MULTIPLE MYELOMA
A GUIDE FOR PATIENTS AND THEIR FAMILIES
If you or a loved one has been diagnosed with multiple myeloma, having accurate information about the disease and its treatment can help you make the best healthcare decisions. Fox Chase Cancer Center’s hematologic oncologists have put together this guide to help you understand multiple myeloma and the range of treatment options available.

### INSIDE THIS GUIDE

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>What Is Multiple Myeloma?</td>
<td>2</td>
</tr>
<tr>
<td>M-Proteins and Myeloma</td>
<td>2</td>
</tr>
<tr>
<td>Symptoms</td>
<td>3</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>3</td>
</tr>
<tr>
<td>Plasma Cell Disorders</td>
<td>3</td>
</tr>
<tr>
<td>Diagnosing Multiple Myeloma</td>
<td>4</td>
</tr>
<tr>
<td>Staging</td>
<td>5</td>
</tr>
<tr>
<td>Primary Myeloma Treatment</td>
<td>5</td>
</tr>
<tr>
<td>Induction</td>
<td>5</td>
</tr>
<tr>
<td>Consolidation</td>
<td>5</td>
</tr>
<tr>
<td>Maintenance</td>
<td>6</td>
</tr>
<tr>
<td>Relapsed and Refractory Disease</td>
<td>6</td>
</tr>
<tr>
<td>Additional Components of Treatment</td>
<td>7</td>
</tr>
<tr>
<td>Radiation</td>
<td>7</td>
</tr>
<tr>
<td>Targeted Therapy</td>
<td>7</td>
</tr>
<tr>
<td>Surgery</td>
<td>7</td>
</tr>
<tr>
<td>CAR T-Cell Therapy</td>
<td>7</td>
</tr>
<tr>
<td>Fox Chase-Temple University Hospital Bone Marrow Transplant Program</td>
<td>8</td>
</tr>
<tr>
<td>About Bone Marrow Transplants</td>
<td>9</td>
</tr>
<tr>
<td>Types of Bone Marrow Transplants</td>
<td>10</td>
</tr>
<tr>
<td>Autologous Transplants</td>
<td>10</td>
</tr>
<tr>
<td>Allogeneic Transplants</td>
<td>10</td>
</tr>
<tr>
<td>Haploidentical Transplants</td>
<td>10</td>
</tr>
<tr>
<td>Bloodless Transplants</td>
<td>10</td>
</tr>
<tr>
<td>Clinical Trials</td>
<td>11</td>
</tr>
<tr>
<td>Why Choose Fox Chase?</td>
<td>12</td>
</tr>
</tbody>
</table>

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WHAT IS MULTIPLE MYELOMA?

Multiple myeloma is a type of blood cancer that forms in the plasma cells (a type of white blood cell), which are found primarily in the bone marrow, the soft tissue in the center of the bone. Bone marrow is where red blood cells, white blood cells and platelets are produced; they all perform different functions that are critical to keeping the body healthy. Normal plasma cells are an important part of the immune system, making antibodies that attack and kill germs.

Lymphocytes (lymph cells) are one of the main types of white blood cells in the immune system and include T cells and B cells. The different types of white blood cells fight germs in different ways. When B cells respond to an infection, they become plasma cells. A healthy person has fewer than five plasma cells per 100 blood cells.

Multiple myeloma occurs when plasma cells become deranged through an unexplained chromosomal abnormality that causes them to keep replicating and dividing, instead of dying when they become old or damaged. This abnormal genetic change turns plasma cells into myeloma cells or malignant plasma cells. Rather than making protective antibodies, the myeloma cells produce an abnormal antibody called an M-protein that has no power to clear an infection, but instead can cause tumors, kidney damage, bone destruction, and impaired immune function.

These myeloma cells make millions of copies of themselves, all with the same genetic abnormality. This is often referred to as a clone of cells that crowds out healthy blood cells and spreads throughout the body.

M-Proteins and Myeloma

Like plasma cells, myeloma cells make antibodies, but they are all copies of one specific type of antibody and they do not help to fight disease. These antibodies are a clone of myeloma cells and are therefore called monoclonal proteins or M-proteins. Myeloma cells make uncontrolled M-proteins, usually in very large amounts.

M-proteins are made of two light protein chains and two heavy protein chains, just like normal antibodies. Light chains are proteins made by plasma cells, which also make immunoglobulins. Immunoglobulins help protect against infection and illness, and they are formed when light chains link up with heavy chains, another type of protein.

