

Treatments May Alleviate and Reverse Central Nervous System Radiation Necrosis

By Jill Delsigne

Although radiation therapy is effective against many tumors of the brain and spine, it also damages normal tissue.

One of the most debilitating types of damage is radiation necrosis of the central nervous system (CNS). But in recent years, treatments have been found that can slow—and in some cases reverse—this damage.

CNS radiation necrosis may cause any of the following

symptoms: abnormal headaches, seizures, personality changes, difficulty concentrating or reading, a sense of slowing down, focal weakness, or problems with speech. These symptoms can appear during or just after radiation therapy (acute injury), within a few weeks or months after treatment (early delayed injury), or 6 months to many years after treatment (late radiation injury). Acute and early delayed injuries can usually be reversed with steroid therapy, and sometimes they appear to spontaneously resolve. Late radiation injury is the most serious kind of damage and usually is irreversible.

Prevalence and causes

A retrospective study from The University of Texas MD Anderson Cancer

Center found that CNS radiation necrosis developed in 36 (24%) of 148 patients treated with radiation and chemotherapy after surgical resection of glial tumors; of those patients, 16 (44%) had both necrotic lesions and recurrent or residual tumors. Several studies have shown that combining radiation therapy and chemotherapy increases the incidence of brain necrosis to three times that seen with radiation therapy alone. This combination disrupts the blood-brain barrier, which allows chemotherapy to more effectively target tumor cells; unfortunately, this disruption of the blood-brain barrier also makes normal brain tissue vulnerable to damage.

Even though radiation necrosis was first reported more than 60 years ago, potential mechanisms for this condition



These magnetic resonance images of a child with radiation necrosis show the typical "Swiss cheese" or "soap bubble" enhancement pattern of necrotic lesions.



Bevacizumab with chemotherapy shows promise in germ cell tumors



Postsurgical treatments for early-stage testicular cancer House Call Patients and caregivers find support online



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Alleviating Central Nervous System Radiation Necrosis [Continued from page 1]

have only recently been discovered. It has been shown that CNS radiation necrosis is associated with increased cytokine production. According to this model, radiation therapy causes vascular abnormalities in the brain that reduce blood vessel density, ultimately restricting the blood supply to brain tissue (chronic ischemia). Ischemia, in turn, causes infiltrative tumor cells and adjacent astrocytes to respond by producing cytokines, such as vascular endothelial growth factor (VEGF), to help the tumor cells or astrocytes survive. In addition to irradiation, some chemotherapy drugs also cause ischemia and may exacerbate necrosis.

Irradiation of the CNS can also produce damage to the myelin sheath of neurons (demyelination). This appears to be caused by the effect of radiation on the oligodendrocytes that make and repair the myelin covering neuronal axons. This effect is seen early on magnetic resonance images of most patients treated with radiation therapy, with or without chemotherapy.

Diagnosis

CNS radiation necrosis is difficult to diagnose accurately because it often appears the same as a progressive tumor on diagnostic imaging. Radiation necrosis usually occurs at the treatment site but can also be distant, usually near a cerebral ventricle; necrosis can also be diffuse or multifocal and resemble tumor metastasis.

Ashok J. Kumar, M.D., a professor in the Department of Diagnostic Radiology at MD Anderson, was the first author of a seminal study published in 2000 of imaging patterns that differentiate radiation necrosis from brain tumors. According to Dr. Kumar, diagnosing radiation necrosis remains difficult, but experienced physicians can recognize the patterns of necrosis and treat it early. Dr. Kumar said radiation necrosis lesions have a "Swiss cheese" or "soap bubble" enhancement pattern on magnetic resonance imaging (MRI). However, this pattern does not provide a definitive diagnosis.

On diffusion-weighted MRI, which

"[T]he fact that even short treatment with bevacizumab seems to turn off the cycle of radiation damage further confirms the central role of VEGF in the process."

- Dr. Victor Levin

measures the magnitude and direction of free water movement, tumors tend to restrict water movement, whereas necrosis tends to increase water mobility. On magnetic resonance spectroscopy, necrotic lesions tend to exhibit reduced levels of *N*-acetyl aspartate and creatine, whereas tumors tend to exhibit high levels of choline. Magnetic resonance perfusion, which measures the relative cerebral blood volume, can indicate necrotic lesions, but this modality also detects fast-growing tumors that exceed their blood supply.

