

NOTES:

# Information on STEM CELL TRANSPLANTS

## What is a Stem Cell Transplant?

A stem cell transplant is an infusion of stem cells following high-dose chemotherapy. The infused cells effectively rescue the patient from the toxic effects of the chemotherapy on the bone marrow. The infusion process is similar to a blood transfusion.

There are two types of stem cell transplants: autologous and allogeneic. In an autologous transplant, the patient's own stem cells are infused. In an allogeneic transplant, donor stem cells are infused.

## The vast majority of stem cell transplants for myeloma are autologous.

## This pamphlet focuses on autologous transplants.

When stem cell transplants were first developed, the stem cells were obtained from the patient's bone marrow; hence, the procedure was known as a bone marrow transplant. Stem cells are now collected from the patient's circulating (or peripheral) blood; hence, the procedure is now known as a peripheral blood stem cell transplant.

## Myeloma Treatment

High dose chemotherapy (HDT) with an agent called melphalan is one of the most effective therapies for myeloma. This procedure can be made safer and more effective by the use of blood stem cells, which are able to form all the elements of the blood.

Initial treatment for many myeloma patients often involves combinations of anti-myeloma agents to get the patient into remission. The level of response and outcome can be markedly improved by the use of HDT.

HDT is very effective at killing myeloma cells, but is also toxic to blood-forming stem cells in the bone marrow. If given alone without stem cells support, it inhibits blood cell production permanently, leading to inadequate numbers of red blood cells, white blood cells and platelets, each of which perform essential functions. Without adequate blood cell counts, patients experience multiple life-threatening complications.

- Red blood cells carry oxygen from the lungs throughout the body
- White blood cells fight infection
- Platelets form clots to control bleeding from injuries

Permanent blood cell suppression can be prevented by infusing healthy blood-forming stem cells collected from the patient's bloodstream 18 to 24 hours after the HDT has been given.

The HDT with stem cell rescue regimen includes flushing stem cells out of the bone marrow into the peripheral blood, from which they can be collected. These healthy stem cells are collected and stored after the patient has responded to initial anti-myeloma agents. High doses of chemotherapy are

This information about Stem Cell Transplants and other patient education materials are available at [www.myeloma.uams.edu](http://www.myeloma.uams.edu)

then administered to wipe out the remaining myeloma cells in the bone marrow and a subsequent infusion of the stored stem cells “rescues” the bone marrow and stimulates production of normal, healthy cells. This regimen is very effective and can produce long-lasting response, with the capability of putting myeloma into complete remission. The stored stem cells “rescues” the bone marrow and stimulates production of normal, healthy cells. This regimen is very effective and can produce long-lasting response, with the capability of putting myeloma into complete remission.

### Successes

The Myeloma Institute has successfully employed stem cell transplantation since the program’s founding in 1989. We pioneered the use of two back-to-back transplant procedures, known as a Tandem Transplant. This approach has been an integral component of the Myeloma Institute’s Total Therapy treatment regimen. Through the use of this procedure, survival rates have increased dramatically, resulting in significant cure rates.

The Myeloma Institute was the first to perform stem cell transplants on an outpatient basis and to demonstrate the safety of transplantation in elderly patients and those with renal failure.

The Myeloma Institute prefers doing transplantation on an outpatient basis unless medical factors necessitate hospitalization. The outpatient setting keeps patients in a comfortable, normal environment and reduces the risk of hospital-acquired infections.

### Process

#### Quick overview

- 1) Induction: The patient is treated with induction chemotherapy to decrease the number of myeloma cells in the bone marrow.
- 2) Mobilization, Harvest & Collection: The patient is treated with a medication to increase the number of stem cells and push them out of the bone marrow into the circulating blood, from which they can be collected (harvested).

- 3) Storage: The harvested stem cells are frozen for use at a later time when they are needed. We collect enough stem cells for multiple stem cell transplants.
- 4) Conditioning & Stem Cell Infusion: The patient receives high-dose therapy (HDT), followed by infusion of thawed stem cells to restore normal blood cell production.
- 5) Recovery: Blood counts fall over five days in response to the HDT, but engraftment (reproduction and growth) of the infused cells normally occurs by day 10 to day 14.

### Induction chemotherapy

Pre-transplant chemotherapy is known as induction treatment. The aim of induction treatment is to reduce the amount of myeloma in the bone marrow before stem cells are collected. Stem cells that are collected when the patient is in remission are less likely to be contaminated by myeloma cells. Courses of induction chemotherapy usually last for several months and are given in cycles. The number of cycles varies, depending on the individual’s response to the treatment.

