An Overview of Hematologic Malignancies

Hematologic malignancies are cancers that affect blood, bone marrow, and lymph nodes. This classification includes various types of leukemia (acute lymphocytic [ALL], chronic lymphocytic [CLL], acute myeloid [AML], chronic myeloid [CML]), myeloma, and lymphoma (Hodgkin’s and non-Hodgkin’s [NHL]).

History

Although solid tumors such as breast malignancies were described and treated as early as 1500 BCE in ancient Egypt, the first description of a hematologic malignancy did not occur until 1832, following the introduction of an innovative achromatic microscope by Joseph Lister in 1830. Thomas Hodgkin, one of the most prominent pathologists of his time, used Lister’s microscope to describe tissue abnormalities associated with an enlargement of lymphoid tissue, spleen, and liver. This form of lymphoma was later named for him by Samuel Wilks, who described the same disease 33 years later. Numerous physicians in the early 19th century had observed that some of their patients had abnormally high levels of white blood cells, leading them to call the associated condition weisses blut, or “white blood.” The first definitive descriptions of leukemia came in 1844 from Rudolph Virchow, a German politician and physician with wide-ranging interests in cell biology, pathology, and anthropology. Myeloma was also first described in 1844, when Samuel (Continued on page 3)
From the Medical Director

Blood is a marvelous fluid containing cells, proteins, nutrients, and much more.

Some blood cells carry oxygen to all the tissues of the body; others fight infection, help identify self vs. nonself, and help to maintain the integrity of our vascular system and keep us from bleeding. It is no wonder that when a malignancy involves the blood cells or the organs that form them, the results can be devastating.

Baylor Charles A. Sammons Cancer Center at Dallas has a long history of treatment, research, and education in the area of hematologic malignancies. The Blood and Marrow Transplant Program was established in 1983 and has performed more than 4,800 transplants. In the past year, more than 170 patients participated in more than 40 hematologic malignancy clinical trials throughout our system.

In this issue of CancerUpdate, we focus on our Hematologic Malignancy Program. The lead article provides an overview of hematologic malignancies through the ages—and here at Baylor Sammons Cancer Center. Other articles highlight our blood and marrow transplantation program, hematopathology, and the use of precision medicine in the treatment of hematologic malignancies.

I hope that you find this issue informative and useful. Please feel free to “circulate” it.
Solly first documented the case of a patient with “mollities ossium” (soft bones). One year later, Henry Bence Jones found that the urine of a mollities ossium patient exhibited a peculiar thermal solubility caused by the presence of a protein that became known as Bence Jones protein. Ultimately, Bence Jones proteins were identified as free monoclonal immunoglobulin light chains. By 1900, J. H. Wright reported that myeloma tumors originated from plasma cells. Wright’s patients may have been the first in whom X-rays demonstrated characteristic lytic lesions in the ribs.

Demographics of Hematologic Malignancies

Taken together, hematologic malignancies accounted for 9% of all newly diagnosed cancers in the United States last year. As shown in the accompanying table, lymphomas (especially NHLs) are much more common than leukemias or myeloma. With the exception of ALL and Hodgkin’s lymphoma, these diseases tend to be associated with increasing age. This will be progressively more important with the rising average age of the U.S. population: the number of people who are >65 years old will double during the first third of the 21st century, as will the number of people >85 years old. In addition to having an increased incidence of hematologic cancers, older patients may have reduced tolerance for intensive therapy, underlining the importance of developing less toxic, targeted treatment approaches.

Demographic Data for Hematologic Malignancies in the United States

<table>
<thead>
<tr>
<th>Type of disease</th>
<th>Estimated new cases for 2012*</th>
<th>Estimated deaths for 2012*</th>
<th>Median age at diagnosis**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia (all types)</td>
<td>47,150</td>
<td>26,830</td>
<td>66</td>
</tr>
<tr>
<td>Acute lymphocytic</td>
<td>6,050</td>
<td>1,440</td>
<td>14</td>
</tr>
<tr>
<td>Chronic lymphocytic</td>
<td>16,060</td>
<td>4,580</td>
<td>72</td>
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<tr>
<td>Acute myeloid</td>
<td>13,780</td>
<td>10,200</td>
<td>66</td>
</tr>
<tr>
<td>Chronic myeloid</td>
<td>5,430</td>
<td>610</td>
<td>64</td>
</tr>
<tr>
<td>Myeloma</td>
<td>21,700</td>
<td>10,710</td>
<td>69</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>79,190</td>
<td>43,120</td>
<td>64</td>
</tr>
<tr>
<td>Hodgkin’s</td>
<td>9,060</td>
<td>1,190</td>
<td>38</td>
</tr>
<tr>
<td>Non-Hodgkin’s</td>
<td>70,130</td>
<td>18,940</td>
<td>66</td>
</tr>
</tbody>
</table>

* Data from the American Cancer Society, 2012
**Data from the Surveillance, Epidemiology, and End Results (SEER) database, 2005–2009

A Brief History of Treatment Approaches

Nearly 200 years ago, when the first description of Hodgkin’s lymphoma was published, hematologic cancers were quickly and uniformly fatal in most cases. Today’s treatments can result in extended remissions and, for some cancers, cures.

In the last half of the 19th century, a common treatment for CML and Hodgkin’s lymphoma was arsenic, given as a combination of arsenic trioxide and potassium bicarbonate known as Fowler’s solution. Around the turn of the 20th century, palliative radiation treatment was introduced for the treatment of leukemia. Shortly after it came into wide use in the 1920s, it was discovered that radiation could be a cause as well as a treatment for leukemia. This association was detected because many early radiologists tested the strength of radiation from their machines on their own arms, looking for a dose that would produce erythema. Not surprisingly, many developed leukemia.

In the late 1940s, after the Second World War, chemotherapeutic agents began to be developed, including alkylating agents (derived from research on mustard gas during the war), adrenocortotropic hormones, and folic acid antagonists. As the result of numerous trials of multidrug therapy, some of which were initially criticized as “unscientific” and “toxic,” today nearly 70% of children with leukemia and 80% of children and adults with Hodgkin’s lymphoma are cured. Remission is common in adults with acute leukemia.
Progress in the treatment of myeloma has been slower. Urethane was used with little benefit until 1960, when phenylalanine mustard (melphalan) became the standard of care. New treatments, including proteasome inhibitors and thalidomide analogues, have yielded better results, and derivatives of these agents are currently the focus of intensive research.

In 1913, the New York Times reported on an attempt to treat ALL with a blood transfusion from the patient’s twin brother. This concept of replacing diseased cells with healthy ones eventually saw fruition in the development of autologous and allogeneic stem cell transplantation. Autologous transplants are now used routinely in the treatment of myeloma and aggressive NHL, with the expectation of a cure in the right setting. They are also used for the treatment of low-grade NHL, with somewhat less success. Allogeneic transplants are standard treatment for AML, ALL, and selected patients with CLL, with curative intent.