Myeloma cells tend to make more light chains than needed to form a complete M-protein. This leads to excess light chains that aren’t attached to a heavy chain, called free light chains. High levels of free light chains are found in the urine of some myeloma patients and can be a marker for this disease.
Symptoms

Multiple myeloma symptoms vary from person to person. Sometimes there are no symptoms and the disease is discovered through routine bloodwork or when a test is done for another condition. Other times, symptoms occur that may prompt you to consult with your physician, although they could indicate many other conditions as well. These include:

- Bone pain, especially in the spine or ribs
- Unexplained kidney failure or frequent infections
- Weakness of the arms or legs
- Extreme fatigue
- Bruising or bleeding easily
- Frequent fevers
- Breathing problems

Risk Factors

The most significant risk factor for multiple myeloma is advancing age. Less than 1 percent of cases are in people younger than 35; most people are at least 65 years old when diagnosed. Other risk factors for myeloma include:

- **Gender**: Men are more likely to develop the disease.
- **Race**: Black people are about twice as likely to be diagnosed as white people.
- **Family history**: The chance of developing myeloma increases if a parent or sibling had it as well.
- **Obesity**: Being overweight or obese increases the risk of myeloma.

Having any of these risk factors does not mean you will develop multiple myeloma. Many people with myeloma have no risk factors.

Plasma Cell Disorders

Along with multiple myeloma, there are numerous types of plasma cell dyscrasias (disorders), which are characterized by production of an abnormal protein. Some of these plasma cell disorders become multiple myeloma and many of them are also treated similarly to multiple myeloma. These plasma cell disorders include:

- **MGUS (Monoclonal Gammopathy of Undetermined Significance)** represents two-thirds of all plasma cell disorders. Doctors see evidence of abnormal protein but no other evidence of multiple myeloma. The incidence increases with age and occurs in up to 5.3% of people age 70 and older. Only 1% of patients with MGUS progress to a more serious condition each year and no treatment is needed or helpful unless it progresses.
- **Amyloidosis**: Amyloidosis is closely related to myeloma. It can be its own disease or a component of some forms of myeloma. It occurs when an abnormal protein called amyloid builds up in the organs and interferes with their normal function.
  - **Light chain amyloidosis**: The most common type of amyloidosis, light chain amyloidosis can affect the heart, kidneys, liver and nerves. Sometimes when the body produces light chains, the protein forms an unusual matrix that sticks together in an odd way and gets deposited into unique places. These deposits of abnormal protein (called amyloid) can cause organ failure.
- **Waldenstrom macroglobulinemia (WM)**: The cancer cells in people with WM have similarities to those seen in both multiple myeloma and non-Hodgkin lymphoma.
- **Extramedullary plasmacytoma** involves a single clump of myeloma cells outside the bone marrow. Plasmacytomas can form in the skin, muscle, lungs or almost any other part of the body.
DIAGNOSING MULTIPLE MYELOMA

A diagnosis of multiple myeloma is based on identification of a clone of plasma cells in the bone marrow or a collection of clonal plasma cells outside the bone marrow. Diagnostic tests may include the following:

- **Bone marrow biopsy:** coring a small piece of the bone and looking at the cells inside the bone where the marrow resides, to determine if there are excess numbers of plasma cells
- **Blood or urine tests:** check for the presence of abnormal M-protein or beta-2-microglobulin that can help diagnose and indicate level of aggressiveness
- **Sensitive imaging tests** of the bone such as magnetic resonance imaging (MRI), computed tomography (CT), or positron emission tomography (PET) scan
- **Skeletal survey:** series of X-rays of all or most of the bones in the body to look for damage
- **Physical exam** and medical history

It usually takes at least a few days to receive a test report that confirms a diagnosis, although the time varies for each patient. Your physician will provide your results as soon as possible, along with a thorough explanation and answers to any questions you have. At that time, your physician will recommend potential procedures and a treatment plan tailored to your diagnosis.

Accurate diagnosis is crucial for developing the best plan for treating your type and stage of multiple myeloma. Fox Chase’s hematopathologists — pathologists who specialize in the diagnosis of blood cancers — have specific expertise for properly diagnosing blood cancers and other blood diseases. These specialists are not available at all healthcare centers and are most often found at comprehensive cancer centers.
STAGING

After a patient is diagnosed with cancer, doctors will try to determine whether it has spread and how far. This process is called staging. The stage of a cancer describes how much cancer is in the body. It helps determine how serious the cancer is and the best treatments.

