Total-Body Irradiation for Bone Marrow Transplantation

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Total-body irradiation (TBI), when given as part of bone marrow transplantation (BMT), works by enhancing immune suppression and by exerting a tumoricidal effect. The modality has been made less toxic because of new approaches to delivering TBI, such as fractionation, and partial organ shielding, Colleen Lawton, MD, professor at the Medical College of Wisconsin, Milwaukee, said at the 1998 American Society for Therapeutic Radiology and Oncology meeting.

Total-body irradiation has continued to play a pivotal role in the conditioning regimens for BMT, which has become a common modality in the treatment of both acute and chronic leukemias and myelodysplastic disorders, as well as relapsed Hodgkin’s and non-Hodgkin’s lymphomas. Transplantation is also gaining favor in the treatment of aggressive multiple myeloma, breast cancer (autologous transplantation), neuroblastoma, Ewing’s sarcoma, and relapsed testicular carcinoma. In addition, BMT has a role in benign but fatal diseases, such as refractory aplastic anemia, some congenital deficiency disorders, and, experimentally, in some autoimmune disorders.

Stem-cell transplantation also looks promising in the treatment of primary progressive multiple sclerosis (MS). Patients qualifying for the experimental protocols are bed-bound and likely to die of their disease within 2 years. In half a dozen or so patients who have received this therapy, disease status has substantially improved and lesions have regressed, as measured on magnetic resonance imaging (MRI). In laboratory models of an MS-like syndrome, TBI prior to transplantation decreases the likelihood of disease progression to a greater extent than does transplantation without TBI. Therefore, TBI may have an adjunctive role in this new approach, Dr. Lawton predicted.

The closer the donor-recipient match in terms of HLA antigens, the lower the transplant-related mortality. Therefore, HLA-matched sibling donors offer the best chance for success. Unfortunately, only 25% to 30% of patients have an ideal match. Therefore, there is a heavy reliance on partially matched, related donors and unrelated, matched donors. The National Marrow Donor Program has greatly facilitated the pairing of patients with nonrelated, matched donors, offering Caucasians a 30% to 40% chance of locating an HLA-identical unrelated donor. However, non-Caucasians have a much poorer chance of finding a matched donor, and there is a great need for donors from all non-Caucasian races to help remedy this problem.

More Effective, Less Toxic TBI Regimens

Advances have been made in rendering TBI more effective and less toxic through greater understanding of marrow recovery. Even when large amounts of marrow are exposed to high doses of radiation, marrow recovery can occur as long as significant portions of the marrow have been shielded. In breast cancer patients, Sykes and colleagues showed that 30 Gy, delivered at 2 Gy per fraction, seemed to be the tolerance beyond which marrow regeneration did not occur.[1] At or above a radiation dose of 30 Gy, 50 (96%) of 56 sternal biopsies showed little or no marrow regeneration.

The response of the peripheral blood cells days after irradiation varies, depending on cell type. Lymphocytes, being the most sensitive cells in the peripheral blood, clearly diminish shortly after the delivery of the TBI. The effect on granulocytes is seen after 1 to 2 days, with regeneration in 20 to 24 days. Platelet effects are seen after 2 to 3 days, with regeneration in 14 to 21 days. The least sensitive cells, the erythrocytes, recover the fastest. The magnitude of the respective cytopenias depends not only on the radiation dose but also on the normal lifespan of the respective circulating cell and its inherent sensitivity to radiation, Dr. Lawton pointed out.

Several lines of evidence support a total dose/fractionation relationship in TBI, especially in T-cell-depleted, unrelated, or mismatched donor transplants. Data show that increasing doses of TBI correlate with increased engraftment, that a single dose of TBI is more immunosuppressive than the same total dose conventionally fractionated, and that bone marrow myeloid eradication is greater with hyperfractionation (with the total dose slightly increased over a single dose).