An explosion of technological developments from 1975 to 2000 allowed the introduction of the first rationally designed targeted therapies. Based on an ever-growing knowledge of the signaling pathways involved in carcinogenesis, the promise of these drugs is to effectively treat specific tumors in specific patients, while avoiding the side effects associated with traditional chemotherapy.

In this relatively short period of time, the whole way we look at CML has changed. With the introduction of imatinib and related agents, CML is becoming a truly chronic disease. This is why we want to continue research.”

Alan M. Miller, MD, PhD

Clinicians at Baylor Sammons Cancer Center are involved in 37 clinical trials testing various approaches to improving treatment outcomes for patients with hematologic cancers. These studies are administered through Baylor Research Institute or through the US Oncology network. They represent alliances with industry (e.g., Seattle Genetics, Celgene, Pfizer, Eisai), with other institutions (e.g., Mayo Clinic, Johns Hopkins), and with collaborative groups (e.g., Southwest Oncology Group, Multiple Myeloma Research Consortium). Some pilot studies or early stage translational patient trials may be funded through the Baylor Sammons Cancer Center’s Research Grant Program, an internal funding mechanism that is supported by the Baylor Health Care System Foundation. Many of these studies are designed to test new targeted agents (small molecule TKIs, antibodies, antibody-cytotoxic agent combinations) to see how they will fit into the standard armamentarium of available treatments, particularly stem cell transplant. Some are investigating new classes of cytotoxic agents, including proteasome inhibitors for the treatment of multiple myeloma. And some are focusing on diseases such as ALL in adults, in which progress to date has been limited in comparison with the success seen in the treatment of children. In addition to advanced phase III trials, a large number of phase I/II trials are in progress at the Innovative Clinical Trials Center, a new facility at Baylor Sammons Cancer Center that offers patients coordinated access to clinical examinations, infusions, imaging studies, sample collection for lab work, and follow-up associated with trial participation. These early stage clinical trials are an essential component in bring-
ing new treatments from the bench to the bedside, and they can also offer a new direction for patients with few remaining treatment options.

For the last 3 years, a Hematologic Malignancy Steering Committee has come together each month at Baylor Sammons Cancer Center to discuss all potential research protocols available for our patients. The goal is to foster integration between our transplant and nontransplant hematologic malignancy teams and to endeavor to have a well-rounded menu of trials available for our patients.

With the recent launch of the Baylor Sammons Cancer Center network, the power of numbers can be brought to bear on recruitment for clinical trials. The inclusion of the medical centers at Fort Worth, Plano, Garland, Irving, Grapevine, and Waxahachie increases the number of analytic patients with hematologic cancers treated last year to more than double that seen at the Dallas center alone (498 vs. 237). The patient nurse navigator system works to identify patients from other centers who might be candidates for active trials. We are also working to help open clinical trials at some of the regional sites, so the flow of patients will not be unidirectional.

Facilities at Baylor Sammons Cancer Center

While some patients with hematologic cancers may receive some or all of their treatments on an outpatient basis at the Baylor Sammons Cancer Center Outpatient Blood and Marrow Transplant (BMT) Clinic, hospitalization is frequently required for at least part of their treatment, especially if they receive a stem cell transplant. Baylor T. Boone Pickens Cancer Hospital provides two floors with 48 beds for patients with hematologic cancers. The BMT unit occupies a 24-bed induction unit on the 7th floor. A 24-bed nursing unit on the 6th floor handles overflow from the BMT unit, as well as serving hematologic oncology patients who require hospitalization for other reasons. All rooms in the hospital are attractive and spacious and include space and facilities for caregivers to stay with the patients while they receive treatment. This is important, since the length of stay for transplant patients may extend to 3 weeks or longer.

Many hematologic oncology patients come to Baylor Sammons Cancer Center from locations outside of Dallas to receive stem cell transplants. Twice Blessed House, a

*Patient room at Baylor T. Boone Pickens Cancer Hospital*
program of Baylor Health Care System, provides affordable housing for transplant patients (including organ transplant) and their caregivers coming from more than 50 miles away during the evaluation process and after transplant if they require transitional care. Housing is provided at reduced rates in 44 fully furnished apartments close to Baylor Sammons Cancer Center. Twice Blessed House offers van transportation to and from treatment, local shopping areas, churches, etc., as well as providing a sense of community for people undergoing the transplant experience.

Another option for long-term stays in the Dallas area will be provided by Hope Lodge, a patient and caregiver housing project being developed through a collaboration between Baylor University Medical Center at Dallas and the American Cancer Society. There are currently 33 other Hope Lodges across the country, funded by private donations to the American Cancer Society. The facility will be built on a 1.5-acre plot of land donated by Baylor Dallas. It will provide free lodging and support for 50 cancer patients and their caregivers who have to travel more than 50 miles one way to Dallas for care at Baylor Sammons Cancer Center or at other institutions in the Dallas area. Guests are provided with private bedrooms and bathrooms but share communal living and kitchen areas. This offers an opportunity to get to know other patients, meet their families, share meals, and exchange tips. Maria Clark, regional vice president of the American Cancer Society, is excited about the collaboration with Baylor Dallas. She commented: “When you don’t have housing or transportation, sometimes the option is to abandon treatment. We are trying to remove those obstacles. We share the enthusiasm of Baylor about the potential for Hope Lodge to really make a difference for cancer patients and their families who travel to Dallas.”

In the rest of this issue of CancerUpdate, we focus on recent progress and ongoing research in the major components of successful treatment for hematologic oncology patients: stem cell transplantation through the Baylor Dallas BMT program, new directions in targeted therapy, and advances in hemopathology.
Pursuing Excellence in Hematopoietic Stem Cell Transplantation: The Blood and Marrow Transplant Program at Baylor University Medical Center at Dallas

Stem Cell Transplantation at Baylor Dallas

Stem cell transplantation using bone marrow-derived stem cells was pioneered by a team at the Fred Hutchinson Cancer Research Center led by E. Donnall Thomas, MD, whose work was recognized with a Nobel Prize in Physiology of Medicine in 1990. Thomas began his work in the late 1950s. At that time, bone marrow transplants were used only as a last resort; survival rates were grim, and many patients developed life-threatening complications. Clinicians were aware of the importance of matching blood types, but tissue typing based on 8 to 12 different genes was still an infant science with seemingly insurmountable technical limitations. Thomas learned to match tissue types between recipients and donors, leading to the first transplant using a matched sibling donor in 1969, and the first matched transplant from an unrelated donor in 1977.

