

New Targeted Therapy Offers Hope to Patients with Blastic Plasmacytoid Dendritic Cell Neoplasm, Related Diseases

By Joe Munch

The treatment of common hematological malignancies is based on reams of study data and years of physician experience with the diseases. But such information is often limited for rare, little-researched blood cancers like blastic plasmacytoid dendritic cell neoplasm (BPDCN). This situation may soon change, thanks to the discovery of a new molecular target, which has led to a spate of innovative treatment approaches and the first dedicated clinical trials for this uncommon malignancy.

"When I first became interested in BPDCN about 7 years ago, there was practically nothing on it, but now there's an explosion of research going on," said Naveen Pemmaraju, M.D., an assistant professor in the Department of Leukemia at The University of Texas MD Anderson Cancer Center. "A number of exciting and novel clinical trials and ap-

Photos taken before (left) and after 4 months of treatment with SL-401 show improvement in skin lesions in a patient with blastic plasmacytoid dendritic cell neoplasm. Reprinted with permission from Frankel AE, et al. Blood 2014;124:385–392.

proaches are rapidly coming out for this disease, which previously had no available therapies."

And these advances in BPDCN also have implications for related diseases.

A rare, aggressive disease

Although BPDCN has been long recognized as a distinct clinical entity, its name has changed frequently. Previously known as natural killer blastic cell lymphoma, CD4+ CD56+ hematodermic tumor, blastic natural killer lymphoma, and natural killer cell leukemia, among other names, BPDCN was

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“Now that we’re seeing that CD123 can be targeted in BPDCN, we’re running a new clinical trial of SL-401 dedicated to this other set of relatively rare diseases.”

– Dr. Naveen Pemmaraju

given its current designation by the World Health Organization in 2008.

“BPDCN was once thought to be an exceedingly rare tumor. But now, with better pathology, classification, and recognition, it appears to be a bit more common than previously believed,” Dr. Pemmaraju said. To illustrate this point, he said, “This year, I’ve had one or two patients per month referred for BPDCN treatment. In contrast, our institution saw only approximately 26 confirmed BPDCN patients from 1998 to 2014.”

BPDCN is primarily a disease of the bone marrow and blood cells, but unlike most other leukemias, BPDCN can also affect the skin. “This is a predominant feature of the disease,” Dr. Pemmaraju said. BPDCN, which tends to occur in older men, can also affect the lymph nodes and has a predilection for the central nervous system and brain.

“BPDCN is also a startlingly aggressive disease, on the order of acute leukemias like acute myeloid leukemia [AML] and some high-risk acute lymphoblastic leukemias [ALLs],” Dr. Pemmaraju said. “We have patients who can go from presenting with skin-only disease to a terminal acute leukemic phase in a year or less.”

Owing to the rarity of BPDCN, there has been very little research into its treatment, which is largely borrowed from the other leukemias. Thus, patients with BPDCN typically receive a combination of AML and ALL treatments that may include multi-agent

intensive chemotherapy (e.g., cyclophosphamide, doxorubicin, vincristine, and prednisone [CHOP] or cyclophosphamide, vincristine, doxorubicin, and dexamethasone [hyperCVAD]), central nervous system prophylaxis, radiation therapy, and stem cell transplantation, along with skin treatment as needed.

“But even with those aggressive therapies, the median overall survival for BPDCN patients historically has been only 1–2 years,” Dr. Pemmaraju said. “This is unacceptable to us as providers and researchers.”

A new target in BPDCN

CD123 (also known as interleukin-3 receptor) is a cell-surface protein involved in the proliferation and differentiation of hematopoietic cells. Whereas normal hematopoietic cells have no or low CD123 expression, virtually all BPDCN cells overexpress CD123. This overexpression ramps up the production of BPDCN cells, enabling them to overcrowd normal, healthy cells.

“CD123 is so primitive in its expression that some researchers think that it is carried on leukemia stem cells, the early or primordial cells that may be predecessors to some of the cells that give rise to these cancers,” Dr. Pemmaraju said.