If diagnostic tests indicate you have multiple myeloma, your doctor will use the information gathered to classify your disease as stage I, stage II or stage III. Staging depends on various factors, including the amount of myeloma cells in the body and the amount of damage the myeloma cells have caused.

Fox Chase commonly stages multiple myeloma based on simple blood tests, dividing among the three stages and then an A and a B component based on whether the kidney function has been preserved. Hematologic specialists commonly look for these four factors in blood tests:

- A low level of albumin, the blood’s most abundant protein, can indicate more aggressive myeloma
- A high level of beta-2-microglobulin, a protein found on the surface of almost all cells in the body, helps measure the amount of myeloma cells in the body
- The level of LDH (enzyme) goes up when tissues are damaged by disease
- The specific gene abnormalities (cytogenetics) of the cancer will be checked

Getting the right diagnostic tests is extremely important as it will help ensure the most accurate treatment approach.

PRIMARY MYELOMA TREATMENT

Once a definitive diagnosis of multiple myeloma has been made, the first step is to gauge how advanced the disease is. Some patients present with very early disease or may have a precursor condition that requires only observation.

We will recommend a treatment plan personalized for your unique condition. Treatment depends on the stage and aggressiveness of your myeloma, as well as your age, health history and personal goals. We will strive to treat your condition with an individualized approach in the least invasive way possible with combination therapies that give you the best chance of a successful outcome.

At Fox Chase, first-line treatment of multiple myeloma typically involves three phases:

INDUCTION

This stage is considered initial therapy and is typically treated with targeted therapies, a combination of oral medications and injections. More and more in recent years, novel therapies (immunomodulatory agents, proteasome inhibitors and monoclonal antibodies) have replaced cytotoxic chemotherapy as the main treatment of myeloma. Novel therapies spare the normal tissues from damage by the chemotherapy and are more effective in eliminating the cancer cells.

Many patients respond well to this treatment. Our specialists follow patients’ blood counts and track the status of the myeloma based on the amount of abnormal protein in the blood or urine.

CONSOLIDATION

Although the induction treatment is effective at killing sensitive myeloma cells, it is very common for some resistant cells to linger in the bone marrow. After patients have responded well to initial therapy, consolidation aims for an even better response through a single course of very high-dose chemotherapy and an autologous stem cell transplant. This means the patient’s own healthy stem cells are

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collected and used later to rescue their blood counts and replace diseased or damaged bone marrow.

Multiple studies have shown that patients stay in remission longer and have more durable responses with this approach. Stem cell transplants are also a key treatment option for relapsed and refractory myeloma. The Fox Chase-Temple University Hospital Bone Marrow Transplant Program is a national leader in performing transplants for patients with multiple myeloma and other blood cancers.

After the stem cell transplant, patients then usually undergo a couple of additional chemotherapy cycles and convert to maintenance therapy afterward. With this intense consolidation treatment, the specialists at Fox Chase are finding that many patients have no lingering signs of multiple myeloma.

MAINTENANCE

After treatment, the patient may switch to maintenance therapy, which usually consists of one drug that patients will stay on indefinitely as long as it continues to keep their disease under control.

Relapsed and Refractory Disease: What This Means for Multiple Myeloma Patients

In many cases, multiple myeloma is very sensitive to initial treatment and patients commonly go into remission. But there may be some cancer cells that are just inherently resistant to those treatments, and over time, they start to multiply and the disease comes back or relapses.

With multiple myeloma, almost all patients will experience a relapse or will see the disease become refractory (where it stops responding to treatment). One common treatment option for these cases is a bone marrow transplant. Patients receive high-dose chemotherapy with the goal of trying to kill off the very resistant cancer cells. Then, stem cells are re-infused into the patient, which allow the patient’s cell counts to recover more quickly.

Our oncologists and bone marrow transplant specialists are experienced in treating patients with relapsed and refractory disease, offering the latest therapies and clinical trials.