In humans receiving a non-T-cell-depleted allogeneic transplant from a matched sibling, it has been
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fairly well demonstrated that no one TBI regimen produces more favorable engraftment rates, because engraftment is virtually 100% for these types of patients. However, with more difficult grafts, both animal and human studies have shown that with increasing TBI dose or with the addition of total lymphoid irradiation (to increase immune suppression) to standard TBI, engraftment rates improve. This may occur because the lymphocytes have a "very small shoulder" on the cell survival curve, meaning that their likelihood of repair, even with fractionation, is small. The same is true for leukemic or other cells targeted for killing. Fractionation, therefore, should be beneficial, Dr. Lawton said.

Compared with single-dose irradiation, fractionation also appears to be less toxic to normal tissues, which are also affected by TBI at some level, with the lung being the principal dose-limiting organ of concern. Multiple clinical regimens have supported this notion, and to date, dramatic sparing of the lung and intestines has been shown with more fractionated regimens, she said.

**Commonly Used TBI Schedules**

In the first published description of a dedicated TBI unit in North America, the patient was placed in a room with a radiation source and a canary was placed in a cage near the patient. Death of the canary during the delivery of the radiation was a signal to discontinue the radiation. Considerable advances since that time have made TBI much safer.

The most commonly used TBI schedule in the United States is 1,200 cGy in six fractions, delivered either once or twice daily, without shielding. But if you are doing T-cell-depleted transplants or transplants from mismatched or unrelated donors, data from multiple centers would suggest that 12 Gy in six fractions is not enough, Dr. Lawton said.

In a small series from the Fred Hutchinson Center in Seattle, 20 patients with matched donors were studied, 11 of whom received 1,200 cGy in six fractions (the standard dose) and 19 of whom received 1,575 cGy at 225 cGy per fraction. Engraftment was unsuccessful in 6 of the 11 patients treated with the 1,200 cGy in six fractions. As the TBI dose increased, nonengraftment was decreased, presumably because immunosuppression was enhanced.

When you don't get a graft in, the patient usually dies. And the likelihood of getting a successful second graft in is small. It's exceedingly important that you get the initial graft in, Dr. Lawton stressed.

In a similar situation with T-cell-depleted transplants, Memorial Sloan-Kettering researchers also found that 20 of 22 matched transplants were successfully engrafted, compared to only 10 of 20 mismatched transplants. The dose of radiation used in this study was 1,320 cGy. The authors concluded that a more intensive preparatory regimen is needed to achieve engraftment. One way to do so, according to Dr. Lawton, is to increase the TBI dose.

Although the most common schedule is 12 Gy in six fractions, there are indications for higher doses, especially in unrelated or mismatched transplants where you may need increased immune suppression. You can get increased immune suppression from the TBI, and this will help the graft to take, she said. Use of hyperfractionated TBI to doses above 12 Gy (ie, 13.50 to 14 Gy) is one way to successfully increase engraftment rates for these unrelated or mismatched transplants.

In terms of positioning the patient for TBI, no one method has proved to be superior. However, with what-ever position is chosen, there should be 10% dose homogeneity, Dr. Lawton said. This means, that, in general, the anterior/posterior-posterior/anterior (AP/PA) technique is preferred over the lateral technique. A range of beam energies are acceptable, as long as beam spoiling of the higher-energy beams is performed to ensure that the dose to the skin surface is delivered as prescribed.

**Toxicity**

The principal dose-limiting organ of TBI is the lung. Interstitial pneumonitis from TBI remains a problem for patients who undergo transplantation because it accounts for approximately 40% of transplant-related deaths. Early studies found that the occurrence of pneumonitis was related to the dose rate of TBI, and that very low dose rates (on the order of < 2 cGy/min) were necessary to avoid this side effect. However, numerous investigators have since shown that higher dose rates and total doses can be safely delivered, as long as they are fractionated.

In fact, the development of hyperfractionated TBI was based on the hypothesis that one could decrease the incidence of pneumonitis while increasing the dose to achieve a higher engraftment rate. By escalating the dose of TBI, the engraftment rate was unquestionably improved; however, mortality in patients who received higher TBI doses without partial lung shielding was increased, mostly due to lung toxicity.