In addition to its overexpression in BPDCN, CD123 is overexpressed in a number of other hematological disorders—including AML, chronic myeloid leukemia, myelodysplastic syndrome, chronic myelomonocytic leukemia (CMML), and myeloproliferative neoplasms—albeit to a lesser extent than in BPDCN.

“CD123 is differentially expressed between leukemia cells and normal cells,” said Marina Konopleva, M.D., Ph.D., an associate professor in the Department of Leukemia. “This principle can be exploited to target the receptor and destroy leukemia cells without harming normal cells.”

Targeting CD123

The CD123-targeting agent furthest along for BPDCN treatment is SL-401,

a recombinant fusion protein comprising a diphtheria toxin fused with interleukin-3. The drug’s origins can be traced to the work of Dr. Arthur Frankel, now at The University of Texas Southwestern Medical Center in Dallas.

The interleukin-3 domain of SL-401 binds to CD123 on the cancer cells, which then take up the entire molecule. “Once the agent has been internalized by the cells, the release of the diphtheria toxin essentially stops protein synthesis, and the cells die from within,” Dr. Konopleva said.

The results of a multicenter pilot trial of SL-401, published in *Blood* last year, are promising. Of nine patients with recurrent or chemotherapy-refractory BPDCN who were evaluable for response, five had a complete response and two had a partial response after just one cycle of SL-401. The median response duration was 5 months (range, 1–20+ months).

“It was an active drug to say the least,” Dr. Pemmaraju said. “Some of these patients’ debilitating skin lesions disappeared, the bone marrow disease improved, and the lymph nodes improved.”

“It’s clear that BPDCN is highly sensitive to this approach,” Dr. Konopleva agreed. “And we’re hoping that SL-401 could be used instead of or in conjunction with stem cell transplantation to improve patients’ survival outcomes.”

The study reported few grade 3 or 4 toxic effects—thrombocytopenia, transaminase elevations, neutropenia, and hyponatremia—all of which were transient. The hyponatremia and milder adverse effects experienced by some patients appeared to be related to vascular leak syndrome. The low-grade effects included hypoalbuminemia, edema, hypocalcemia, uremia/elevated creatinine, fatigue, and headache; although these usually resolved within a few days, persistent hypoalbuminemia was managed with parenteral albumin and diuretics.

“The differential expression of CD123 between tumor and normal cells is very important, because otherwise

you'd see more toxic effects." Dr. Konopleva said. "CD123 is expressed on a fraction of normal hematopoietic stem cells, causing some degree of suppression of normal bone marrow. Liver function abnormalities are common in patients who receive SL-401, but it's not very clear why this is the case.

"So we still see some toxicity," Dr. Konopleva continued, "but we believe that at least for the malignancies that express very high levels of the receptor, like BPDCN, there's clearly a therapeutic window where SL-401 can affect the tumor without causing major side effects."

Positron emission tomography/computed tomography scans taken before (left) and after 6 months of treatment with SL-401 show shrinkage of involved inguinal lymph nodes (arrows) in a patient with blastic plasmacytoid dendritic cell neoplasm. Reprinted with permission from Frankel AE, et al. Blood 2014;124:385-392.

Beyond BPDCN

Following the promising findings of the pilot study of SL-401 in BPDCN patients, clinical trials of the drug at MD Anderson and other centers are now enrolling patients with other hematological diseases. "Oftentimes in oncology, discoveries from rare diseases can spur research in other tumor types," Dr. Pemmaraju said. "That's what's happened here."

AML

Drs. Pemmaraju and Konopleva, as part of an interdisciplinary team of collaborators, are now conducting a multicenter phase I/II trial of SL-401 that includes patients with AML as well as those with BPDCN.

The investigators have just submitted the preliminary results of their trial to the American Society of Hematology and hope to present these findings at the society's annual meeting in December.

While earlier studies of SL-401 have indicated potential activity against AML, Dr. Pemmaraju said, "The results of our ongoing trial will shed more light on this subject."

"I think it remains to be seen what the benefit in AML will be," said Dr. Konopleva, the trial's principal investi-

gator. "There's a lot of hope that SL-401 will be successful, but I think we need more data to determine that."