None of these imaging modalities can differentiate necrosis from tumor progression (or necrotic lesions mixed with a recurrent tumor) definitively. Even invasive tests such as biopsy cannot definitively distinguish between necrosis and recurrent cancer owing to sampling error. Experienced physicians and radiologists can learn to recognize signs that indicate a high probability of necrosis versus tumor progression. A diagnosis of CNS radiation necrosis instead of cancer is not cause for relief, however. Necrosis can have the same debilitating effects as a tumor and can even be fatal if unchecked.

Treatment

Until just a few years ago, treatment for CNS radiation necrosis was restricted to alleviating its symptoms. Physicians have long prescribed corticosteroids to control swelling and psychostimulants to address psychomotor slowing and fatigue in patients with CNS necrosis. Corticosteroids also help counteract the radiation-induced vascular damage that can disrupt the blood-brain barrier. Sometimes symptoms return if patients stop using the steroids, so problems arising from chronic steroid use must also be treated. Anticoagulants, such as warfarin or heparin. can slow the progression of necrosis in some patients. Hyperbaric oxygen treatment can help restore oxygen concentrations to a normal level in order to encourage angiogenesis. Patients can also undergo brain surgery to remove necrotic tissue.

In 2009, a group at MD Anderson revolutionized treatment options for radiation necrosis. They found that bevacizumab, a monoclonal antibody that prevents blood vessel growth in tumors by blocking VEGF, also causes necrotic lesions in the brain to regress, reversing radiation damage. This observation spurred the design of a doubleblind, placebo-controlled phase II trial of bevacizumab as a therapy for CNS radiation necrosis. Treatment involved four cycles of bevacizumab (7.5 mg/kg intravenously every 3 weeks). At a median 10 months' follow-up, 9 of the 12 patients treated with the drug had necrotic lesion shrinkage on MRI. This trial provided class I evidence of the efficacy of bevacizumab as a treatment for CNS radiation necrosis.

"Just the fact that bevacizumab works has helped us understand much more about what happens in radiation necrosis," said Victor A. Levin, M.D., a professor emeritus in the Department of Neuro-Oncology at MD Anderson and the senior researcher on these studies. "We presume necrosis is related to the release of cytokines like VEGF, since bevacizumab is very specific and only reduces VEGF levels. We think aberrant production of VEGF is involved with radiation necrosis of the brain, and the fact that even short treatment with bevacizumab seems to turn off the cycle of radiation damage further confirms the central role of VEGF in the process." Astrocytes try to protect neurons by expressing VEGF,

but this strategy threatens the brain by causing a leak in the blood-brain barrier. Bevacizumab turns off this cytokine loop and reduces plasma leakage across brain capillaries, thus reducing brain edema.

MD Anderson researchers presented at the Society for Neuro-Oncology conference in November 2011 on the ability of diffusion-weighted MRI to predict which patients are most likely to benefit from bevacizumab treatment.

Although some researchers have claimed that a larger study is needed to validate bevacizumab as a standard treatment for CNS necrosis, Dr. Levin asserts that the success of each treatment outside of a research study adds to the growing evidence of its efficacy. He currently treats primary brain tumor patients as part of the Kaiser Medical Group in California and continues to prescribe bevacizumab, both pre-emptively to minimize radiation damage and after treatment to reverse radiation necrosis.

While research for treatments continues, advances in radiation therapy may reduce the incidence and severity of CNS necrosis and other side effects by minimizing radiation damage to healthy tissue. Dr. Levin said that proton therapy may prove to be such an advance because radiologists can calculate the trajectory of the proton to pinpoint the release of energy to occur precisely when the proton reaches the tumor cell, minimizing damage to the surrounding healthy tissue. Although this new technique also has caused instances of radiation necrosis, Dr. Levin is hopeful that it will lead to fewer cases of radiation necrosis compared with other treatment modalities.

These exciting developments in radiation therapy and treatment options for CNS radiation necrosis offer hope for CNS cancer patients and survivors.

FOR MORE INFORMATION

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BRIEF

Bevacizumab With High-Dose Chemotherapy Shows Promise for Cisplatin-Refractory Germ Cell Tumors

Bevacizumab given concurrently with high-dose chemotherapy elicits encouraging results in patients with treatment-refractory germ cell tumors, according to the preliminary results of an ongoing phase II study.