Dr. Thomas recently passed away, but during his long career he trained hundreds of physicians in the developing science of stem cell transplantation. One of these, Edward Agura, MD, now serves as medical director of the Blood and Marrow Transplant (BMT) Program at Baylor Dallas. Dr. Agura heads up a team of seven physicians with 130-plus years of combined experience in stem cell transplantation. In 2011 alone, they performed 256 transplants, with more than 4,800 transplants performed since the program’s inception in 1983. Patients who come to Baylor Dallas for a stem cell transplant will usually spend 2 to 3 weeks in the BMT unit of Baylor T. Boone Pickens Cancer Hospital. A multidisciplinary care team
physician, pharmacist, social worker, dietitian, and nurse) visits each patient daily to coordinate care. The unit is staffed with 44 nurses, 9 patient care technicians, and a full-time oncology pharmacist. Many nurses have an OCN (oncology-certified nurse) classification, and some have experience in intensive care units (ICUs). Newly hired nurses undergo an oncology internship as well as specialty classes in bone marrow transplant.

The rooms for patients are ICU-equipped and HEPA-filtered. They are larger than usual to allow caregivers to have their own space for relaxing, sleeping, watching television, or working at a desk. Caregivers also have access to two areas in the hospital for showering, washing clothes, or just relaxing. Unique support services are provided for patients during their stay, including acupuncture, massage, fitness classes in a supervised gymnasium, aromatherapy, art therapy, and music therapy.

Baylor has a primary care model for transplantation that persists for the life of the patients. Even if they are no longer in Dallas, their transplant doctors continue to monitor their care. According to Dr. Agura: “Quality of life after the transplantation is a major endpoint. We are not just here to transplant patients and send them home; aftercare can involve as much expertise as the actual transplant process. To facilitate this while allowing the patients to return home, we partner with their hometown doctors. We provide ongoing expertise—usually by telephone—to help manage longer-term issues such as infection prevention, immune recovery, and physical and mental strengthening. By following patients in this primary care model, we can help to provide long-term quality of life.”

According to the Center for International Blood and Marrow Transplant Research (CIBMTR) and the National Marrow Donor Program® (NMDP), the Baylor Dallas BMT program is in the top 14 of programs nationwide in terms of number of unrelated donor transplants done each year. Of the top programs, the patients at Baylor Dallas have among the highest levels of complexity before transplant, yet routinely have results that exceed expectations. JaNeene L. Jones, RN, FACHE, chief operating officer at Baylor T. Boone Pickens Cancer Hospital and Baylor Charles A. Sammons Cancer Center, commented: “The BMT program is a very important collaborative effort that offers a highly sophisticated clinical service to patients and families.”

Baylor T. Boone Pickens Cancer Hospital
Advances in Stem Cell Transplantation
Stem cell transplantation has seen significant progress since its inception. Improved supportive therapies have made the procedure safer. There are better techniques to mobilize stem cells and more effective approaches for preventing infection during and after transplantation and engraftment. For allogeneic transplantations, one of the most significant developments has been the recognition that the quality of the donor stem cells and immune cells are what can ultimately cure the patients, not the completeness or intensity of the conditioning regimen. As a result, preparatory regimens are becoming less intense and less toxic, and are geared instead toward ensuring that the new immune system engrafts powerfully, with greater ability to fight infection and patrol for residual cancer cells. This lower-intensity approach, combined with improved supportive care and toxicity management, means that older patients who may not have been good candidates for stem cell transplantation 10 years ago are now receiving transplantations on a regular basis. For example, the upper age limit to be considered for transplantation in the mid 1990s was 55 for autologous transplantation and 45 for allogeneic transplantation. Today, it is not unusual to have patients in their 70s successfully undergo transplants, and one recent patient at Baylor Dallas was 82.

New Ways of Finding Donors for Stem Cell Transplant: The Registry and Beyond
The very first marrow transplants (in the 1950s) were done on patients whose cancers did not infect their marrow, making self-donation possible. Leukemia, on the other hand, is a disease of the marrow, and treatment requires the transplantation of healthy marrow from a donor with a similar tissue type. This type of transplant is called allogeneic. Before the discovery of human tissue typing in the 1960s, all allogeneic transplants from unmatched donors failed. With the discovery of tissue matching, early successes occurred, but were limited by the fact that only siblings had a chance of being perfect matches and only 1 in 3 patients who needed a transplant had a matched sibling who could serve as a donor. When more efficient approaches for tissue typing started to be available, unrelated donors became a possibility. To widen the opportunity for a good match, the National Marrow Donor Program® (NMDP) initiated the Be The Match® Registry, a national database of donors that includes cooperative agreements with donor registries worldwide. Potential donors can go to a center where they live to be matched and to donate their stem cells. (You can find a center close to you at www.bethematch.org). Currently, more than 10 million people in the United States have volunteered to be donors, with an additional 8.5 million donor volunteers worldwide. A patient’s likelihood of having a donor on the Be The Match® Registry who is willing and able to help save a life is estimated to range from 66% to 93%, depending on race and ethnicity. Being tested is simple, and involves no more than a cheek swab.

What exactly constitutes a match? A key finding from the Nobel Prize–winning research of Dr. Thomas was the critical importance of tissue type matching for a successful transplantation. Originally, six tissue antigens were examined (three maternal, three paternal). With the idea that more antigen matches would mean a better transplantation outcome, this number was ultimately expanded to 10 or 12. Opinion has now come full circle, however, and many believe that striving to match 10/10 or 12/12 tissue antigens is excessive; if the transplantation is done early in the treatment cycle, an 8/8 match should be sufficient to achieve good results. The chances of finding a match in the registry increase substantially with this lower level of stringency. Importantly, the more intervening treatments between diagnosis and transplantation, the less the matching matters, and the greater likelihood that the transplant will not be a success. Early use of transplantation increases the chance of success.

Despite this worldwide initiative, some patients do not have the good fortune or the time to locate a perfect donor. Clinicians from the BMT program are also using a new approach called haploidentical transplantation. This technique uses donors that are half-matched to the recipient. With certain modifications to standard protocols—the conditioning regimen is adjusted to suppress the immune system rather than completely destroying it, and the immune system is “rebooted” with additional drug therapy after the transplantation—
successful results can be obtained even with this low level of matching. This means that parents, siblings, or children may be suitable donors. With this option, nearly all patients with blood cancers have potential matches.

Being a donor used to be a daunting task and discouraged some from volunteering. The number of volunteers took a great leap forward with the development of techniques to harvest stem cells from peripheral blood rather than from bone marrow. Prior to this, the donor was taken to an operating room and anesthetized. Multiple bone punctures were made on each posterior iliac crest to aspirate a quart or more of bone marrow. Today, donors receive an injection of filgrastim, a synthetic form of granulocyte colony stimulating factor, which causes bone marrow cells to be released into the peripheral blood where they are collected through apheresis. Results of a large collaborative study recently published in the New England Journal of Medicine (October 18, 2012) showed that stem cells collected from the peripheral blood were as effective as bone marrow stem cells for transplantation. Not surprisingly, the peripheral blood technique was strongly favored by donors.