Today, with selective organ shielding, we can go to significantly higher TBI doses than we ever thought we could without it, Dr. Lawton said.
Other Uses of Irradiation During the Transplant Process

Irradiation has a number of other uses during the transplant process: treating splenomegaly, treating the central nervous system (CNS), boosting of local disease, and boosting of known or potential testicular disease. In the treatment of splenomegaly, radiation is used most commonly in patients with chronic myelogenous leukemia (CML) as a means of avoiding surgery. Data from a European randomized trial of CML patients who were given 10 Gy over 3 days initially showed no improvement in disease-free survival. (There was often a delay between the spleen irradiation and the conditioning regimen, which is problematic, Dr. Lawton pointed out.) However, an updated analysis of this study identified an intermediate group of patients who actually benefited from spleen irradiation, such that the relapse rate at 8 years was 8% with splenic radiotherapy and 30% without.

“So I think there is still a role for splenic irradiation,” Dr. Lawton said. At our institution, if you have mild splenomegaly, you do get radiation as a boost prior to TBI, but if the splenomegaly is more prominent we generally take the spleen out surgically.

A radiation boost to localized disease is often used in patients with leukemias and lymphomas who have bulk disease, and also in patients receiving solid tumor transplants. The recommended dose is based on tumor type, but is generally 10 Gy at 2 Gy per fraction for leukemias and lymphomas when boosting is done in conjunction with TBI.

Administering radiation boosts to the testicles remains controversial; however, data from Memorial Sloan-Kettering support the use of a 4-Gy boost to the testicles in addition to TBI, based on the occurrence of relapses in 4 of 28 patients who received no boost to the testicles, compared with 0 of 600 who had the boost.

“This testicular boosting is done to decrease the risk of testicular relapse in patients with leukemia. At our institution we don’t routinely use it, although we certainly will do it in patients who are on a protocol requiring testicular boosting. It’s clearly controversial; nevertheless, you can’t ignore the data from Memorial Sloan-Kettering,” Dr. Lawton commented.

Early and Late Sequelae of TBI

“One of the most important things that we as radiation and medical oncologists can do is to help the patients understand the sequelae of TBI—what effects are related to the radiation and, just as importantly, what effects are not related to the radiation,” Dr. Lawton said.

In terms of acute sequelae, nausea and vomiting can occur within an hour of delivery of TBI; however, current antiemetics have made actual vomiting a very uncommon phenomenon. The antiemetics work very well and should always be used, she stressed.

Most patients develop parotiditis. This usually begins on the second or third day of fractionated TBI and can be treated simply with analgesics. If used as part of the transplant maneuver, steroids also relieve the parotiditis fairly quickly.

Diarrhea is also common and can be managed with antidiarrheal agents. Skin erythema is not generally seen, except when certain chemotherapeutic agents are part of the conditioning regimen. Hair loss is a near-universal problem, but hair grows back within 3 to 6 months. Fatigue is very common.

Late sequelae can be numerous. It is important that patients understand what is and is not attributable to the radiation, Dr. Lawton said. I like to explain the risks of total body irradiation from a head to toe perspective, so that I don’t overlook anything.

Cataracts

Cataracts can occur after transplantation, either as a result of the TBI or as a consequence of the steroids administered for immune suppression. When cataracts are due to the radiation, they usually occur years after the TBI and their occurrence is clearly related to dose and fractionation.

Data collected in the mid-1980s in Seattle showed that single-dose TBI was associated with an incidence of cataracts of up to 80%, vs no TBI or fractionated TBI, for which the incidence of cataracts was only about 20%. Updated information has confirmed these findings. Single-dose TBI with or without steroids carried a very high risk for cataracts in this series of patients, which supports the benefits of fractionation. However, even with fractionated TBI, if steroids were used the incidence of cataracts was still approximately 50%. Fractionated TBI without steroids, or steroids without TBI, produce virtually the same results with regard to cataract formation.

