Ureter Cancer (8th ed., 2017)

T	Primary Tumor
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Ta	Papillary noninvasive carcinoma
Tis	Carcinoma *in situ*
T1	Tumor invades subepithelial connective tissue
T2	Tumor invades the muscularis
T3	For renal pelvis only: Tumor invades beyond muscularis into peripelvic fat or the renal parenchyma. For ureter only: Tumor invades beyond muscularis into periureteric fat
T4	Tumor invades adjacent organs, or through the kidney into the perinephric fat.

N*	Regional Lymph Nodes
NX	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis
N1	Metastasis ≤2 cm in greatest dimension, in a single lymph node
N2	Metastasis >2 cm in a single lymph node; or multiple lymph nodes *Note: Laterally does not affect the N classification.

M	Distant Metastasis
M0	No distant metastasis
M1	Distant metastasis

Histologic Grade (G)

For urothelial histologies, a low- and high-grade designation is used to match the current WHO/ISUP recommended grading system:

LG	Low-grade
HG	High-grade

For squamous cell carcinoma and adenocarcinoma, the following grading schema is recommended.

GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated

Table 4 – AJCC Prognostic Groups

	T	N	M
Stage 0a	Ta	N0	M0
Stage 0is	Tis	N0	M0
Stage I	T1	N0	M0
Stage II	T2	N0	M0
Stage III	T3	N0	M0
Stage IV	T4	NX	M0
	Any T	N1	M0
	Any T	N2	M0
	Any T	Any N	M1

Standard 4.6 Monitoring Compliance with Evidence Base Guideline: Study regarding Stage 0a, I, II, and III cancer of the bladder by Dr. Jeremy Bonzo.

Study Population/ Methodology

From January 2016 to December 2017, the medical records ofpatients who were diagnosed with cancer of the bladder at OLBH were retrospectively analyzed through chart review. Stage breakdown was as follows:

Stage

- 0a: 37.5%
- 0is: 0%
- I: 12.5%
- II: 37.5%
- IIIa: 6.25%
- IIIb: 6.25%
- IV: 0%

Analysis/Results:

All patients were seen in consultation at Bellefonte and had initial resection and staging by Bellefonte or Bellefonte affiliated Urologists. Of the 16 patients, 4 patients (25%) received additional treatments at other hospitals or tertiary care centers.

Stage 0a:

- 83% (5/6) of patients received intravesical mitomycin within 24 hours after TURBT; *Recurrence rate for Low grade Ta bladder cancer is 50% , most within one year of TURBT. A single dose of intravesical chemotherapy within 24 hours of TURBT (ideally within 6 hours) is recommended in the absence of bladder perforation because it decreases the recurrence rate by 13%.*
- 33.3 % (2/6) had a tumor recurrence within 1 year and both were re-resected and given induction BCG + maintenance BCG immunotherapy which is within guidelines for recurrent low grade cancer.
- 66.6% (4/6) had follow up surveillance consistent with NCCN guidelines (cystoscopy 3, 12 month, then annually for 5 years; no cytology recommended). Of the other two patients, one was recommended annual cystoscopy and the other cystoscopy and cytology every 6 months for 3 years.

Stage I:

- NCCN guidelines were followed for 100% (2/2 patients). Re-resection which is recommended by guidelines was recommended for both patients but one patient passed away from pulmonary disease and another was lost to follow up.

Stage II:

- 75% (3/4) patients with initial muscle invasive bladder cancer who underwent cystectomy and urinary diversion received neoadjuvant chemotherapy consistent with NCCN guidelines. *NCCN recommends neoadjuvant systemic chemotherapy before cystectomy because randomized trials have shown that it achieves a 5% absolute improvement in overall survival at 5 years after treatment.*
- 1 patient experience stroke and passed away after bladder tumor resection.
- 1 patient developed high grade upper tract urothelial cancer and was not felt to be an adequate surgical candidate for required surgery (nephro-ureterectomy and cystectomy)
- 1 patient had abnormal variant disease (sarcomatoid differentiation) and was referred to tertiary center, follow up treatment/staging is unknown
- 1 patient had bladder sparing protocol and had maximal TURBT, chemo-radiation (5-FU/mitomycin) consistent with NCCN guidelines.

Stage IIIA:

- 1/1 patient with muscle invasive bladder cancer did not receive neoadjuvant chemotherapy and was pT3aN0Mx at cystectomy. They received adjuvant chemotherapy (gemcitabine/ cisplatin) consistent with NCCN recommendation. Patient subsequently developed mediastinal metastasis. *Meta-analysis suggests a survival benefit to adjuvant therapy for pathologic T3, T4, or N+ disease at cystectomy.*

Stage IIIB:

- 1/1 patient with muscle invasive bladder cancer received neoadjuvant chemotherapy (MVAC) and then underwent cystectomy and urinary diversion and was pT2N2Mx at cystectomy. He was offered adjuvant treating with PDL-1 trial but deferred. Developed inguinal node biopsies positive recurrence and started on PDL-1 inhibitor.