This approach works about 90% of the time. Occasionally, however, the yield of stem cells is poor. For these individuals, a second injection of a type of stem cell “grease” called plerixafor releases stem cells from the bone marrow, causing them to come pouring out of the bones. This compound is mainly used in the autologous setting. It has markedly improved stem cell collection, making it quicker and getting better results.

If a particular patient in need of a transplant still cannot find a match or obtain stem cells from a living donor, umbilical cord stem cell banks, which exist in the United States and around the world, are an additional source of stem cells. Previously used only to treat children, umbilical cord blood stem cell transplantation has now been demonstrated to be effective in adults. Cord blood stem cells are so young and immunologically naïve that they do not require the same degree of matching as adult stem cells. The NMDP was selected by the U.S. government to operate the nation’s Cord Blood Coordinating Center. In this role, it encourages expectant parents to donate umbilical cord blood to the Be The Match® Registry.

Ongoing Research in Stem Cell Transplantation

There have been important advances in the field of stem cell transplantation over the last 15 years, but significant limitations and toxicities remain. Thus, every patient who comes to the Baylor Dallas BMT program for treatment is asked to participate in some form of research for the betterment of future patients. Ongoing research is investigating new ways to address the major issues of stem cell transplantation: preventing infection, preventing graft-versus-host reaction, and preventing recurrence. Examples of ongoing research are:

- For a healthy person, vaccines against shingles, cytomegalovirus, and Herpes simplex are a straightforward way to lessen the risk of these infections. For a transplanted patient, such vaccinations might pose unknown problems of safety or efficacy. Several clinical trials are investigating the safety of these vaccinations for transplant patients.

- A set of trials is using half-matched parents or siblings as donors for patients with hematologic cancers.

- Genetic testing is being done before transplant to identify specific genetic loci that will help in determining how strong the conditioning regimen needs to be.

- T cells are key players in graft-versus-host reaction, a significant complication of transplantation. In a new study, donor cells are being manipulated genetically to insert an on/off switch inside the donor’s T cells. If graft-versus-host reaction begins, the switch can be turned off by administration of a specific agent, resulting in death of the T cells.

- Patients are being vaccinated against their own cancers to improve their immune systems after transplantation, making it more likely that residual tumor cells will be eradicated.

Baylor Dallas BMT Program Comprehensive Plan

A multidisciplinary group of physicians on the medical staff, nurses, finance officers, social workers, and administrators convenes yearly to assess the Baylor Dallas BMT program: its strengths and weaknesses, opportunities, and threats. The purpose of the group is to continue an iterative process that is evolving the 3-year strategic plan for the program. Priorities for the next several years are assessed and
adjusted. The group monitors quarterly reports and recommendations from work groups in the areas of service, quality, finance/growth, research/technology, and marketing.

Where We Are; Where We Are Going

Advances in drug therapies have transformed some diseases, once fatal, into chronic illnesses. Examples of this are AIDS and CML, for which a lifetime regimen of pills has proved lifesaving or obviated the need for a more rigorous therapy such as transplantation. However, one of the great challenges in cancer medicine remains: Only 1 in 5 patients who might stand to benefit from a transplant treatment are ever referred to a transplant center by their doctor. Clearly, education on this point for referring doctors is needed.

The revolution in genetic detection of illness and assessment of prognosis will shape the future of medicine and of transplantation. Already we are seeing that many patients with leukemia, thought to be curable without transplantation because old methods had determined that they had “normal genetics,” are being discovered to have hidden genetic mutations; the use of modern technology has clarified their prognosis and established the need for transplantation as a part of their treatment plan.

Some day, this new genetic information will lead the treating oncologists to the “right pill” or set of pills to turn the cancer into a chronic illness. For now, however, stem cell transplant remains a critical part of the treatment approach for most patients with hematologic cancers. With the continuing development of stem cell transplant technology, more patients are becoming eligible for transplants, more donor cells are available, and outcomes are improving. To optimize the chances of a successful outcome, all hematologic cancer patients should have a stem cell transplant consultation early on in their treatment plan. Brian Berryman, MD, medical oncologist/hematologist on the medical staff at Baylor Dallas and attending physician for the Baylor Dallas BMT unit, said: “Ideally, we would like to see patients with hematologic malignancies very early in the process. It takes time to undergo tissue typing, find donors, sort out insurance, and weigh all the options.”

Texas Cancer Vaccine Symposium

JANUARY 22, 2013 - 8 AM TO 6 PM

10th floor of the Charles A. Sammons Cancer Center, 3410 Worth St., Dallas, TX 75246

Pre-registration is required.

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Precision Medicine in the Treatment of Patients with Hematologic Malignancies

Multiagent chemotherapy can be curative for certain hematologic malignancies, including childhood acute lymphoblastic leukemia, certain cases of Hodgkin’s and non-Hodgkin’s lymphoma, and adult acute leukemia. Moderate toxicity is associated with many of these regimens, triggering the search for better treatments that will more directly target specific cells or molecular pathways within cells.

Targeting Specific Cells: Monoclonal Antibodies

With the advent of monoclonal antibody (MoAb) technology in the late 1970s, it became possible to produce antibodies that target specific antigens on the surface of tumor cells. Ideally, the antibodies target an antigen present at high concentrations on tumors cells and absent or present at low concentrations on normal cells. MoAbs, either as single agents or in combination with chemotherapy, have improved treatment outcomes for several types of cancer, with increased time to progression, survival time, and quality of life. A variety of mechanisms have been proposed by which MoAbs can kill neoplastic cells, including induction of apoptosis, cell growth inhibition, and complement-mediated cytotoxicity, among others.

Rituximab, a chimeric human/mouse MoAb that targets the CD20 antigen on the surface of B lymphocytes, was approved by the US Food and Drug Administration (FDA) in 1997 for the treatment of relapsed and refractory NHL. The CD20 antigen is a 33-kDa protein expressed by mature B cells and most malignant B cells, but not by pre-B cells or differentiated plasma cells. The amount of CD20 expressed varies with different cancers (expression is very high in follicular lymphoma, but low in chronic lymphocytic leukemia) and with the stage of differentiation in normal B cells. The combination of rituximab with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) chemotherapy has shown a survival advantage compared with CHOP alone for the treatment of diffuse large B-cell lymphoma and several other B-cell lymphomas. Rituximab as a single agent typically has a favorable side effect profile. Because it causes a depletion of B lymphocytes needed for antibody production, it may impair the immune system for several months after treatment. Otherwise, it does not appear to affect blood counts or to produce any of the toxicities typically seen with normal chemotherapy. (See sidebar on page 15 to read the personal experience of a patient with follicular lymphoma treated with rituximab.)