Myeloproliferative neoplasms and CMML

Dr. Pemmaraju, extending what he's learned about BPDCN to other rare hematological diseases, is the principal investigator for another clinical trial of SL-401, this one for patients with high-risk myeloproliferative neoplasms. This group of chronic blood disorders includes the three classic myeloproliferative neoplasms: polycythemia vera (excess red blood cells), essential thrombocythosis (excess platelets), and myelofibrosis (abnormal bone marrow resulting in decreased red blood cell production). Other, rarer myeloproliferative neoplasms include hypereosinophilic syndromes (also called hypereosinophilic disorders) and systemic mastocytosis.

"Among the three classic myeloproliferative neoplasms, myelofibrosis is the most deadly; it can turn into an acute process very quickly," Dr. Pemmaraju said. "We see patients with such varied outcomes with myelofibrosis—for example, a person with lower-risk disease may have decades to live, but a patient whose disease transforms or starts as

high risk may have only a few years."

Although myeloproliferative neoplasms are more common than BPDCN, they have very few U.S. Food and Drug Administration–approved therapies. In fact, myelofibrosis has only one, ruxolitinib, which is for intermediate- to high-risk disease. And the only standard therapies for CMML are those already approved for myelodysplastic syndrome. However, studies have shown that in some cases, myeloproliferative neoplasms and CMML express CD123.

"So we have these other life-threatening blood cancers that have little to no

standard therapy," Dr. Pemmaraju said. "Now that we're seeing that CD123 can be targeted in BPDCN, we're running a new clinical trial of SL-401 dedicated to this other set of relatively rare diseases."

The multicenter four-arm trial is currently enrolling patients with myelofibrosis, CMML, systemic mastocytosis, and advanced symptomatic hypereosinophilic disorders.

Minimal residual disease

Researchers also want to see if SL-401 can prevent relapse in patients with high-risk disease that is in remission. Dr. Konopleva is the principal investigator for a phase I/II clinical trial of SL-401 in AML patients with minimal residual disease.

"It's believed that this approach may be most effective in targeting the CD123-expressing stem cells that survive standard chemotherapy," Dr. Konopleva said. "Patients with high-risk AML in remission may or may not have detectable residual disease, but based on their clinical experience, we know that their survival is very short and they relapse early on; and cytotoxic chemotherapy usually doesn't help to cure them."

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Targeted Therapy

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By eliminating the stem cells of minimal residual disease, Dr. Konopleva said, she and her colleagues hope to prevent relapse. “We are hopeful that this approach will be very beneficial, because some of the other maintenance approaches with chemotherapy have not shown substantial benefit. We hope we can change that,” she said.

Emerging strategies

The recombinant fusion protein approach used in SL-401 for targeting CD123 is the furthest along, but other ways of targeting CD123 are in the works.

“We’re very interested in CD123 as a tumor-specific antigen, and of course there are other approaches that we can use to target it,” Dr. Konopleva said.

Such approaches include the use of monoclonal antibodies conjugated with cytotoxic agents, which have been shown in preclinical trials to target and destroy CD123-expressing cells; “naked” antibodies against CD123, which have shown promise in AML patients with minimal residual disease; T cells engineered to express CD123-specific chimeric antigen receptors; and bispecific T cell engager antibodies, which can be engineered to link T cells to CD123-expressing tumor cells.

“We’re going to learn as much as we can about CD123’s modulation behavior before, during, and after therapy. We’ll continue to explore all tumors, solid and hematological, to see which of these express CD123 and in what proportion,” Dr. Pemmaraju said. “Once we identify the tumors that could be targeted, we can develop clinical trials that are safe and efficacious for testing new treatments.” ■

FOR MORE INFORMATION

Dr. Naveen Pemmaraju.....713-792-4956

Dr. Marina Konopleva.....713-794-1628

FURTHER READING

Frankel AE, Woo JH, Ahn C, et al. Activity of SL-401, a targeted therapy directed to interleukin-3 receptor, in blastic plasmacytoid dendritic cell neoplasm patients. *Blood* 2014;124:385–392.