Recommendations/Follow up:

Non-muscle invasive bladder cancer: Recommend reinforcing importance of post-operative mitomycin-C instillation for papillary appearing low grade tumors as per NCCN guidelines to decrease tumor recurrence. Recommend reinforcing recommended NCCN follow up after diagnosis for low grade Ta bladder cancer to include cystoscopy at 3, 12 months and annually for 5 years without cytology.

Muscle invasive bladder cancer: Recommend reinforcing importance of consideration of neoadjuvant chemotherapy prior to cystectomy and urinary diversion for appropriately selected patients per NCCN guidelines.

2018 Cancer Data Summary

Percentage of OLBH Cancer Incidence by Primary Site

TONGUE	1%	OTHER SKIN	1%
SALIVARY GLANDS	1%	BREAST, FEMALE & MALE	22%
GUM & HARD PALATE	1%	CERVIX	2%
OROPHARYNX	2%	ENDOMETRIUM (CORPUS UTERI)	2%
OTHER ORAL CAVITY	1%	OVARY	1%
ESOPHAGUS	2%	OTHER FEMALE GENITAL ORGANS	2%
STOMACH	2%	PROSTATE	8%
SMALL INTESTINE	1%	BLADDER	8%
COLON	11%	KIDNEY	2%
RECTUM/ANUS	4%	OTHER URINARY ORGANS	1%
LIVER	1%	BRAIN	1%
PANCREAS	1%	THYROID	2%
OTHER DIGESTIVE TRACT	1%	NON-HODGKIN'S LYMPHOMAS	12%
LARYNX	1%	LYMPHOCYTIC LEUKEMIAS	1%
TRACHEA, BROCHUS, LUNG-SMALL	3%	MYELOID LEUKEMIAS	1%
TRACHEA, BROCHUS, LUNG-NSC	18%	OTHER LEUKEMIAS	1%
MALIGNANT MELANOMA	12%	BENIGN/BORDERLINE BRAIN, CNS	1%

Cancer Registrar's Report

OLBH began its cancer registry in 1991 to collect data from every patient diagnosed or treated for cancer at the hospital. The data plays an important role in the ongoing evaluation of cancer care. The cancer registry is a computerized data collection and analysis center that contributes to patient treatment, planning, staging, and continuity of care through data retrieval, annual analysis, and long term follow-up.

The OLBH cancer registry is a member of Kentucky Cancer Registry (KCR) and the American College of Surgeons (ACOS). Information is submitted annually to Kentucky Cancer Registry and the National Cancer Data Base, which is designed to provide an annual review of patient care, a comparative summary of hospital cancer statistics and data edit report.

All information collected for the registry is kept strictly confidential. General data however, is available for presentations, publications, reports, etc. For more information regarding the OLBH cancer registry, please call **Barb Fitzpatrick, CTR,** at **(606) 833-3252**.

2018 Cancer Committee

Dr. Kirti Jain, Chairman
Medical Oncologist-Hematologist

Dr. Phillip Lackey
Surgeon, Cancer Liaison

Dr. Brian DeFade
Urologist, Co-Cancer Liaison

Rose Guy-Chapman
Pastoral Care

Dan Spreacker
Pastoral Care

Dr. Jeremy Bonzo
Urologist

April Broun, MSW

Susan Coburn-Somon, MSW

Christy Coovert, BSN, RN, OCN
Breast Health Navigator

Dr. John Darnell, VP, CMO

Brandi Fields, MSN, RN
VP Patient Care Services

Barb Fitzpatrick, CTR

Anna Hampton, BSN, RN
Quality Improvement

Leigh Ann Holt,BSN, RN
Lung Health Navigator

Kim Jones, BSN, RN
Manager of Palliative Care

Dr. Anshu Jain
Radiation Oncologist

Dr. Terry Justice
Radiation Oncologist

Dr. Venu Konala
Oncologist–Hematologist

Shelly McComas, Pharm-D

Christi McKinney, MSN, CIC, OCN
Infection Prevention & Control/
Oncology Service Line