MoAbs against other tumor cell surface antigens have met with varying levels of success. Several agents based on a MoAb directed against CD33 (lintuzumab, gemtuzumab ozogamicin) have been developed as treatments for acute myeloid leukemia, but have subsequently been withdrawn from the market. On the other hand, alemtuzumab, a MoAb directed against the CD52 antigen, has shown promising results. CD52 is expressed on human B and T cells, natural killer cells, eosinophils, and macrophages. Alemtuzumab is FDA-approved for the second-line treatment of chronic lymphoid leukemia and has also been used in the treatment of T-cell lymphoma. Milatuzumab targets the CD74 antigen. It is currently being studied for the treatment of multiple myeloma, NHL, and chronic lymphocytic leukemia. Epratuzumab targets the CD22 antigen on B lymphocytes and is being evaluated for the treatment of NHL.

Immonoconjugates are MoAbs linked with cytotoxic drugs or radiation emitters, delivering the toxic agents directly to the tumor cell. The protease-cleavable linker is designed to be stable in the bloodstream but to release the cytotoxic agent after internalization into the tumor cells. Brentuximab vedotin and inotuzumab ozogamicin are immunoconjugates currently being studied in clinical trials at Baylor Charles A. Sammons Cancer Center at Dallas.
Targeting Specific Pathways: The Imatinib Model Opens the Door

Over a relatively short period of time, the tyrosine kinase inhibitor (TKI) imatinib has totally changed the treatment paradigm for chronic myeloid leukemia (CML). Prior to the introduction of imatinib, treatment for CML involved toxic chemotherapy followed by stem cell transplantation for definitive treatment.

This picture changed with the introduction of the targeted agent imatinib. The hallmark of CML is a reciprocal t(9,22) (q34;q11) chromosomal translocation (the Philadelphia chromosome). This rearrangement results in a BCR-ABL fusion gene that encodes a protein with a deregulated tyrosine kinase activity. The deregulated activity leads to an intracellular phosphorylation cascade resulting in cell proliferation, migration, differentiation, and apoptosis. Imatinib acts by competitive inhibition of the adenosine triphosphate (ATP) binding site, preventing BCR-ABL autophosphorylation, tyrosine kinase activity, and subsequent downstream activity.

The results of the International Randomized Interferon versus STI571 (IRIS) phase III trial reported in 2001 showed that imatinib was significantly superior to the combination of interferon-alpha and cytosine arabinoside for newly diagnosed CML patients in the chronic phase. The FDA approved imatinib for the first-line treatment of CML in 2002.

Four targeted agents—imatinib, nilotinib, dasatinib, and bosutinib—are now commercially available for the treatment of CML. Nilotinib and dasatinib have higher potency than imatinib and are more likely to result in a complete response (cytogenetic or molecular). Bosutinib, a third-generation TKI that has just been commercially released, is a dual-kinase inhibitor, impacting the autophosphorylation of both Abl and Src kinases. Early studies indicate that patients who have developed resistance to imatinib, nilotinib, or dasatinib may respond to bosutinib.

These successes in targeted treatment have come about because of the well-defined genetic abnormality associated with Philadelphia chromosome-positive CML. As we learn more about critical signaling pathways in other hematologic cancers, the model will translate to more effective treatment strategies for other diseases.

Research at Baylor Charles A. Sammons Cancer Center

Currently, 37 clinical trials and research studies at Baylor Sammons Cancer Center are exploring improved treatment options for hematologic cancers. Some trials are testing the safety and efficacy of new agents, but most are exploring innovative ways of combining agents for greater efficacy.

Combination Therapy with Proteasome Inhibitors for Multiple Myeloma

Proteasomes are intracellular protein complexes responsible for degrading proteins into their constitutive amino acids, providing the raw material for new protein synthesis.

Mechanism of Action of Imatinib (IM)

Mechanism of action of imatinib (IM). IM blocks adenosine triphosphate (ATP) binding to BCR-ABL and inhibits the ability of BCR-ABL to induce increased cell proliferation.
Bortezomib is a first-generation proteasome inhibitor that acts by binding to the catalytic site of the proteasome with high affinity and specificity. It is currently recommended for primary induction therapy in combination with dexamethasone, lenalidomide, melphalan, and/or prednisone for the treatment of patients with multiple myeloma. It is also recommended as a single agent or in combination with liposomal doxorubicin as salvage treatment for multiple myeloma. Researchers are continuing to investigate the best uses of bortezomib in this patient group, in particular, the best ways to use it in combination with other agents. At Baylor Sammons Cancer Center, a number of trials are ongoing, including:

- A phase II study of three bortezomib-based consolidation treatments for patients completing induction therapy and stem cell transplantation for newly diagnosed multiple myeloma
- A phase I study of ganetespib (a heat shock protein 90 inhibitor) and bortezomib in patients with relapsed and/or refractory multiple myeloma
- A phase II study of bortezomib/dexamethasone with or without elotuzumab. Elotuzumab is a humanized MoAb directed against human CS1, a cell surface antigen that is highly expressed on multiple myeloma cells and normal plasma cells.
- A phase I study of ARRY-520, a small molecule inhibitor of the kinesin spindle protein, in combination with bortezomib and dexamethasone for relapsed/refractory multiple myeloma

The safety and efficacy of the second-generation proteasome inhibitor carfilzomib is being tested in combination with pomalidomide (a derivative of thalidomide) and dexamethasone for relapsed multiple myeloma.

An Immunoconjugate for the Treatment of Lymphoma

Brentuximab vedotin (SGN-35) is an immunoconjugate consisting of the anti-CD30 MoAb brentuximab linked to the antimitotic agent monomethyl auristatin E. The CD30 antigen is found primarily on T cells, so this compound has been very effective against T-cell lymphomas and Hodgkin’s lymphoma. The compound received accelerated approval from the FDA in August 2011 for the treatment of relapsed or refractory anaplastic large-cell lymphoma and relapsed or refractory Hodgkin’s lymphoma that is CD30-positive.

Studies under way at Baylor Sammons Cancer Center are evaluating brentuximab vedotin for the treatment of CD30-positive NHL and as front-line therapy for Hodgkin’s lymphoma in adults aged 60 and above.

An Immunoconjugate in Combination with Rituximab

Inotuzumab ozogamicin is an immunoconjugate consisting of an anti-CD22 MoAb and calicheamicin, a cytotoxic agent that is a natural product of bacteria. Both inotuzumab and rituximab target B lymphocytes. A phase III trial is assessing the effectiveness of these two agents in combination compared with the investigator’s choice of therapy in patients with relapsed or refractory CD22-positive aggressive NHL.