Laparoscopic Free Omental Lymph Node Transfer Offers a Powerful Alternative for Lymphedema

By Bryan Tutt

Armed with new laparoscopic and microsurgical techniques, surgeons are revisiting the use of omental flaps to safely and effectively treat lymphedema in breast cancer patients.

“Lymphedema is a horribly morbid disease without a cure,” said Alexander Nguyen, M.D., an assistant professor in the Department of Plastic Surgery at The University of Texas MD Anderson Cancer Center. Paraphrasing the consensus statement of the International Society of Lymphology, he added, “The closest thing we currently have to a cure is microsurgery.”

Vascularized lymph node transfer—in which lymph nodes are transplanted from one part of the body to another using microsurgical techniques—has been shown to improve lymphedema symptoms and reduce the volume of affected limbs. In some cases, however, the use of such flaps can cause lymphedema at the donor site.

In search of a donor site

The groin and supraclavicular lymph nodes are often used as donor sites for vascularized lymph node transfers to treat lymphedema of the arm. However, the removal of lymph nodes from these sites sometimes results in lymphedema of the leg or contralateral arm.

The safety of lymph node transfers has been improved by a treatment algorithm developed by Dr. Nguyen and colleagues in the Department of Plastic Surgery. Dr. Nguyen has also worked with Franklin Wong, M.D., Ph.D., a professor in the Department of Nuclear Medicine, to map the lymph nodes in

the donor sites so that surgeons can identify and spare those most essential to the limb.

Despite measures that reduce the likelihood of donor site lymphedema following lymph node harvest, the possibility remains. This is especially true for obese patients, who are at higher risk for postoperative lymphedema. “Unfortunately,” Dr. Nguyen said, “a person who is at risk for lymphedema in the upper extremity may also be at risk for lymphedema of the lower extremity.”

To find lymphatic tissue that could be harvested without causing lymphedema elsewhere in the body, Dr. Nguyen revisited a donor site that had shown promise in the past: the omentum.

New techniques for an old idea

In addition to its abundant lymphatic structures, the omentum has immunogenic properties that fight infection. Dr. Nguyen reasoned that these properties would benefit patients with lymphedema, many of whom experience recurring infections in the form of cellulitis or lymphangitis.

Using the omentum as a flap donor site for lymphedema treatment was not a new idea. Surgeons performed omentum transfers to treat lymphedema of the arm and leg more than 40 years ago, but there were risks associated with the open procedure used to access the omentum and especially with the use of a pedicled flap. “Forty-plus years ago, surgeons needed to open the abdomen and didn’t transfer the omentum as a free flap; they left it attached to the blood supply,” Dr. Nguyen said. “This left a large incision to recover from and a vascular clothesline for the intestines to get twisted around, and patients had bowel obstructions and other devastating complications.” Thus, even though using the omentum as a donor site yielded good results for the lymphedema—over 50% of patients reported improvement—surgeons stopped performing the procedure because of the risks involved.

lymphatic Flap Transfers for Lymphedema Treatment

Left: An omental flap removed laparoscopically is ready to be used as a free flap in a lymphedematous limb. Right: Fluorescence imaging highlights the omentum's lymphatic structures. Images courtesy of Dr. Alexander Nguyen.

Dr. Nguyen and Hiroo Suami, M.D., Ph.D., an assistant professor in the Department of Plastic Surgery, hypothesized that modern surgical techniques could reduce these risks while improving the lymphatic quality of the flap. “We have a team of surgeons who are cross-trained in various techniques,” Dr. Nguyen said. “So we developed a procedure that combines supermicrosurgery, routine microsurgery, and laparoscopic surgery to perform a laparoscopic free omental lymphatic flap transfer.”

In the new procedure, surgeons use a minimally invasive technique to harvest the omental lymphatic tissue. “We map the lymphatic structures of the omentum,” Dr. Nguyen said, “and then we harvest the critical lymphatic structures of the right half of the omentum, which has more lymphatic structures and larger blood vessels.”

The flap is transplanted to the recipient arm or leg and can be placed proximally or distally as determined by preoperative imaging and physical examination. Microsurgical techniques are used to anastomose blood vessels in the omental flap to both an artery and a vein to provide adequate perfusion. The surgeon also performs a lymphovenous anastomosis, connecting the lymphatic vessels in the flap with the venous draining system.

