

## Metastatic Bladder Cancer

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New: 2007: Chemo plus surgery for metastases improves survival:

Impact of multimodal treatment on survival in patients with metastatic urothelial cancer. Abe T, Shinohara N, Harabayashi T, Sazawa A, Maruyama S, Suzuki S, Nonomura K. Department of Urology, Hokkaido University Graduate School of Medicine, Sapporo, Japan.  
Eur Urol. 2007 Oct;52(4):1106-14. Epub 2007 Mar 6. PMID: 17367917

Innovative Treatments - Newer Chemotherapeutic Drugs; C Barone, Oncologia Medica ,Università Cattolica S. Cuore, Roma, Dec.. 2005

May 2005: advantage of  
further chemo after pre-op chemo, cystectomy and lymph node  
involvement [click here](#)

Chemo-surgery yields 92% survival in metastatic  
TCC in those with single, small volume metastases who respond to chemotherapy: Octoboe, 2004: Is there a role for surgery in the management of metastatic urothelial cancer? The M. D. Anderson experience. Siefker-Radtke AO, Walsh GL, Pisters LL, Shen Y, Swanson DA, Logothetis CJ, Millikan RE. Center for Genitourinary Oncology and Department of Medical Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, 77030-4009, USA. PUBMED

Prolonged remission in a patient with transitional  
cell carcinoma of the bladder developing brain metastases  
after systemic chemotherapy: a case report.

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{/niftybox}Transitional Cell Carcinoma of the Urinary Tract

Diagnosis, symptoms and treatments for common metastases

Metastatic cancer in all its many forms is a formidable foe. Metastatic cancer ('mets') means that cancer cells have traveled through the bloodstream or lymph system to form a secondary tumor of the same biological make up. Only 5% of people have metastases when their bladder cancer is discovered.

Transitional cell carcinoma of the bladder and/or upper urinary tract most commonly mestastasizes to the lymph nodes, lung, bone, liver and brain, although it can appear almost anywhere. Treatments for metastatic bladder cancer vary according to the site of spread, prior therapies and the needs of individual.

If someone is diagnosed as having lymph node or involvement or tumor

outside the bladder, the option of cystectomy may be withheld (not considered worth the morbidity or the costs).

Metastatic disease is considered incurable; however a subset of patients who have stage IV disease which is local, or 'regional', such as minimal extension to pelvic organs or small volume metastases to regional lymph nodes may benefit from cystectomy with or without adjuvant chemotherapy or radiation. Chemotherapy or radiation are the treatments of choice, as well as cystectomy with an ileal conduit for palliation of symptoms.

For the NCI treatment summaries for Stage IV, metastatic or recurrent bladder cancer, [click here](#)

Chemotherapy agents that have shown activity in metastatic bladder cancer include paclitaxel, docetaxel, ifosfamide, gallium nitrate, and gemcitabine.

Molecular targets are being investigated and are of interest to those looking for options; One ongoing phase I/II trial using Herceptin plus Taxol chemotherapy appears like a hopeful option for those with Her2-overexpressed, metastatic TCC. Paclitaxel and Radiation Therapy With or Without Trastuzumab in Treating Patients Who Have Undergone Surgery for Bladder Cancer

Benefits from treatments include control of symptoms and possible prolongation of life. The most important concerns are:

Will further treatments improve my quality of life?

Will benefits outweigh risk and discomfort?

Will further treatments add to survival?

What feels most comfortable to me?

Do I feel I can manage the side effects of each treatment option? What kind of support will I have from family or friends? Outside agencies?

For help finding a second opinion [click here](#)

For a good list of links to financial aid, [click here](#)

Many studies cite the addition of 2-3 months to a person's life as justification enough for aggressive chemotherapy. Ask your doctor how many patients he's treated with the same therapy and how the patients did. Palliation of symptoms alone is still a valid goal in metastatic cancer.

Because the needs of metastatic patients are highly individual and many of the treatments are still experimental, there are no standard guidelines available to either the patient or the doctor. In some cases the decision is determined by whose opinion you seek — a surgeon will recommend surgery, an oncologist chemotherapy or a radiation oncologist radiation therapy. Often, the patient and family must decide on the course of treatment. .

When faced with two different opinions about treatment, consider seeking a third opinion from a nationally recognized cancer center. Although it

can be very difficult to focus in the face of metastases, it's important to take the time needed to investigate available options before coming to a decision.

New treatment modalities are being investigated in clinical trials for advanced bladder cancer; given that existing therapies are often inadequate, participation in clinical trials is often recommended for those with a stage IV bladder cancer diagnosis. See clinical trials

#### Diagnosis, symptoms and treatments for common metastases and complications

CT scans, MRI scans, sonograms, x-rays, bone scans are among the most commonly used diagnostic tests. PET scans may pick up things that CTs miss. A newer method which combines both the PET and the CT is even more accurate at finding metastases than PET.