Side effects of induction treatment, including nausea, fatigue and anemia, can be managed so the patient has minimal discomfort and interruption to daily life.

### Stem Cell Mobilization & Harvesting

Chemotherapy causes a drop in blood cell counts. A medication called granulocyte colony stimulating factor (GCSF) can be used to stimulate growth of new blood stem cells and move them into the circulating blood from which they can be collected. The process of stimulating growth of new blood stem cells and moving them into circulating blood is known as mobilization.

Blood stem cells in circulating blood are known as peripheral blood stem cells. When the peripheral blood stem cell count is high enough, the cells are withdrawn (i.e. “collected” or “harvested”).

If a patient has received chemotherapy, peripheral blood stem cell collection typically begins just as blood counts start to recover. If a patient has received just GCSF and no chemotherapy, collection typically begins when the white blood cell count begins to rise. Since the time during which increased production of peripheral blood stem cells is limited, and because the first days of collection are the most important, patients must be in Little Rock for frequent blood work assessments.

Mobilization of stem cells can sometimes be challenging for patients who have been previously treated for their disease. In such cases, patients may be given daily injections of plerixafor, a medication that forces the release of stem cells in the bone marrow into the bloodstream. This can improve mobilization and increase the number of stem cells harvested.

### Side effects of mobilization

The most common side effects of mobilization with GCSF are temporary general and bone aches, joint pain and fever, all of which can be treated with mild painkillers. Common side effects of chemotherapy used for mobilization include nausea, loss of appetite, skin rash, general weakness and loss of hair.

Side effects of plerixafor may include nausea, diarrhea, dizziness, headache, joint pain and irritation at the injection site.

### Stem Cell Collection

Peripheral blood stem cells are collected, or harvested, through a process called apheresis. A blood cell separator machine draws blood from the body, separates the different types of blood cells, draws off the stem cells and then returns the rest of the blood cells back to the patient. The machine operates a very rapid withdrawal and return of blood, necessitating a central venous line that is placed in the chest wall by interventional radiology or a surgeon prior to the start of the collection process.

The number of apheresis procedures for sufficient collection differs for each person. Two or three collections over consecutive days are usually required to collect a sufficient quantity of cells for most patients. Each procedure may last up to four hours.

A marker on the cell surface called CD34 is used to determine the quantity and quality of stem cells that have been collected.

The minimum number of stem cells needed for a successful transplant is roughly two million per kilogram of body weight. However, we collect enough stem cells for multiple transplants.

### Stem Cell Storage

In the Cell Therapy Processing Lab a protective agent is added to the collected stem cells. This prevents water in the cells from forming ice crystals, which would permanently damage the stem cells during the freezing process.

Stem cells are placed in special bags and then stored in liquid nitrogen. Frozen stem cells can be stored indefinitely.

UAMS has a specialized apheresis unit and processing lab with tight controls and thorough tracking and monitoring. The units are accredited by the Foundation for the Accreditation of Cellular Therapy (FACT). FACT is an accrediting organization that addresses all quality aspects of cellular therapy treatments: clinical care, donor management, cell collection, cell processing, cell storage and banking, cell transportation, cell administration, cell selection, and cell release. FACT-accredited organizations voluntarily seek and maintain their accreditation through a rigorous process.

### Transplantation

In order to prepare the body for transplant, the patient receives high-dose chemotherapy (HDT), usually melphalan. The main function of HDT is to destroy the cancerous myeloma cells.

Infusion of the stem cells typically takes place 18 to 24 hours after completion of the conditioning chemotherapy regimen. The actual infusion takes about 15 minutes. If the volume of cells to be infused is especially large, the infusion can be spread over two days.

After the stem cells are infused there is a waiting period of about five days, during which the counts of white cells, red cells and platelets will drop. The process of the transplanted cells “taking” and beginning to grow in the bone marrow is referred to as engraftment. The time from transplant to engraftment is between 10 and 20 days. During this time period, when blood counts are low, patients usually feel their worst and are at risk for infection. Transfusions of red blood cells and platelets are given, if needed, to support the blood counts.

### Side effects of Stem Cell Transplantation

The Myeloma Institute places an emphasis on supportive care throughout the entire treatment and recovery process. We do everything possible to minimize side effects and discomfort.