Other Compounds Under Study

Additional phase II studies are testing these agents:

- Alvocidib: A synthetic N-methylpiperidinyl chlorophenyl flavone compound that inhibits cyclin-dependent kinases and down-regulates cyclin D1 and D3 expression, resulting in G1 cell cycle arrest
- CDCT2980S: An immunoconjugate consisting of the anti-CD22 MoAb antibody MCDT2219A linked to monomethyl auristatin E
- CAL-101: A small molecule inhibitor of the delta isoform of the 110-kDa catalytic subunit of class IA phosphoinositide-3 kinases

These are only a selection of the wide variety of clinical trials under way at Baylor Sammons Cancer Center to improve treatment outcomes for patients with hematologic cancers. Many new agents continue to be developed and await testing in well-designed clinical trials. It is a slow process, but one that is gaining momentum. Barry Cooper, MD, medical director of clinical hematology at Baylor University Medical Center at Dallas, commented: “As we learn more and more about the mutations that trigger tumors, basic science is giving us increased opportunities to design drugs that are extremely specific. It’s a very exciting time in terms of the management of hematologic malignancies.”
"If I’m going to be in a life-and-death situation, I’m really lucky to have come to work at a place that is two blocks from Baylor Sammons Cancer Center."

Steven J. Phillips, MS, PhD, RBP

Steven J. Phillips, MS, PhD, RBP, is currently chief biological safety officer for Baylor Research Institute. Nine years ago, he was living and working near Chattanooga, Tennessee. In spring of 2003, as he got ready for work one morning, he noticed what he thought was “a small pimple” on his forehead—except that this pimple never went away. Eventually, his concern drove him to a dermatologist, who biopsied the small lesion. It turned out to be a metastasis from a follicular lymphoma. Subsequent imaging studies discovered the primary in the right axilla.

Steve began treatment with an oncologist in Chattanooga, who started him on a regimen of chlorambucil and prednisone. He commented that the treatment was relatively benign, with few side effects. “Unfortunately,” he said, “it didn’t do anything for the tumor.”

By the end of that summer, Steve had relocated to Atlanta and began seeing another oncologist, who started him on a treatment regimen containing a chemical cocktail (5-fluorodeoxyuridine, mitoxantrone, dexamethasone) and the targeted agent rituximab. “I could feel the rituximab working at the first treatment,” he said. “The affected areas on my forehead and in the axilla started itching almost immediately.” He relocated to Dallas in mid-treatment, continuing to receive his therapy at Baylor Sammons Cancer Center. By December of that same year, the tumors were completely gone.

Steve completed his treatment 8 years ago and remains tumor free. He continues to return for follow-up. In looking back at his experience, he said: “If I’m going to be in a life-and-death situation, I’m really lucky to have come to work at a place that is two blocks from Baylor Sammons Cancer Center.”

North Texas Multidisciplinary Lung Cancer Symposium

The second annual North Texas Multidisciplinary Lung Cancer Symposium was held on October 13, 2012. This day-long event focused on recent advances in lung cancer, with residents, fellows, nurses, and physicians in attendance. Faculty from across the country presented the latest information on a number of topics. These topics included the identification of patients who need to be screened as well as use of helical computed tomography for screening, the scope and frequency of follow-up after treatment, the importance of a coordinated team approach for preoperative physiologic testing of the patient to determine the feasibility of surgical resection, the ways different interventional pulmonary techniques can be incorporated into lung cancer treatment, the use of surgery versus chemotherapy and radiation therapy in stage III lung cancer, harnessing the immune system for treatment of lung cancer, molecular advances and targeted therapies in non–small cell lung cancer, and the status of treatment in small cell lung cancer. In addition to the lectures, open discussions led by a moderator were initiated after each group of talks, allowing the participants to ask questions of either a particular speaker or the panel of speakers. It was a day for all involved to learn about many of the new advances in the identification and treatment of lung cancer.
Hematopathology: Combining Old and New Tools to Improve Diagnosis and Predict Outcome

The Division of Hematopathology in the Department of Pathology at Baylor University Medical Center at Dallas occupies the third floor of the Caruth Laboratory building at Baylor Dallas. Last year, approximately 1,800 bone marrow biopsies and 1,100 lymph node specimens were sent to the Division of Hematopathology for evaluation.

The modern discipline of hematopathology combines morphological analysis of stained cells with the tools of cytogenetics, molecular biology, and immunology to provide accurate diagnosis and assessment of prognosis for patients with hematologic cancers. As director of hematopathology, John R. Krause, MD, oversees morphological and immunohistochemical analyses of all blood, bone marrow, and lymph node specimens sent from Baylor University Medical Center at Dallas or Baylor Charles A. Sammons Cancer Center. Additional analyses (flow cytometry, cytogenetics, molecular diagnostics, etc.) are performed at med fusion, an advanced medical testing and clinical trials company located in Lewisville, Texas.

The Foundation of Modern Hematopathology

“If I have been able to see further, it was only because I stood on the shoulders of giants.” This expression, often attributed to Sir Isaac Newton, describes very well the steady and painstaking progress that laid the foundation for the modern discipline of hematopathology. Key steps in this progress were:

- 1902: James Homer Wright developed Wright’s stain to help differentiate white blood cell types.
- 1952: T. C. Hsu discovered the hypotonic technique for improved chromosome visualization, ushering in the birth of modern cytogenetics.
- 1960: Peter Nowell and David Hungerford described the Philadelphia chromosome in chronic myelogenous leukemia; it was the first chromosome aberration to be associated with a specific type of cancer.
- 1971: Maximo Drets and Margery Shaw described G-banding, allowing the identification of specific chromosomes and chromosome segments and leading to a revolution in cancer cytogenetics.

Until the 1960s, cells from patients with hematologic malignancies were assessed largely through morphological analysis of Wright’s- or hematoxylin-stained cells from blood smears, bone marrow aspirates or biopsies, or lymph node biopsies. With the advent of improved methods for studying human chromosomes, specific chromosome aberrations were identified through meticulous cytogenetic analysis and began to be associated with different types of cancer. As a result of these studies, we now know that acquired clonal chromosome abnormalities are found in malignant cells of most patients with hematologic malignancies.

While these types of studies are still the cornerstone of hematopathologic analysis, the tools of modern immunology and molecular biology have significantly advanced the speed and accuracy with which we can diagnose hematologic malignancies and predict their outcome.

Modern Tools of Hematopathology

**Fluorescence in situ hybridization (FISH)** involves the labeling of DNA probes with fluorochromes (e.g., fluorescein or rhodamine), followed by hybridization onto cells fixed on a slide. Centromere-specific probes are available that can mark a pair of chromosomes, tracking gains or losses of chromosomes on both metaphase and interphase cells. Larger probes that contain specific genes can be used to screen for translocations. FISH has advantages over routine microscopic analysis of metaphase chromosomes (karyotyping): it does not require dividing cells; it is highly sensitive and specific; and it is less expensive and less time-consuming than...
karyotyping. Unlike karyotyping, however, it does not provide information about specific breakpoints in chromosome rearrangements, and its usefulness is limited by the number of available probes. FISH studies are diagnostically useful and also provide information about residual disease. In addition, FISH may help in detecting early progression to malignancy in people with myelodysplastic or preleukemic disorders.