Although high-dose chemotherapy alone is curative for many patients with recurrent germ cell tumors, a low rate of event-free survival is seen in patients with recurrent disease whose tumors have developed cisplatin resistance or who present with high levels of tumor markers at the time of relapse.

The purpose of the study was to determine whether the addition of the antiangiogenic drug bevacizumab to high-dose chemotherapy helps control germ cell tumors. Bevacizumab inhibits vascular endothelial growth factor, a protein that is highly expressed in metastatic germ cell tumors. Bevacizumab also increases drug penetration into tumors.

The 23 patients enrolled so far in the study have undergone a median of 4 prior chemotherapy regimens (range, 2–6 regimens). Sixteen of the patients have undergone prior surgery to remove metastases. The patients received bevacizumab (5 mg/kg) 1 week before each of 2 cycles of high-dose chemotherapy with stem cell support. The first chemotherapy cycle consisted of a novel regimen of gemcitabine with docetaxel, melphalan, and carboplatin; the second cycle consisted of ifosfamide, carboplatin, and etoposide. Patients received an autologous stem cell infusion after each cycle.

The most prominent side effect of the first cycle of high-dose chemotherapy

was mucositis, which resolved. Three patients died of infections unrelated to their tumors following the first cycle of chemotherapy.

Of the remaining 18 patients, 15 received the second cycle of high-dose chemotherapy at a median of 49 days (range, 38–66 days) after their first stem cell infusion. All patients tolerated the second chemotherapy cycle well. Residual lesions were resected in 8 patients, with biopsy findings of necrosis or mature teratoma in all cases. At a median follow-up time of 25 months, the event-free survival rate was 68%.

Researchers from The University of Texas MD Anderson Cancer Center presented the study's preliminary results in an abstract at the annual meeting of the American Society of Clinical Oncology in June.



Quarterly discussion of cancer types for which there is no standard treatment or more than one standard treatment

Early-Stage Testicular Cancer

Postsurgical treatment varies according to tumor stage and histology

By Sunni Hosemann

Introduction

Inguinal orchiectomy is the standard initial treatment for patients who present with a testicular mass considered suspicious. The diagnosis and staging of testicular cancers are then made by pathological analysis, and subsequent management decisions are guided by the tumor's histologic subtype and assigned stage.

Most testicular cancers (95%) are germ cell tumors either seminomas (40%) or non-seminomas (60%)—and this discussion is limited to those types. Tumors are considered non-seminomas if they contain any histological component that is not pure seminoma.

Serum tumor markers—specifically, the beta subunit of human chorionic gonadotropin (β -hCG) and alpha fetoprotein (AFP)—also have a role in staging and treatment decisions for testicular cancers. According to Louis Pisters, M.D., a professor in the Department of Urology at The University of Texas MD Anderson Cancer Center, elevated β -hCG levels may be seen in patients with seminomas or non-seminomas, but elevated AFP levels are seen only in patients with non-seminomas. Therefore, tumors are categorized and treated as non-seminomas when increased AFP is present, even if pathological analysis has not detected a non-seminoma tumor component.

In this discussion, early-stage disease refers to stages IA and IB (pT1–pT4, N0, M0). These stages include primary tumors that are limited to the testis and those that involve adjacent structures (tunica albuginea, tunica vaginalis, spermatic cord, or scrotum) with or without evidence of lymphovascular invasion (LVI) but have not involved regional lymph nodes or metastasized to distant sites.

Testicular cancer

The National Cancer Institute estimates that 8,590 new cases of testicular cancer and 360 testicular cancer–related deaths will occur this year. Testicular cancer is highly treat-

able and curable and is often detected early. The survival rate for all men with testicular cancers is 95%; for men with early-stage disease, it is over 99%. "The cure rate for stage I disease approaches 100%, and even metastatic disease is curable," Dr. Pisters said. "But it is not 100%, and we still see patients who die of both seminoma and non-seminoma."

More than half of the testicular cancer cases in the United States are diagnosed in men between the ages of 20 and 34 years. Testicular cancers in older men are more commonly found to be seminomas. Non-seminomas tend to be more aggressive.