Many times metastasis first makes its presence known by causing symptoms. These symptoms differ according to the site of spread and how far advanced the cancer is.

#### Lymph Nodes

Lymph node involvement may be detected after surgery during the pathology work-up, or by the individual or doctor during a physical exam. Adenopathy, or enlarged lymph nodes may be biopsied (fine needle aspiration biopsy).

Lymph nodes are found between the groin and the head, with the inguinal nodes in the groin being the ones most commonly affected by TCC.

In cases where regional (pelvic) lymph nodes are found to be involved either before or during surgery many experts feel that surgical removal of these nodes can actually be curative. For more info here at WebCafe see: [Survival Advantage with Lymph Node Removal](#)

If lymph nodes metastasize after surgery has been done, chemotherapy and/or radiation is preferred over further surgery as the disease is now considered systemic. In some cases, chemotherapy can gain significant periods of disease-free survival.

#### Further Chemo after Pre-op Chemo for lymph node metastases

A presentation at the 2005's American Urological Association's meeting discusses the usefulness of further chemo following neo-adjuvant (pre-op) chemo, cystectomy and lymph node involvement found after surgery. See the abstract [here](#)

#### Lung involvement

Symptoms usually include shortness of breath and a chronic cough. Lung metastases rarely cause pain. Metastasis can also show up as fluid produced by the cancer, which can collapse the lung. Lung metastases can be treated with chemotherapy; steroids can help relieve symptoms. Fluid in the lung can be drained in various ways.

Lung metastasis are most often treated with combinations of chemotherapy drugs with M-VAC being the most commonly used.

### Brain Metastasis

The most common symptom is headache that lasts over a long period. Radiation is usually given to shrink brain metastases. Steroids may help to reduce any swelling in the brain, and anti-seizure medication can be administered when appropriate. Chemotherapy doesn't work well on brain metastases

Surgery may be an option in certain cases (preferable one small lesion or tumor). Studies have shown that the used of combined modalities (ie: surgery+chemo and/or whole brain radiation) give better results than single mode therapy. One study showed that younger age, single metastasis, surgical resection, whole brain radiation therapy, and chemotherapy were associated with prolonged survival. Stereotactic radiosurgery (the 'gamma knife') is sometimes used, though few institutions have the equipment.

More info can be found on the Memorial Sloane Kettering Cancer Center site, covering symptoms, diagnosis and treatments: [Metastatic Brain Tumors](#)

### Liver Metastasis

Symptoms include weight loss, appetite loss, gastrointestinal disturbances, fatigue and fever. Liver metastasis is usually diagnosed by a liver scan. When pain (caused by the expanding liver pressing on the membrane that encases it) becomes too difficult to tolerate, the liver may be radiated to shrink it. Chemotherapy is usually used for liver metastases.

### Bone Metastasis

Aside from causing pain in up to 70% of people afflicted, the most serious implication of bone metastasis is that they increase the possibility of "pathological fractures", so named because they are due to problems within the bone itself rather than to external factors.

Metastatic bone lesions can be described as osteolytic, osteoblastic and mixed. The osteolytic lesions are most common where the destructive processes outstrip the laying down of new bone. Osteoblastic lesions result from new bone growth that is stimulated by the tumor. Microscopically, most lesions are mixed.

Treatment for bone metastasis is normally palliative. An assessment of the risk of pathological fracture must be made by an experienced orthopaedic surgeon. Lesions that do not represent a risk for fracture may be treated with radiation or by appropriate chemotherapy directed at the tumor.

When a weight-bearing bone, such as the leg is involved, your doctor may suggest an operation to support the bone and prevent a break. This procedure will involve reinforcing the bone with internal splints and may help relieve pain and prevent a break. The goals of surgery are to preserve stability and function of the musculoskeletal system as well as alleviate pain.

The ribs, pelvis and spine are usually first affected. Pain, which resembles ordinary low back pain or a disease such as arthritis, is usually the first sign. Standing up on the bone may compress it, causing more pain than when lying down.

Another risk from bone metastasis is hypercalcemia (a higher concentration of calcium compounds in the bloodstream). This condition can cause a number of symptoms, including dehydration, loss of appetite, nausea, thirst, fatigue, muscle weakness, kidney problems, restlessness, confusion and even death.

For an article with everything you wish you never needed to know about bone metastases: <http://www.emedicine.com/radio/topic88.htm#section~mri>

#### Zometa for bone metastases/hypercalcemia

Bisphosphonates work by slowing down the actions of bone cells.