MULTIDISCIPLINARY EXPERTISE

All patients with multiple myeloma receive comprehensive treatment and supportive care to control pain and prevent clot formation, skeletal complications, and viral infections. Because Fox Chase uses a multidisciplinary approach to treatment, many different physician specialists are part of the team:

- **Hematopathologists**, who specialize in diagnosing blood cancers and can differentiate between different subtypes of myeloma and other blood disorders
- **Infectious disease experts**, who treat patients undergoing transplants who develop low blood counts or infections
- **Orthopedic surgeons**, who help heal and repair bone fractures and damage sometimes experienced as a side effect of multiple myeloma
- **Radiation oncologists**, who have special expertise in providing pain relief, through radiation therapy, to multiple myeloma patients
- **Pulmonologists and cardiologists**, who can address potential lung or heart complications after transplants

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ADDITIONAL COMPONENTS OF TREATMENT

Radiation
For myeloma, radiation is used most often to treat an area of bone damage or a plasmacytoma that is causing pain. Radiation therapy can be used as the only treatment for a solitary plasmacytoma, or a single mass of myeloma cells.

To treat cancer, radiation therapy uses high-energy rays that damage the genes in cells. This treatment either kills the cancer cells or stops new ones from being produced. External beam radiation therapy (EBRT) is the most common type of radiation therapy used for solitary plasmacytomas. A machine outside the body delivers radiation to the cancer site.

Targeted Therapy
Targeted therapy is a precise type of cancer treatment, targeting proteins that control how cancer cells grow, divide and spread. These drugs can treat myeloma in different ways:

- **Angiogenesis inhibitors** block the growth of new blood vessels that feed myeloma cells in the bone marrow
- **Proteasome inhibitors** block the removal of unwanted proteins from cells and enables myeloma cells to die
- **HDAC inhibitors** block the action of histone deacetylase enzymes and may cause cell death
- **Monoclonal antibodies** are made in the lab and attach to proteins on cancer cells, labeling them for destruction by the body’s immune system
- **Immunomodulators** help the body’s immune system find and attack cancer cells

Surgery
Surgery can be used to remove a solitary plasmacytoma outside the bone if it can’t be treated by radiation alone and is causing symptoms. Radiation therapy may be given before or after surgery. If myeloma causes bone fractures, surgery can be used as treatment.

Slow-Growing Myelomas
Some cases of myeloma grow slowly and patients are asymptomatic. These are referred to as indolent or smoldering myeloma. These patients tend to be closely monitored rather than treated immediately. As important as it is to identify patients at high risk of disease progression, it is equally important to avoid overtreating patients with indolent diseases. In most cases, however, treatment will be needed eventually.

CAR T-CELL THERAPY FOR RELAPSED AND REFRACTORY MULTIPLE MYELOMA
The FDA recently approved the first chimeric antigen receptor (CAR) T-cell immunotherapy for the treatment of patients with relapsed or refractory multiple myeloma. Fox Chase is now offering this therapy (Abecma [idecabtagene vicleucel]) to eligible patients.

CAR T-cell therapies involve blood being drawn from the patient so that their T-cells can be extracted. The T-cells are then sent to a specialized lab where scientists genetically modify them to recognize their cancer cells. The newly altered T-cells are multiplied in the lab and then sent back to the hospital where they are infused back into the patient to find and destroy their cancer cells.

In the clinical study that led to the approval of Abecma, a rapid and durable response was seen in a majority of patients.

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Through our highly ranked Bone Marrow Transplant Program, Fox Chase Cancer Center and Temple Health physicians provide bone marrow and stem cell transplantation and other complex treatment options to improve long-term outcomes for patients with multiple myeloma and other blood-related disorders. Our multidisciplinary program includes board-certified hematologic oncologists with specific expertise in transplantation and caring for patients undergoing transplants and cellular therapy.

For the second year in a row, our BMT Program’s performance for one-year survival is above the expected survival rate – when compared to similar patients transplanted throughout the United States, according to a risk-adjusted analysis performed by the Centers of International Blood Marrow Transplant Research (CIBMTR). Our program was one of 17 U.S. transplant centers that achieved this recognition in 2020 and is the only center with this distinction in the tri-state area (Pennsylvania, New Jersey, and Delaware).

We perform 100-150 blood and bone marrow transplants each year at our state-of-the-art facility, which is solely dedicated to performing transplants, and every member of our team is specially trained in blood and bone marrow transplantation with extensive experience in managing all transplant types.