“Compared to the groin or supraclavicular flap, I think that the omental flap is much more powerful.”

– Dr. Alexander Nguyen

Promising results

The omental flap's lymphatic structures are mapped intraoperatively using lymphography. “When we inject the indocyanine green dye into the flap, it just flies through the omentum, confirming its lymphatic effectiveness,” Dr. Nguyen said. “In lymph node transfers from other donor sites, the dye doesn't move as quickly; it just sits there.” Similar results are seen on postoperative lymphograms.

The new procedure was first performed in November 2013 in two patients with lymphedema of the arm following surgery for breast cancer. “These patients' lymphedema has improved, their arms are lighter, and the skin quality is better—the skin used to be like leather, and it's now softer,” Dr.

Nguyen said. He added that both patients had experienced frequent infections in their lymphedematous arms before surgery but not afterward.

Dr. Nguyen has since seen similar results in more than 20 patients treated with the procedure. Only one patient experienced flap loss, Dr. Nguyen said, and this most likely was caused by concurrent venous hypertension of the leg. None of the patients has had donor site complications.

“We've had success early on,” Dr. Nguyen said. “I've had patients who no longer wear compression garments and who are off the maintenance antibiotics they needed for recurrent infections.”

Moving forward

The infection-fighting properties of the omentum also make omental flaps useful for other reconstructive procedures. Dr. Nguyen said he has used laparoscopic omental flap transfers to repair pelvic defects, perform scalp reconstructions, cover chest defects, and correct breast reconstruction defects. These flaps have also been used to treat head and neck lymphedema.

For cancer survivors with lymphedema of the arm or leg, Dr. Nguyen said, the omental flap offers promise as an effective treatment without the risk of lymphedema in another limb near the donor site. “Compared to the groin or supraclavicular flap, I think that the omental flap is much more powerful,” Dr. Nguyen said. “Long term, this may be the game changer.” ■

FOR MORE INFORMATION

Dr. Alexander Nguyen.....713-794-1247

ADDITIONAL RESOURCES

Nguyen AT, Suami H. Laparoscopic free omental lymphatic flap for the treatment of lymphedema. *Plast Reconstr Surg.* 2015;136:114–118. (Supplemental video: <http://links.lww.com/PRS/B336>.)

Naproxen Shows Potential for Chemoprevention in Patients with Lynch Syndrome

By Jill Delsigne

People with Lynch syndrome face a high risk of colorectal cancer. But researchers think that reducing this risk may be as easy as taking a daily over-the-counter pill.

Chemoprevention in Lynch syndrome

Up to 5% of colorectal cancers are caused by Lynch syndrome, which results from germline mutations in the DNA mismatch repair genes. Lynch syndrome increases the risk of colorectal cancer from around 5% to 50%–80%.

Researchers have found that chemoprevention with daily high-dose aspirin can reduce the cancer risks associated with Lynch syndrome. However, the potential for gastrointestinal bleeding or other problems from the long-term use of high-dose aspirin may discourage physicians from prescribing this treatment.

A possible alternative to high-dose aspirin for chemoprevention was found when a mouse model of Lynch syndrome showed that naproxen was a more effective chemoprotective agent than aspirin. This chemoprotective effect was seen even at relatively low doses of naproxen. On the basis of these results, the National Cancer Institute approached Eduardo Vilar Sanchez, M.D., Ph.D., an assistant professor in the Department of Clinical Cancer Prevention at The University of Texas MD Anderson Cancer Center, to arrange a phase I placebo-controlled double-blind trial of naproxen in participants with Lynch syndrome. He and his colleagues are studying the safety of naproxen in this group as well as the molecular changes that the drug induces in the normal colorectal mucosa.

Clinical trials

In the ongoing trial, study participants receive a daily dose of placebo or 440 mg or 220 mg of naproxen. Both naproxen dosages are similar to the over-the-counter recommended dose (one or two 220-mg tablets).