#### Short term side effects

Common side effects from high-dose chemotherapy (HDT):

##### ■ Myelosuppression

HDT typically decreases bone marrow activity, resulting in fewer red blood cells, white blood cells and platelets. Red blood cell and platelet infusions can be given if necessary.

##### ■ Nausea

This is controlled with an anti-emetic drug to prevent nausea and vomiting

##### ■ Sore mouth, also known as mucositis

Chemotherapy drugs attack fast-dividing cells, which include the cells lining the mouth and digestive system. This can cause mild to moderate inflammation and changes in taste or more painful ulcers and difficulty eating and drinking. Sucking on ice cubes when receiving HDT can help reduce the risk of mucositis.

##### ■ Altered taste and smell

This is normal. Sense of taste and smell will return in time.

##### ■ Fatigue

Feeling very tired, sleeping more than usual and having difficulty concentrating are common. Fatigue might persist longer than other symptoms, but eventually the fatigue will diminish.

##### ■ Hair Loss

While hair may thin during the induction phase of treatment, hair loss typically occurs two to three weeks following HDT. The hair will regrow after three to six months.

##### ■ Peripheral Neuropathy

Chemotherapy drugs can cause degeneration of peripheral sensory and motor nerves and cause tingling or burning sensation in the hands and feet and balance problems. Medications can help reduce inflammation of the nerve endings. It is important to report peripheral neuropathy to your healthcare provider.

##### ■ Shingles

Caused by the chickenpox virus, shingles can develop after the transplant. You will receive medication before the transplant to prevent shingles. Side effects related specifically to the infusion of stem cells result primarily from a preservative that is used in the cell storage process. Medications are given before the infusion process to lessen nausea, vomiting and chills. Other side effects can include:

- Distinct odor of the cells in body excretions for the first 24 to 36 hours after the infusion
- Distinct taste of the preservative. Peppermints can help.

Additionally, during the period of time between infusion of stem cells and the body’s production of new blood cells, patients are at risk of infection, anemia and bleeding. This is caused by the low counts of white blood cells, red blood cells and platelets. During this **Neutropenic Stage** when the immune system is compromised, patients must be

diligent about taking precautions to avoid infection. For example, fresh fruits and vegetables must be thoroughly cleaned under running water. Meticulous hygiene, including mouth hygiene, diligent hand washing and use of protective masks in public areas are essential. Patients are routinely placed on preventive antibacterial, antiviral and antifungal medications.

#### Long term side effects

With advances in anti-myeloma agents and supportive care treatment, patients undergoing high-dose chemotherapy with autologous stem cell transplantation can expect to make an excellent recovery and experience improved quality of life. However, there can be long-term risks, especially with increased lengths of survival.

##### ■ Infertility

Patients are given the opportunity to store eggs or sperm before treatment starts.

##### ■ Organ damage

In particular, interstitial lung disease (characterized by progressive scarring of lung tissue) can result from high-dose chemotherapy or from frequent respiratory infections. The heart and kidneys are also at risk. Testing done prior to the transplantation process provides a baseline of normal function. Organ function is monitored throughout the course of therapy.

##### ■ Secondary cancers

Chemotherapy drugs work by damaging the DNA in cells. Most normal cells can repair the damage. Damage that is not repaired can potentially result in secondary cancers, such as leukemias or lymphomas.

#### Is Stem Cell Transplant Right for Every Patient?

Not all patients with myeloma are candidates for transplantation. Each individual patient is thoroughly assessed to determine the optimal type of therapy.

Factors that influence whether or not stem cell transplantation is appropriate include:

- Type of myeloma
- Disease stage and aggressiveness
- Response to treatment
- Chromosome and genomic indicators
- Overall health status and activity level

The Total Therapy approach at the Myeloma Institute typically includes stem cell transplantation early in the treatment process. This is based on the premise that killing cancerous myeloma cells in the beginning offers the patient the best chance of a long-lasting remission and cure. Evidence supports the use of stem cell transplantation.

While highly successful, this approach is not always the best for each and every patient. Through the use of sophisticated diagnostic testing, including genomic analysis, Myeloma Institute physicians can determine the ideal course of treatment and optimal timing of treatment for each individual.

While the autologous stem cell transplantation process may seem daunting, the benefits can be substantial and can outweigh the temporary discomforts and disruptions to one’s daily life. The Myeloma Institute utilizes transplantation when in the best interest of the patient. In all cases, care plans are customized for each patient in order to achieve the best possible results.