**Flow cytometry** analyzes multiple characteristics of single cells, including cell size, cytoplasmic complexity, DNA or RNA content, and a wide range of membrane-bound and intracellular proteins. Cells flowing in single file in a stream of fluid are drawn individually through an interrogation point, where they are hit with a beam of monochromatic light (typically a laser). Incident light that scatters at different angles is collected and passed through a series of filters and mirrors to analyze specific wavelength bands. This scattered light is useful for distinguishing differences in size and cytoplasmic complexity. For example, an increase in blast cells in bone marrow is a marker for malignancy in patients with preleukemic conditions. Cellular DNA/RNA content can be assessed with the use of fluorescent dyes that intercalate the nucleic acid molecule. The dye fluoresces at the interrogation point, with a signal strength that reflects the amount of DNA. Immunophenotyping uses antibodies against cell surface proteins to identify specific types of white blood cells. Immunophenotyping as part of the diagnostic workup for leukemias and lymphomas offers a rapid and effective means of providing a diagnosis, as well as confirming diagnoses reached using other approaches.

**Molecular diagnostics** includes molecular assays (reverse transcriptase–polymerase chain reaction [RT-PCR], microarray analysis) for specific genes associated with known chromosome rearrangements in hematologic cancers. These assays can be used as a diagnostic aid and also offer a more precise estimate of residual disease than routine differential counts or cytogenetic analysis.

**Modern Hematopathology in Action:**

**Acute Promyelocytic Leukemia**

Acute promyelocytic leukemia (APL) is a distinct subtype of acute myeloid leukemia, characterized by a severe coagulopathy often present at diagnosis. Examination of blood or bone marrow cells reveals characteristic cells with hypergranular morphology and frequent Auer rods in the leukemic cell population. Auer rods, clumps of granular material that form elongated needles visible in the cytoplasm, are occasionally seen in other acute myeloid leukemias, but they are almost always observed in APL.

The combination of clinically apparent coagulopathy and characteristic leukemic cells is a strong indicator of APL. However, for the first 20 years after it was first described, the probable diagnosis did little good, as there was no effective treatment and the mortality rate was near 100%. Then, in 1977, Janet Rowley and coworkers reported that APL is associated with a balanced chromosome translocation between chromosomes 15 and 17, designated as t(15;17) (q22;q12-21). By 1990, it was known that this translocation, found in 95% of patients with APL, resulted in the fusion of the promyelocytic (PML) gene on chromosome 15 and the retinoic acid receptor-α (RARα) gene on chromosome 17. The abnormal receptor coded by the fused gene cannot be activated with physiologic doses of retinoic acid, resulting in the inhibition of myeloid cell differentiation.

This knowledge, gained from the tools of cytogenetics and molecular biology, opened the door to effective therapy for patients with APL. The APL blasts are extremely sensitive to the differentiating action of all-trans retinoic acid, which activates the abnormal retinoic acid receptor, resulting in a dramatic clinical response in patients. Arsenic trioxide is also effective, targeting and degrading the abnormal receptor. With these therapies, in combination with conventional chemotherapy, most patients with this once-fatal disease can now be cured.
Although the PML/RARα fusion is detectable by FISH in most patients with clinically defined APL, the diagnosis should be confirmed with molecular diagnostic testing. This allows the identification of variants that are resistant to all-trans retinoic acid because they do not involve the PML site or involve different breakpoints within the PML site. Ideally RT-PCR in combination with karyotyping should be used to detect these rare molecular subtypes.

**Training the Hematopathologists of Tomorrow**

The field of hematopathology, which once progressed at a slow and measured pace, is now in a period of explosive change, with new techniques and refinements of established techniques becoming available all the time. To train practitioners in this rapidly changing field, focused training programs are necessary, in addition to the standard pathology residency.

Now in its fourth year, the program accepts one fellow each year. Candidates must have completed a pathology residency. During the year they spend in the program, they typically spend 8 months working directly with Dr. Krause at Baylor Dallas, 1 month working in pediatrics at Cook Children’s Hospital in Fort Worth, and 3 months at med fusion gaining experience in flow cytometry, molecular diagnostics, and cytogenetics. Because of the high volume and diversity of patients at Baylor Dallas, Baylor Dallas has applied for a second fellowship position for the program.

**FISH Analysis for PML/RARA t(15;17) translocation, which occurs in acute promyelocytic leukemia.** PML is located on chromosome 15q and identified with an orange dot. RARA is located on chromosome 17q and identified with a green dot. In the translocation, there is a fusion of red and green, resulting in a yellow dot (see arrow).

(Photograph used with permission from D. Saurabh Gupta of med fusion, Lewisville, TX.)

Although the PML/RARA fusion is detectable by FISH in most patients with clinically defined APL, the diagnosis should be confirmed with molecular diagnostic testing. This allows the identification of variants that are resistant to all-trans retinoic acid because they do not involve the PML site or involve different breakpoints within the PML site. Ideally RT-PCR in combination with karyotyping should be used to detect these rare molecular subtypes.

**Welcome to New Members of the Medical Staff at Baylor Charles A. Sammons Cancer Center at Dallas**

**James Fleshman, MD**—Chair of the Department of Surgery, Baylor University Medical Center at Dallas

**Pavlos Papavasiliou, MD**—Surgical Oncology

**Keith Cavaness, DO**—Surgical Oncology

**Micah Burch, MD**—Medical Oncology and Hematology

**Carolina Escobar, MD**—Blood and Marrow Transplantation
This campus is dedicated to serving the more than 133,000 residents in McKinney and surrounding communities. Baylor Health Care System’s dedication to providing safe, quality, compassionate care continues to lead us into growing communities like McKinney.

The cancer treatment team at Baylor McKinney includes medical oncologists, surgeons, radiologists, pathologists, and other specialists who work together to provide technologically advanced inpatient and outpatient cancer services for patients in their own community. Currently, Baylor McKinney is working on receiving accreditation from the Commission on Cancer of the American College of Surgeons as an approved cancer program so that it can meet the criteria to become part of Baylor Charles A. Sammons Cancer Center network.