Our BMT Program is fully accredited by the Foundation for the Accreditation of Cellular Therapy (FACT) — the gold standard of excellence for blood and bone marrow transplant programs in the United States — and the National Marrow Donor Program (NMDP). We meet and exceed the rigorous criteria established by these organizations based on the high number of transplants we perform, our level of expertise, and the support personnel available to care for patients.

Our physicians have performed thousands of bone marrow and stem cell transplants, using cells from your own body or from matching donors. The type of transplant you receive is determined by your diagnosis, stage of disease, overall health and age. Our BMT Program is also one of very few in the United States to offer bloodless transplant procedures for patients who request this complex technique.

Other key elements of our BMT Program:

- Patients in need of transplants are not turned away from our program due to their age. Nearly 25% of our patients are older than 65.
- We actively participate in research from our own institutions, the ECOG-ACRIN Cancer Research Group, and the Bone Marrow Clinical Trials Network (BMT-CTN). Our researchers work collaboratively to bring the most promising discoveries from the laboratory into the clinical setting, where they can directly impact patients.
About Bone Marrow Transplants

Bone marrow transplants, also called stem cell transplant, are typically a key component of care for patients with multiple myeloma. A transplant infuses healthy cells into the body to replace damaged or diseased bone marrow. Bone marrow is the soft, spongy center of the bone that contains the stem cells that produce white blood cells, red blood cells and platelets, which all work to keep the body healthy.

Typically, a bone marrow transplant may be needed if:

• Your body cannot make the blood cells it needs because your bone marrow or stem cells have failed.
• Your bone marrow or blood cells have become diseased and need to be replaced with healthy cells.
• You have a disease being treated with high doses of chemotherapy and/or radiation treatment, which destroys both cancerous and healthy cells.

When people hear the term “transplant,” they may typically think of an operation, but a bone marrow transplant is not a surgical process. Stem cells are given back to the body in the same manner as a blood transfusion – the cells are pushed into the IV tubing and travel back to the marrow to start making a new population of healthy blood cells.

Types of Bone Marrow Transplants

Our team offers allogeneic and autologous transplantation, including unrelated donor and related haploidentical transplantation. The type of transplant you receive is determined by several factors, including your diagnosis, the stage of your disease, your overall health, and your age.

• **Allogeneic:** Healthy bone marrow cells come from matched related donors, unrelated donors, or umbilical cord blood.
• **Autologous:** Healthy bone marrow cells come from the patient.
• **Haploidentical:** Healthy bone marrow cells come from related donors that are not a complete match for the patient.

BMT Support Services

The Fox Chase-Temple Bone Marrow Transplant Program offers support services to help you and your family deal with the emotional, physical and social challenges that often accompany transplantation. You will have access to:

• Transplant coordinators who will walk you through all aspects of a bone marrow transplant and coordinate your care
• A complete set of consulting physicians for internal medicine and surgical issues, as well as the close support of a medical intensive care unit when necessary
• Interventional radiologists who assist with placement of indwelling catheters
• Licensed social workers who work closely with patients, caregivers and family during and after the transplant process
• Regular support and educational group meetings
• A board-certified psychiatrist who specializes in psychopharmacology
• A certified nutritionist to help with dietary issues
• Palliative care, which focuses on improving the quality of life for patients and their families through the management of symptoms, pain and stress brought on by a serious illness
• Integrative care, which explores a body/mind/spirit approach to healing

Fox Chase provides a full spectrum of care for every type and stage of myeloma — from detection through survivorship.

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AUTOLOGOUS TRANSPLANTS

Many multiple myeloma patients who respond well to initial therapy have shown even greater improvement when they receive a single course of very high-dose chemotherapy with an autologous transplant. This transplant method involves using the patient’s own previously collected healthy cells.

The course of high-dose chemotherapy overcomes the resistance of lingering cancer cells to treatment, and the autologous transplant acts as a rescue for the patient’s blood counts. The patient’s blood counts recover more quickly, and the process becomes much more tolerable for their system.

Multiple studies have shown that many patients stay in remission longer and have more durable responses with this approach.

ALLOGENEIC TRANSPLANTS

For allogeneic transplants, we make every effort to use donated cells that are as closely matched as we can identify. The best chance for finding a match is with a full sibling, where there is typically about a 25 percent chance of matching.