Bisphosphonates (clodronate, pamidronate, aredia, zometa), a family of drugs used to treat osteoporosis and the bone pain caused by some types of cancer, have been investigated in large trials for breast and prostate cancer with good results at relieving bone pain and perhaps even slowing destructive processes.

Zometa, the youngest and easiest to use of the bisphosphonates, was first approved for the treatment of hypercalcemia. In February, 2002, The FDA approved Zometa (Zoledronic Acid) for patients with documented bone metastases from solid tumors, in conjunction with standard antineoplastic therapy. The trials that led to the approval of Zometa mark the first time any bisphosphonate has demonstrated efficacy in treating bone complications in patients with prostate cancer, lung cancer and other solid tumors (including bladder tumors). see; <http://www.zometa.com/index.html>

One potential side effect of Zometa included kidney damage, which can also occur with other bisphosphonates.

#### Percutaneous Vertebroplasty for Spinal Metastasis

<http://www.managedcaremag.com/archives/0003/0003.percut.html>

This is a relatively new procedure which can relieve pain and strengthen the spinal column if it has been damaged by tumor spread. A cement-like substance is inserted into weak or fractured vertebrae. Pain relief and increased mobility usually occur within a week. Treatments may be done on an outpatient basis using conscious sedations.

## Radiofrequency ablation for bone metastases and other disseminated disease

Although this treatment is not yet readily available to most patients, initial research has shown that radiofrequency ablation can provide local pain relief caused by metastatic disease in the liver, lung and kidney. Patients with very localized disease who may not require more extensive radiation therapy, are bad surgical candidates or who have been previously unsuccessfully treated with radiation therapy are potential candidates.

Radiofrequency ablation is an outpatient procedure whereby a small needle electrode is placed directly into the tumor using CT scan or ultrasound guidance. The high frequency radiowaves sent into the tumor cause heating and local necrosis of the tumor. The procedure takes between 45-90 minutes and can be performed with intravenous sedation. This technique is currently being applied to tumors involving the liver), kidneys, pancreas, adrenal gland and skeleton.

Patient selection criteria are controversial for RFA, so check the protocols on the NIH website or have your doctor call 1-800-411-1222 to see if you qualify.

### Study Trial using Radiofrequency ablation for bone metastases

Summary: A phase I/II clinical trial of percutaneous radiofrequency ablation of bone metastases using ct guidance. Radiofrequency ablation (RFA) is an image-guided minimally invasive treatment for solid tumors. Patients that have not responded to conventional treatment may benefit from palliation with RFA. For more info from the American College of Radiology Imaging Network, [click here](#) ; info on the same trial from the NCI [here](#)

Good article about RFA: [http://www.brown.edu/Departments/Diagnostic\\_Imaging/state/rf-ablation.htm](http://www.brown.edu/Departments/Diagnostic_Imaging/state/rf-ablation.htm)

New avenues of treatment are being investigated: Molecular Therapies Target Bone Metastasis MD Anderson's Oncolog, Feb. 2002

Anemia is extremely common in patients with cancer.

Low hemoglobin levels are associated with diminished quality of life and possibly decreased overall survival. Successful treatment of anemia has undeniable benefits for patients, often yielding dramatic symptomatic improvement.

The following is excerpted from: Negotiating the Terms of Your Death

Medical Advances Give Patients More Control Over How and When They Die  
By Andrea Petersen, Staff Reporter of The Wall Street Journal May 10, 2005; Page D1:

## Relieving Symptoms

The workhorse of pain medication is still morphine, a 200-year-old drug that is effective -- and controversial. That is because very high amounts can depress respiration and even cause someone to stop breathing.

But a number of more advanced pain treatments have been developed in recent years. And perhaps more significantly, palliative-care centers are finding success treating the dying with medications not necessarily meant for terminal illnesses. (There is little research on treating symptoms in the dying because studies of the very ill are difficult to do and there is scant funding.)

Doctors in the palliative-care field have had success using antiseizure drugs such as gabapentin (Neurontin) and valproate (Depakene) to treat nerve pain that often afflicts cancer patients, diabetic patients and those dying from kidney failure. Medications for osteoporosis, such as pamidronate, are now used to treat bone pain in cancer patients. Drugs that are used to treat chemotherapy-related nausea, such as granisetron and ondanesron, are now sometimes used by doctors at New York's Mount Sinai and other palliative-care programs to treat nausea that dying cancer patients may have even after stopping chemo.

Doctors are now using epidurals, such as those commonly used during childbirth, to continuously deliver morphine or other anesthetics such as bupivacaine directly to the spinal cord in patients with severe pain. While there is a risk of infection, it also means that patients can get pain relief without the sleepy, drugged-out feeling that can arise with IV or oral versions of morphine.