Opening of Baylor Medical Center at McKinney

On September 23, 2010, Baylor Health Care System broke ground on a 469,000-square-foot medical center in McKinney, located on 58 acres at the northwest corner of Highway 380 and Lake Forest Drive. The $212 million, 95-bed, four-story hospital and medical office complex has been completed, and Baylor Medical Center at McKinney opened on July 6, 2012.
# New Clinical Trials at Baylor Charles A. Sammons Cancer Center at Dallas

<table>
<thead>
<tr>
<th>Site</th>
<th>Location</th>
<th>Principal investigator</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>Texas Oncology–Dallas</td>
<td>Joanne L. Blum, MD, PhD</td>
<td>A Phase III Clinical Trial Comparing the Combination of Docetaxel Plus Cyclophosphamide to Anthracycline-Based Chemotherapy Regimens for Women With Node-Positive or High-Risk Node-Negative, HER2-Negative Breast Cancer</td>
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<td>Texas Oncology–Dallas</td>
<td>Joyce O’Shaughnessy, MD</td>
<td>International, Multi-Center, Open-label, Treatment Extension Study of Iniparib as Monotherapy or in Combination Chemotherapeutic Regimens in Cancer Patients Who Have Derived Clinical Benefit From Iniparib Following Completion of a Phase 1, 2 or 3 Parental Study</td>
</tr>
<tr>
<td>GU</td>
<td>Texas Oncology–Dallas</td>
<td>Thomas Hutson, DO, PharmD</td>
<td>A Phase 3, Randomized, Double-blind, Controlled Trial of Cabozantinib (XL184) Versus Mitoxantrone Plus Prednisone in Men With Previously Treated Symptomatic Castration-resistant Prostate Cancer</td>
</tr>
<tr>
<td>Hematology</td>
<td>Baylor Dallas</td>
<td>Joseph W Fay, MD</td>
<td>A Phase 1 Study of ARRY-520 and Bortezomib plus Dexamethasone in Patients with Relapsed/Refractory Multiple Myeloma</td>
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<td></td>
<td>Texas Oncology–Dallas</td>
<td>Alan Miller, MD, PhD</td>
<td>A Phase 3, Randomized, Double-Blind, Placebo Controlled Study Evaluating the Efficacy and Safety of GS 1101 (CAL-101) in Combination with Bendamustine and Rituximab for Previously Treated Chronic Lymphocytic Leukemia</td>
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<td></td>
<td>Baylor Dallas</td>
<td>Alan Miller, MD, PhD</td>
<td>Pilot study exploring IDH1/2 and 2-HG as diagnostic tool in AML patients</td>
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<td>Texas Oncology–Dallas</td>
<td>Alan Miller, MD, PhD</td>
<td>A Randomized, Non-Comparative, Open-Label, Multi-center, Phase II Trial Evaluating the Safety and Activity of DCDT2980S in Combination With Rituximab or DCDS4501A in Combination With Rituximab in Patients with Relapsed or Refractory B-Cell Non-Hodgkin's Lymphoma</td>
<td></td>
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<tr>
<td>Neuro-Oncology</td>
<td>Karen Fink, MD, PhD</td>
<td>Randomized, Double-Blind, Placebo-Controlled Trial of Lacosamide for Seizure Prophylaxis in Patients with High-Grade Gliomas</td>
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<td>Baylor Dallas</td>
<td>Karen Fink, MD, PhD</td>
<td>Pilot study exploring IDH mutation and metabolites in malignant Glioma patients</td>
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<td>Skin</td>
<td>Joseph W Fay, MD</td>
<td>IL-15 DC Vaccine in Patients With High Risk Melanoma—A Follow Up Protocol to Baylor IRB # 009-273</td>
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<tr>
<td>Texas Oncology–Dallas</td>
<td>Charles Cowey, MD</td>
<td>Vemurafenib in Melanoma w/ Brain Mets</td>
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<tr>
<td>Texas Oncology–Dallas</td>
<td>Charles Cowey, MD</td>
<td>The TEAM Trial (Tasigna Efficacy in Advanced Melanoma): A Randomized, Phase III, Open Label, Multi-center, Two-arm Study to Compare the Efficacy of Tasigna® Versus Dacarbazine (DTIC) in the Treatment of Patients With Metastatic and/or Inoperable Melanoma Harboring a c-Kit Mutation</td>
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<tr>
<td>Texas Oncology–Dallas</td>
<td>Charles Cowey, MD</td>
<td>Phase II, Randomized Double-blind Study of Efficacy and Safety of Two Dose Levels of LDE225 in Patients With Locally Advanced or Metastatic Basal Cell Carcinoma</td>
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Physicians and their patients can now access information about open clinical trials in oncology at Baylor Sammons Cancer Center by following these steps:

- Go to BaylorHealth.edu/Sammons.
- Click on “Cancer Clinical Trials” on the right-hand menu.
- From the list of studies that appears, click on the study that is of interest to you to view details such as the inclusion/exclusion criteria.

For additional details or questions about the studies, please contact the Office of Clinical Oncology Research Coordination at 214.818.8472 or via e-mail at cancer.trials@baylorhealth.edu.
Site-Specific Tumor Conferences at Baylor Charles A. Sammons Cancer Center at Dallas

At Baylor Sammons Cancer Center, a key element at the heart of our approach to patient care and education is the site-specific tumor conference program. Rather than focusing solely on recommendations for patient care, the site-specific conferences also aim at educating the medical professionals attending the conference. Unlike tumor boards, continuing medical education credit is available for physicians who attend. Because several patients with the same diagnosis are presented at each conference, attendees are provided with an in-depth view from specialists, accompanied by lively discussion.

Most of the site-specific tumor conferences have been relocated to the 10th floor conference center in the new outpatient cancer center. The gynecology and skull base conferences currently remain at their former locations.

For more information about site-specific tumor conferences at Baylor Charles A. Sammons Cancer Center, please call 214.820.4073.

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<thead>
<tr>
<th>Conference Schedule:</th>
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<tbody>
<tr>
<td>Bone and Soft Tissue</td>
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<tr>
<td>Breast</td>
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<tr>
<td>Chest</td>
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<tr>
<td>Endocrine</td>
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<td>GI</td>
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<td>Gynecology</td>
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<td>Head and Neck</td>
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<tr>
<td>Journal Club</td>
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<td>Hematology/Oncology</td>
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<td>Hematology*</td>
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<tr>
<td>Liver</td>
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<tr>
<td>Lymphoma*</td>
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<td>Neuro-oncology</td>
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<td>Pancreas</td>
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<td>Skin</td>
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<td>Skull Base</td>
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<tr>
<td>Stem Cell Transplant*</td>
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<tr>
<td>Urology</td>
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*Rotate during the month
Recent Publications from Baylor Sammons Cancer Center
August 21, 2012 to November 19, 2012


GI CANCER CONFERENCE

2013

LIVER CANCER—WHAT NOW?

Join us for a continuing education event to explore the latest in medical management and surgical advances.

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Register Online/More Information: www.camenaegroup.com