Dr. Eugene DeGiorgio
Radiologist

Dr. Ben Roach
Radiologist

Dr. Steve Woolley
Radiologist

Jodi Renfroe, MA
RDN/Manager, Clinical Dietetics

Dr. Gabriel Rodriguez
Pathologist

Amber Schweickart, OTR/L,CLT

Kathy Skaggs, BSN, RN
Clinical Coordinator, 2 Center

Mary Ann Stephens, APRN

Pamela Stevens, BSN, RN
Manager 2 Center

Margaret Ward, APRN
Advanced Genetics Nurse-Board Certified

Julie Walters
American Cancer Society

Jennifer Wilson
Kentucky Cancer Program

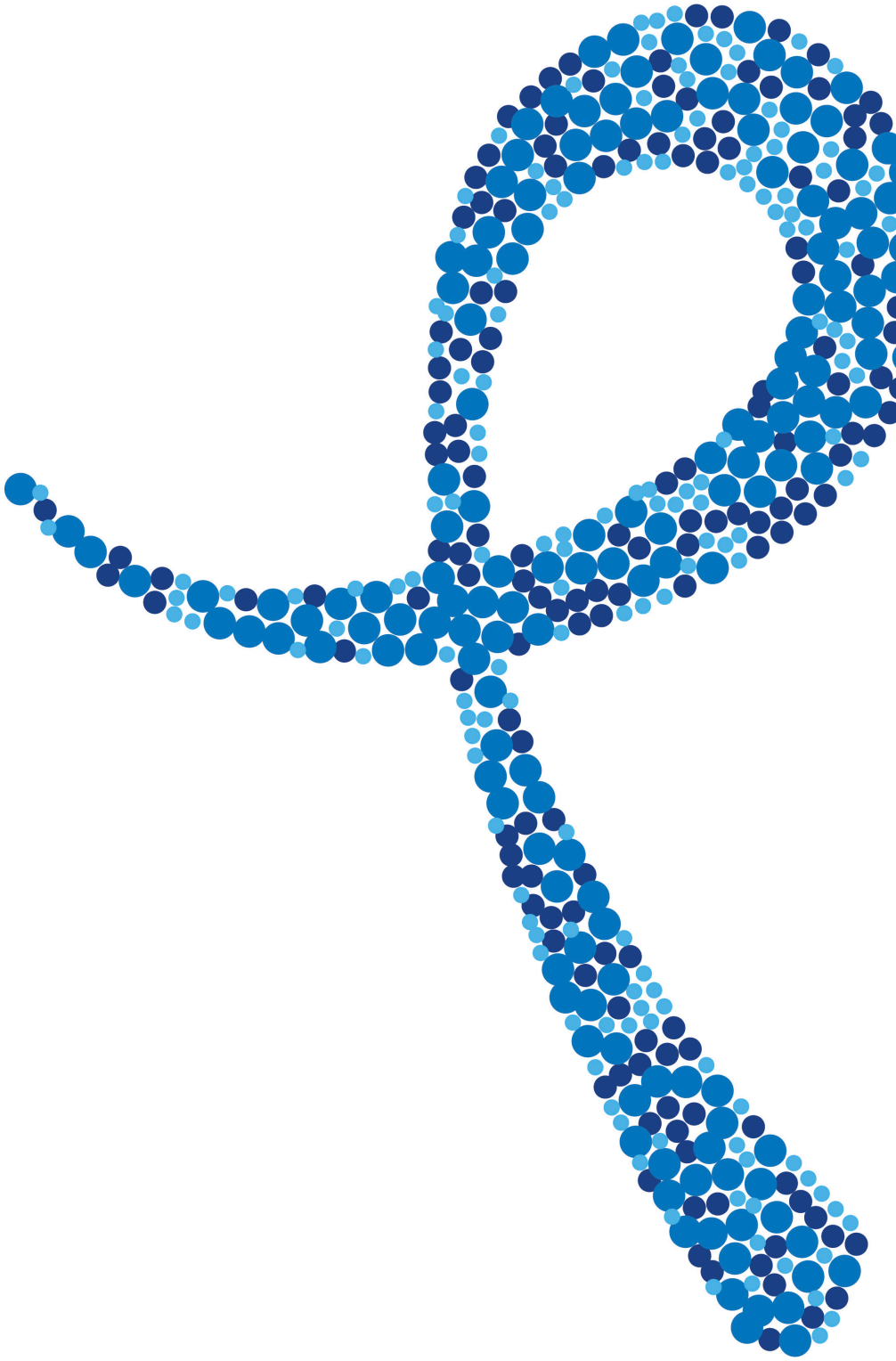
ONS
Oncology Nursing Society

Commission on Cancer

ACR
American College of Radiology
Breast Imaging Center of Excellence

HealthCare
MARKEY CANCER CENTER
Network

OLBH is affiliated with UK Markey Cancer Center. The UK Markey Cancer Center Affiliate Network enhances access to cancer services and programs through collaboration with community hospitals.



Bon Secours

Our Lady of Bellefonte Hospital