Study participants undergo a colonoscopy at baseline and after 6 months of treatment. Researchers measure prostaglandin E2 levels and other proteins in participants' blood, urine, and tissue samples to determine how long-term use of naproxen affects tissues, messenger RNA, and microRNA signatures. The tissue samples are also analyzed for biomarkers that may help determine who will benefit most from naproxen chemoprevention. The researchers are also studying possible side effects such as ulcers, heart attacks, and kidney problems.

The trial has recruited about 30 patients from MD Anderson and other centers. So far, naproxen has been well tolerated, and preliminary safety results were reported in July at the European Society for Medical Oncology's World Congress on Gastrointestinal Cancer. Because the trial is double-blind, efficacy results will not be available until after the trial has been completed.

"At the conference, we also demonstrated the feasibility of recruiting healthy participants with rare genetic mutations into clinical trials," Dr. Vilar Sanchez said. "In the past, it has been challenging to execute and complete clinical trials for carriers of rare mutations." MD Anderson has been particularly successful at recruiting patients for the trial; at annual colonoscopy screenings, patients with Lynch syndrome are invited to participate in the trial. "The trial gives patients with Lynch syndrome opportunities beyond screening and colonoscopies to be involved in research and to actively prevent cancer," Dr. Vilar Sanchez said.

The trial is still accruing patients, with a goal of 60 participants. The phase I trial will end in December 2016, and Dr. Vilar Sanchez plans to launch a

Lynch Syndrome Genetic Counseling and Care

Lynch syndrome, caused by a germline mutation in any of the DNA mismatch repair genes (*MLH1*, *MSH2*, *MSH6*, or *PMS2*), is an autosomal dominant disorder. For this reason, children of patients with Lynch syndrome have a 50% chance of harboring the mutation.

Most guidelines encourage families with one or more members who were diagnosed with colorectal or endometrial cancer before the age of 50 years to be referred for genetic counseling and consideration of genetic testing. Additionally, the Evaluation of Genomic Applications in Practice and Prevention Working Group recommends that any person diagnosed with colorectal cancer be screened for Lynch syndrome so that family members can be notified of their potential risk.

Dr. Vilar Sanchez emphasized that patients with Lynch syndrome and their family members need specialized care. He said that patients with Lynch syndrome should be screened yearly for colorectal cancer and other cancers for which they may have a high risk.

For more information on Lynch syndrome and other hereditary cancer predisposition syndromes, visit <http://bit.ly/1hUJ0bm>. ■

phase II clinical trial in 2017 to investigate whether naproxen at safe doses can prevent cancer. ■

FOR MORE INFORMATION

Dr. Eduardo Vilar Sanchez.....713-745-4929

To learn more about the ongoing clinical trial of naproxen for chemoprevention in people with Lynch syndrome, visit www.clinicaltrials.org and select study No. 2013-0698.



Preparing for a Hospital Stay

What to bring—and what to leave at home—to make your stay more pleasant

Staying at a hospital can be overwhelming; however, preparing for the experience can help make this time away from home a little less stressful. The following is a general overview of items that you should pack before checking in to the hospital.

Important documents

Talk to your doctor or hospital staff to find out which documents you need to bring. These documents can include insurance, Social Security, Medicare or Medicaid, and identification cards. Please note that international patients may need to provide a different set of documents. Place your important documents in a folder that can be closed to make sure they do not get lost.

Ask your health care provider what medical information you should bring. This information might include a list of your medications, including the doses and schedule; medical records such as x-ray films and lab results; and a list of allergies. If the hospital gave you forms to fill out before arrival, be sure to have those completed and ready to go. Bring paper and pens to record any notes or questions.

If you have an advance directive, such as a living will or written power of attorney, bring a copy of it with you. Be sure to make your wishes regarding your health care known to your relatives and the hospital staff.

Clothing and other necessities

The right type of clothing can help you find comfort in a tiresome and sometimes stressful experience. Pack comfortable clothes such as pajamas, nightgowns, or lounge wear. Short sleeve shirts are recommended because an intravenous line will likely be placed in the arm. You should also bring a sweater, bed jacket, shawl, or blanket in case you feel cold. Furthermore, comfortable underwear, socks, non-skid slippers, and a pair of regular shoes could prove to be essential.