Testicular cancers follow a very predictable pattern of spread via the retroperitoneal lymph nodes, which are located behind all the major organs in the abdomen and extend upward along the aorta and vena cava. The lymphatic vessels of the testes follow the gonadal blood vessels as they ascend through the spermatic cord and continue upward along the aorta and vena cava to the renal hila. These lymphatic vessels' location deep in the abdomen, their proximity to major organs, and the distance they span have implications for both surgical and radiation therapies. It is important to note that this pattern of spread initially bypasses the pelvic nodes; therefore, disease in the retroperitoneal lymph nodes would be considered regional.

Notably, the pattern of lymph drainage from the scrotum is different from that of lymph drainage from the testes. Lymph in the scrotum first drains to the lower extremities; thus, it is prudent to avoid enabling the escape of cancer cells from a diseased testicle into the scrotum, which would result in two potential pathways of spread. This is why needle biopsies of the testicle are avoided and orchiectomy is performed via the inguinal route rather than through the scrotum.

Treatment overview

After orchiectomy, the question becomes: is further treatment warranted at this time, or is active surveillance a better option?

For early-stage testicular cancers, the objective of additional treatment is to prevent disease relapse due to subclinical or occult metastases. Thus, postoperative treatment modalities are aimed at the retroperitoneal lymph nodes where the cancer first spreads. Disease recurs in 25%–30% of patients with non-seminomas and 15%–20% of patients

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with seminomas. Fortunately, the cure rate is very high in patients treated for recurrent disease, and their survival is equivalent to that achieved with pre-emptive treatment. However, compared with preemptive treatment, treatment for recurrent disease is more intense and carries higher risks of long-term sequelae.

According to Dr. Pisters, risk stratification is possible for non-seminomas using serum tumor markers and pathological characteristics. Predictors of a high risk for relapse include evidence of LVI or embryonal carcinoma cells' making up more than 80% of the tumor. Relapse occurs in about half of patients with high-risk characteristics.

Postoperative treatment options

Postoperative treatment options for stage IA and IB

seminomas include active surveillance, radiation therapy, or chemotherapy. For non-seminomas, the standard options for stage IA disease are active surveillance or retroperitoneal lymph node dissection (RPLND). The options for stage IB non-seminomas are active surveillance (for T2 only), RPLND, or chemotherapy.

Active surveillance is an option for patients with stage IA or IB seminomas or stage IA non-seminomas. Surveillance is generally not recommended for patients with stage IB non-seminomas because the disease will recur in 50% of these patients, but it is an option for selected patients who are compliant with follow-up. Active surveillance consists of follow-up visits at specified intervals. Evaluations at these visits include abdominal pelvic computed tomography, chest radiography, and monitoring of serum tumor marker levels. Patients with seminomas remain on active surveillance for 10 years, and those with non-seminomas are monitored for 5 years. The time span of these clinic visits is a limiting issue for some patients.



Radiation therapy has long been a standard option for stage IA and IB seminomas. However, according to Karen Hoffman, M.D., an associate professor in the Department of Radiation Or.cology, the treatment paradigm for these tumors has changed over time. Historically, pre-emptive radiation therapy was delivered to lymph nodes in the paraaortic and ipsilateral pelvic regions. "This produced excellent survival rates—near 100%," she said. Thus, for a time, it was standard procedure to treat patients with radiation therapy after crchiectomy.

"However, it became known that the incidence of second malignant neoplasms occurring later in life was increased in these patients and in some cases caused premature deaths," Dr. Hoffman said. Over time, studies confirmed that the radiation field could be reduced to exclude the ipsilateral pelvic nodes and that the radiation dose to para-aortic nodes could be decreased from 3C to 20 Gy without compromising survival. "This was important because we believe that this reduction in field size and radiation dose reduced the risk of radiation-related second malignancies," Dr. Hoffman added.



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Advances such as computed tomography-based planning and proton radiation therapy have resulted in a more precisely targeted delivery of radiation. However, some risk remains, so although radiation is still used elsewhere, it is no longer a preferred option at MD Anderson in patients with no known lymph node involvement. Dr. Hoffman instead discusses the option of active surveillance with all her patients with earlystage disease for whom it is an option.

"Currently, if I treat an early-stage seminoma patient with radiation at all, I use proton therapy," Dr. Hoffman said. Proton beams have a lower entrance dose than conventional photon radiation, deliver the therapeutic dose over a discrete area, and have no exit dose. Therefore, proton radiation treatment of the para-aortic lymph nodes delivers a lower dose to adjacent organs, including the pancreas and gastrointestinal tract. "Although proton therapy has not been around long enough to gauge its long-term effects and has not been compared head-to-head with conventional radiation delivery, we know that it reduces the unnecessary radiation dose to tissues outside the target field, which should decrease longterm side effects," she said.