If a patient doesn’t have a family member who is a close match, there may be other options, including:

- **Donor registries:** Hospitals have access to national and international registries where volunteers have offered to donate their stem cells or bone marrow cells if they are found to be a match. We perform tissue typing on our patients, submit it to the registry, and generate a list of potential matches. If a potential match is found, additional testing is performed, and the cells can be collected remotely and shipped for transplantation.

- **Cord blood:** A national cord blood bank is available, which involves blood taken from the umbilical cord when babies are born. A list of potential matches within this bank can be generated by recording the patient’s blood type and tissue type.

HAPLOIDENTICAL TRANSPLANTS

With haploidentical transplants, a family member may be able to donate cells for a transplant even if he or she is not a match. In the past, mismatched cells often caused serious complications with high rates of graft-versus-host disease, but today we can use a combination of chemotherapy and immunotherapy treatments after the transplant to suppress those cells and try to avoid negative reactions.

BLOODLESS TRANSPLANTS

Some patients may not be able to receive blood or blood products from any person other than themselves, even family members. This may be true for religious reasons, safety, or any other personal reason.

As a result, interest has grown in minimizing blood transfusions and in performing operations or bone marrow transplants without blood or blood products. The Fox Chase-Temple University Health Bone Marrow Transplant Program is a referral center for bloodless transplants, which don’t involve blood or blood products from other donors.

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At Fox Chase, with careful support, we minimize the amount of blood that we take during the course of the transplant, by safely doing blood tests less often and by using much smaller tubes that take less blood for testing.

The red blood cells that our bodies make typically last for months, so most of the cells that patients come into the transplant with are still viable. In addition, the body makes new red blood cells every day, so there is a slow decrease in the blood count. As a result, the outcomes are very similar to those of patients who receive blood products.

**CLINICAL TRIALS FOR MULTIPLE MYELOMA**

Engagement in multiple clinical trials allows Fox Chase to be at the forefront of new treatment options for multiple myeloma. For multiple myeloma patients with relapsed or refractory disease (which has either come back after previous treatment or did not respond to previous treatment at all), clinical trials are often recommended when available. We are proud to be able to offer our patients the most recent advances and most promising treatments for multiple myeloma through these trials.

The cancer treatments used today are products of previous clinical trials, and the trials taking place now will help determine how we approach cancer in the future.

Fox Chase multiple myeloma patients have participated in and now have access to many groundbreaking, state-of-the-art trials. [View a complete list of multiple myeloma clinical trials at Fox Chase.](#)

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**Multiple Bone Marrow Transplants**

Some people have more than one bone marrow transplant:

- After a first transplant, a patient may receive maintenance therapy to keep the abnormal cells at their lowest level for as long as possible – sometimes for years – and then undergo a second transplant whenever the disease strengthens again.
- Some patients may plan to receive two autologous transplants within three months to maximize the chance for a cure.
- Patients with lymphomas who relapse after an autologous transplant can sometimes be cured with an allogeneic transplant.
WHY CHOOSE FOX CHASE?

Fox Chase Cancer Center:

- Has received the highest designation from the National Cancer Institute (NCI) as a Comprehensive Cancer Center, an elite center recognized for excellence in cancer treatment, research, prevention and education
- Offers a multidisciplinary team of physician leaders with strong expertise in treating multiple myeloma
- Provides a full spectrum of care for every type and stage of multiple myeloma — from detection through survivorship
- The Fox Chase-Temple University Hospital Bone Marrow Transplant Program is a national leader in performing transplants for patients with multiple myeloma, leukemia, lymphoma and other blood disorders
- Offers access to clinical trials for emerging and innovative therapies for multiple myeloma

When you or someone you care about is faced with the risk or diagnosis of multiple myeloma, you will want medical advice and care from experienced and compassionate professionals who are leaders in their field. At Fox Chase, we have offered comprehensive approaches to diagnosis, treatment and follow-up support for more than 100 years.

Our multidisciplinary hematologic specialists not only are using some of the latest treatments and technology available, but also are involved in clinical trials and risk assessment research. Clinical trials and research may offer patients access to innovative treatments today and breakthroughs in the future.

In addition, we take a comprehensive approach to treating your condition, with nurse educators, social workers and other specially trained staff members who truly make a positive difference during a difficult time. These support staff members provide emotional support, advice and coping strategies when they are needed most.

We hope that you’ve found this guide to be a useful resource. If you have further questions about multiple myeloma, please contact Fox Chase at 888-539-8205.