Keeping patients symptom-free often requires doctors to juggle multiple medications. If every symptom can't be alleviated, some doctors at hospices and palliative-care programs are now allowing patients to choose which symptoms they want addressed.

There is also some new thinking on morphine itself. Recent studies suggest that morphine, though it can depress respiration, doesn't actually hasten death. A study published last year in the journal *Chest* showed that among 75 patients withdrawn from ventilators that help them breathe, those treated with morphine and anti-anxiety medications died in about the same time as those who weren't treated. The new data have made some doctors more comfortable about using morphine in big enough doses to control pain.

## Mental Health

While deep sadness is normal and expected in dying patients, some doctors say that more-severe symptoms of depression can and should be treated -- even in patients with only a few weeks to live.

Traditional antidepressants, however, such as Prozac and Paxil can take weeks to work, time that some dying patients don't have. Now, doctors in palliative-care programs have found that using Ritalin can lift depression in just days. The approach is new: In 2000, researchers at the Cleveland Clinic published a study showing the efficacy of the drug in lifting depression in critically ill patients, and the practice has grown since then.

Ritalin isn't right for all depressed terminally ill people. Doctors say it shouldn't be used in patients with acute delirium or those with heart-rhythm problems. Physicians increasingly are also focusing on patients' emotional and spiritual health. Patients who are conscious and alert are often encouraged to celebrate their lives and reach out to families and friends.

### When to Die

The decision about when to say "enough" is now much more complicated than just whether or not to turn off the machines. Some doctors are reluctant to push aggressive treatment that will buy only a little time and perhaps cause more suffering.

### Where to Die

The movement in recent years to allow more people to die in their own homes is getting a further push from hospices and palliative-care programs. Home calls from doctors and nurses and portable medical equipment, such as morphine pumps, are making it easier for people to die in familiar surroundings. The National Hospice & Palliative Care Organization's Web site ([www.nhpco.org](http://www.nhpco.org)) allows users to search for local programs.

Andrea Peterson

### When To Stop Active Treatment?

Because of the distinction in practice between active treatment and palliation at the end of life, defining selection criteria for end-of-life services assumes critical importance.

Unless patients and families hear that the likelihood of survival is declining so that informed decision-making can occur, aggressive treatment may proceed without regard to its potential futility, attendant physical and emotional distress, and high costs.

Prognostic estimates are necessary to determine hospice eligibility. In order to qualify for hospice, patients must be certified by their physician as "terminal," defined by law as "six-month life expectancy, assuming the disease runs its normal course."

Evidence indicates that many patients, even those with very advanced disease, begin to plan realistically only after they comprehend that their own survival may be limited. Only then can informed consent discussions be initiated in which the "forgotten option" - that of a well-managed end of life - may be introduced by the compassionate and skillful physician.

Many factors enter into the clinical assessment of patients with cancer who are under evaluation for end-of-life services. In general, the malignancy should be advanced, defined as stage IV with distant metastases, and progressive, with evidence of increased burden of disease and health care utilization. Usually conventional anticancer therapy has become ineffective, is being given for palliative reasons alone, or has been declined. In some cases,

significant nonmalignant comorbid conditions make disease-directed therapy unrealistic. Frequently, the patient or family (or both) have chosen treatment goals focused on comfort and relief of suffering rather than life-prolonging therapy.

Many physicians believe that once therapeutic options have been exhausted, nothing more can be done for patients with advanced disease. Unfortunately, this attitude deprives patients, their families, and the physicians themselves of the opportunity to find comfort and to experience the benefits of care that, even if provided in the patient's home, may be as intensive as that provided in the hospital. The key to a well-managed end of life is careful attention to changing goals of treatment from curative to supportive early enough in the disease process to allow patients and families the time to benefit from palliative care. When events are managed well in alignment with patient and family preferences, all participants may come to remember the end of life as a time that can be challenging, but is often extraordinarily meaningful.

The above section 'When to Stop Treatment' was excerpted in part from the article 'Advanced Cancer and Comorbid Conditions, Prognosis and Treatment' Brad Stuart, Cancer Control 6(2):168-175, 1999. © 1999 H. Lee Moffitt Cancer Center and Research Institute, Inc Selections from 1999 - Volume 6, Number 2 from Cancer Control: Journal of the Moffitt Cancer Center Used with permission from publisher.

Further Reading: July/Aug '00 issue of the Moffitt Cancer Journal: Progress in the Management of Metastatic Bladder Cancer (PDF file: 129Kb] <http://www.moffitt.usf.edu/pubs/ccj/v7n4/toc.htm>

Advances in the Treatment of Metastatic Bladder Cancer Nicholas J. Vogelzang, MD -- Writer: Michelle L. Plante, PharmD, online article at Medscape, registering is required, then search for 'advances bladder' for the article.

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