RPLND is a standard option for patients with stage IA or IB non-seminomas, in whom the surgery usually provides definitive treatment.

RPLND is usually done through a large transabdominal midline incision and involves removing lymphatic tissue from around the great vessels. In the past, the operation involved a full bilateral dissection and usually resulted in nerve damage that caused loss of ejaculation and emission capability. Today, smaller dissection fields are used to spare these nerve bundles and retain as much function as possible.

Standard options for patients with stage IA non-seminomas are pre-emptive RPLND or active surveillance. Some patients who opt for active surveillance will not need further treatment, and those who undergo RPLND when disease recurs have outcomes similar to those of patients who undergo early surgery.

Patients with stage IB non-seminomas who require or want additional treatment rather than surveillance must choose between RPLND and chemotherapy. "The surgery is a large and serious operation—an extensive abdominal surgery," Dr. Pisters said. "Most patients prefer the chemotherapy."

For these reasons, Dr. Pisters said, RPLND has fallen out of favor as a treatment for most of the early-stage testicular cancers discussed here and is rarely used at MD Anderson. The exception is a small subset of patients who have a teratoma with malignant transformation—a rare but very aggressive histologic type for which RPLND is the only option.

Chemotherapy is a standard option for patients with stage IA or IB seminomas or stage IB non-seminomas. According

to Lance Pagliaro, M.D., a professor in the Department of Genitourinary Medical Oncology, chemotherapy is a safe and effective alternative to RPLND or radiation therapy.

For seminomas, the standard adjuvant chemotherapy is carboplatin, which has relatively mild side effects and can be administered on an outpatient basis either as a single dose or in two doses 3 weeks apart. A large randomized trial found equivalent rates of relapse-free survival in patients receiving single-dose carboplatin and patients receiving radiation therapy after orchiectomy.

"Two questions arise, however," Dr. Pagliaro said. "The first is whether we can improve outcomes with two cycles instead of one, and the second is what are the effects after 10 or 20 years or longer?" Answering these questions will require data from follow-up visits over many years. In the meantime, noting that most recurrences are prevented with the first dose, he considers single-dose therapy safer.

In the event of a recurrence during active surveillance or after chemotherapy, treatment outcomes are excellent, but either radiation therapy or intensive combination chemotherapy is required.

"I regard surveillance as the least morbid option for seminomas," Dr. Pagliaro said. "Most are cured without the need for further treatment. Plus, we don't have sufficient data about the long-term risks of some postoperative treatments."

However, Dr. Pagliaro believes that there are patients with early-stage seminomas for whom a single course of carboplatin should be strongly considered. These patients include:

- Patients with tumors larger than 4 cm classified as pT3. "These patients have a higher risk of recurrence—about 1 in 3," he said.
- Patients 50 years or older, in whom seminomas are more common. These patients have fewer concerns about fertility or long-term sequelae.
- Patients of any age who are concerned about future access to health care. This includes men in their teens or early 20s who are currently covered by their parents' insurance policies and whose future insurance coverage is uncertain. Chamatherapy is also an option for patients with store IB

Chemotherapy is also an option for patients with stage IB non-seminomas. For these patients, the most important risk factors are histological type and evidence of LVI. For patients who are considered to be at high risk of recurrence, the chemotherapy options are one or two cycles of bleomycin, etoposide, and cisplatin (BEP). "This is the same chemotherapy that is used for recurrence, but less is given if used up front," Dr. Pagliaro said. "Although two cycles have not been proven clearly superior to one, we know that two cycles reduces recurrence risk from 50% with surveillance to 2%," he said.

No study so far has compared one versus two cycles of BEP directly. However, a large risk-adapted trial that com-[Continued on page 8]

Online Cancer Support Networks

Patients and caregivers find support online



Sometimes you need more than a friend—you need a friend who understands exactly what you're going through. This can be especially true if you or someone close to you has cancer. Even if you have plenty of supportive family members and friends, you may feel as though not everyone "gets it."