As far as toiletries are concerned, remember to bring a toothbrush, toothpaste, skin care products, deodorant, soap, shampoo, hairbrush, earplugs, lip balm, baby wipes, and hand sanitizer. Do not pack anything that is heavily scented. Furthermore, before coming to the hospital, be sure to bathe and remove any makeup, including nail polish. Check with your hospital before bringing electric appliances such as a hair dryer or electric shaver; some hospitals do not allow these. Finally, be sure to pack eyeglasses, dentures, or other assistive devices.

Even though hospitals are safe environments, theft can still occur. For that reason, it would be wise to leave jewelry and other valuables at home. In addition, be sure to label any personal items that do make their way into the hospital. Avoid bringing large amounts of cash. Some hospitals have rooms equipped with personal safes; you may want to find out if your hospital does before bringing valuable items.

Entertainment and decorations

During your hospital stay, you may experience some boredom or need a distraction. Thus, it is a good idea to bring books, magazines, journals, puzzles, games, a deck of cards, or stationery to help pass the time. Portable

crafts that are not messy, such as knitting and stitching, also can be a good source of entertainment.

You may be able to bring devices to listen to music or stream movies; however, many hospitals have strict rules regarding the use of electronic items. Certain devices, such as cell phones, can interfere with hospital equipment and are banned in some hospitals. If cell phone use is not permitted, buy a pre-paid long-distance phone card and bring a list of phone numbers. Reach out to the hospital to get a full list of approved electronic devices.

If you're going to be in the hospital for more than a couple of days, bring photographs, stuffed animals, or other mementos to make your hospital room feel like home. These, along with cards and flowers, can help make your hospital room more inviting and comfortable.

Following these recommendations while preparing for the hospital can help ensure a more pleasant hospital stay. ■

– K. Nair

FOR MORE INFORMATION

- Ask your physician
- Visit www.mdanderson.org
- Call askMDAnderson at 877-632-6789

IN BRIEF

Beta-Blockers May Prolong Ovarian Cancer Patients' Survival

The use of beta-blockers for hypertension or heart disease may prolong survival in patients with epithelial ovarian cancer, a study led by investigators at The University of Texas MD Anderson Cancer Center has reported.

The study's findings, published online in *Cancer* in August, build on research indicating that stress hormones fuel the progression of ovarian and other cancers and show that beta-blockers stifle that effect.

"Beta-blockers target a receptor protein in heart muscle that causes the heart to beat harder and faster when activated by stress hormones," said Anil Sood, M.D., a professor in the Department of Gynecologic Oncology and Reproductive Medicine and the study's principal investigator. "Our research has shown that the same stress mechanisms impact ovarian cancer progression, so these drugs could play a new role in cancer treatment."

The multi-institutional retrospective analysis, which included 1,425 ovarian

cancer patients who received chemotherapy with or without beta-blockers (given for any reason) between 2000 and 2010, revealed that the median overall survival duration of the patients who received beta-blockers (48 months) was significantly longer than that of the patients who did not receive beta-blockers (42 months; $p = 0.04$). Of the 269 patients who received beta-blockers, 193 (71.7%) received adrenergic receptor- β_1 selective agents (SBBs), and 76 (28.3%) received nonselective beta antagonists (NSBBs).

The patients who received NSBBs had a significantly longer median overall survival duration (95 months) than did the patients who received SBBs (38 months; $p < 0.001$). The NSBB results highlight the importance of the adrenergic receptor- β_2 signaling pathway, which NSBBs target, in driving ovarian carcinogenesis.

"While these data are encouraging," Dr. Sood said, "given the retrospective nature of the current study, additional studies are needed before these drugs are used for cancer indications. Feasibility studies are under way that will help guide additional studies."

Two clinical trials, one led by MD Anderson (Study No. 2011-0800), are evaluating the combination of chemotherapy and the NSBB propranolol in patients with newly diagnosed epithelial ovarian carcinoma. ■

"[T]he same stress mechanisms [inhibited by beta-blockers] impact ovarian cancer progression."

— Dr. Anil Sood

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