A fast way to find people who can relate to your experience with cancer is through an online social network for people who have experienced cancer. Online networks such as Cancer Survivors Network, I Had Cancer, and Know Cancer can help point you to people in situations similar to your own, whether you're facing a mastectomy or dealing with an infection after a stem cell transplant. Whether your remission is on the horizon, out of reach, already attained, or uncertain, you can often find someone else in the same boat.

Some networks are for people with a certain type of cancer (e.g., Colon Club, Leukemia and Lymphoma Society), and others target specific demographic groups such as young adults (e.g., Stupid Cancer, Planet Cancer).

Information

Many cancer communities not only link people but also promote discussion. For example, The Cancer Forums has an array of discussion threads for current and former patients and caregivers to share anecdotes and useful links on topics such as specific cancer types. pain, clinical trials, nutrition, and finances. In addition to a survivor message board, the Anderson Network hosts weekly online chats on cancer treatment and related topics with experts from The University of Texas MD Anderson Cancer Center. The Living Room on the Cancer Support Community Web site offers a variety of chat rooms and discussion groups. Because these sites attract members



from all around the world, you're likely to find someone online at any time.

In addition, you can follow the ongoing narratives of other cancer survivors or begin a story of your own through blogs. Many cancer patients maintain blogs over the course of their illnesses; visit Blog for a Cure to find thousands of cancer blogs organized by cancer type, disease stage, and geographic location.

Another archive of personal narratives about cancer is the Voices of Survivors Web site, which collects videos of cancer survivors talking about their experiences and writings by survivors about the idea of survival. Some people opt for simpler means of sharing updates, such as Facebook or Tumblr.

Support

But not all social media are for sharing the details of your life with people you've never met before. To keep only specific people in the loop, you can make your own private Web page for publishing updates, such as written entries and photos, while letting readers post words of encouragement. One such service, CaringBridge, includes a planner to help coordinate care and various tasks between supporters. Similarly, the Cancer Support Community site has an area where you can create a personal Web page with sections for updates, a calendar, links for learning about your specific disease, requests for financial

help, and inspirational photos and quotes.

Of course, there are ways to connect that are more direct than using a computer. For example, the Anderson Network Telephone Support Line (800-345-6324 or 713-792-2553) has a database of around 2,000 survivors and caregivers who are ready to talk. Call the line, and volunteers may be able to link you with a survivor who has gone through treatments or experiences similar to yours. This service is available in English and Spanish, as many survivors in the network are bilingual or speak Spanish only. The survivors who connect through this service are proof that intimidating situations are not hopeless.

A glimmer of hope or a word of encouragement can make a big difference when you're fighting cancer. Online communities, forums, blogs, and other media can be valuable resources; however, remember that any advice you get on the Internet cannot replace a visit with your doctor. You should consult your health care team before making health decisions.

Social networks can empower you and extend your community, making it easier for you to discover useful information and to remember that you're not alone.

– S. Bronson

FOR MORE INFORMATION

- Talk to your physician
- Contact the Anderson Network at andersonnetwork@mdanderson.org, www.facebook.com/AndersonNetwork, or twitter.com/andersonnetwork
- Visit www.mdanderson.org
- Call askMDAnderson at 877-632-6789

The Web sites for the social networks mentioned in this article can

be found by an Internet search using their name, and links to these sites are provided with the online version of this article at www.mdanderson.org/oncolog.

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pared chemotherapy to surveillance after orchiectomy in patients with stage I nonseminomas found a 90% reduction in recurrence rate with only one cycle. Therefore, the difference in recurrence rates between patients who receive one and two cycles of BEP could be relatively small-4% versus 2%. Dr. Pagliaro's current view is that because most recurrences are eliminated with one course, the benefit of less treatment outweighs the risk of treating 100 patients with a second course to prevent two recurrences.

For the average-risk patient with a stage IA non-seminoma, Dr. Pagliaro considers active surveillance the safest choice. But for select patients, such as those who might be less likely to tolerate chemotherapy later or those who have concerns about compliance with surveillance schedules, one course of BEP could be reasonable. "Most long-term chemotherapy effects are associated with three or more courses of therapy," he said. "We have not seen serious treatment effects with only one course."

Patient preferences

Treatment for stage I testicular cancers must be individualized, and substantial discussions are needed to help patients weigh the various options and choose between surveillance and postoperative treatment. In many cases, personal circumstances and preferences weigh as

heavily in the decision as purely medical considerations. In all cases, sperm banking should be discussed before any treatment is initiated.

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