Some very recent data from the European group for BMT shows some interesting information in regards to hyperfractionated TBI, Dr. Lawton said. With single-dose or fractionated TBI we see some difference in the incidence of cataracts, but the biggest reduction was for hyperfractionated—their version of hyperfractionated is more than six fractions—where the incidence of cataracts was less than 10%. They also found a dose rate phenomenon related to cataract
formation but didn't subselect their hyperfractionated group, so it's hard to know whether the dose-rate phenomenon will be important or not if you hyperfractionate the TBI.

**Pediatric Transplantation**

Growth and development problems are clearly big issues in pediatric transplantation. Data from the University of California, San Francisco, showed that pediatric patients undergoing transplants for either leukemia or benign disease demonstrated diminished growth, although delayed or arrested puberty was not as common in children with benign disease as in those with leukemia. Neuropsychological evaluations showed diminished scores in all patients in both groups; interestingly, however, there was 100% recovery within 3 years. Other studies have suggested that growth delay occurs more commonly in patients who have a transplant and have had prior cranial irradiation, Dr. Lawton said.

"I think this is really important information for parents to understand. TBI delivered in prepubertal patients will cause growth and development delays," she commented.

Fertility is also an important issue related to transplantation in young people. It is generally accepted that more than 95% of males will become azoospermic and more than 95% of postmenarchal females will become amenorrheic following transplantation. Some interesting data from Seattle in the mid-1980s showed that the likelihood of normal gonadotropin levels in menstruating females was less than 10% post-TBI, and the incidence of subsequent pregnancy was approximately 5%. While fertility in males was affected somewhat less often, only 2 of 41 males had normal spermatogenesis. Fertility appears to recover sooner in males than in females. Although some males and females do recover their fertility, patients need to understand that the likelihood of fertility loss after TBI-containing transplantation is very high.

Recent data suggest, however, that some ovarian recovery does occur post-transplantation. In one study of females who were premenarchal at the time of TBI, four of five eventually achieved menarche. However, 100% of females who were post-menarchal at TBI had evidence of ovarian insufficiency, Dr. Lawton reported.

"This is definitely an age-related phenomenon. If you were younger than 18 in this study, 100% were ultimately able to menstruate, but if you were older than 18, only 15% achieved menarche. It is very important to understand those nuances," Dr. Lawton stated.

The scenario is similar for males, according to a recent study from Minnesota that focused on 270 patients who underwent BMT and TBI at an average age of 25 years. Again, older age at transplant increased the risk of gonadal dysfunction, similar to the previous study. Radiation clearly plays a role, Dr. Lawton said.

"With sperm-banking and the ability to freeze eggs today, there are ways of getting around the fertility problems, but this still remains a major issue," she said.

Fractionation also seems to play a significant role in thyroid dysfunction. Single-dose TBI is associated with a 23% to 73% incidence of thyroid dysfunction; with fractionation, the incidence is lower. Hypothyroidism is usually mild and does resolve spontaneously in some cases. Hypothyroidism increases in incidence over time and can occur late; therefore, patients must be followed over the long term.

**Interstitial Pneumonitis**

Interstitial pneumonitis, as previously mentioned, remains a problem, and one which can be influenced by fractionation. Interstitial pneumonitis can be either infectious or idiopathic, although these two causes are interrelated. Although the radiation cannot be blamed directly for the infectious component, damage from radiation may pave the way for an infection to occur more easily.

Approximately 40% of transplant-related deaths are still related to interstitial pneumonitis. The common clinical presentation includes dyspnea, fever, nonproductive cough, and hypoxia. The chest x-ray shows bilateral interstitial infiltrates. Histologically, there is edema, fibrosis, and alveolar exudates. The condition usually occurs within 90 days after transplantation.

Interstitial pneumonitis incidence depends on total dose and fractionation. Patients who receive doses of 12 Gy in six fractions or higher need to be seriously considered for lung shielding. There are two ways to shield the lung. One method is to decrease the radiation dose to correct for the heterogeneity issue and the other is to decrease dose beyond the total dose prescribed.

"At our institution, using a hyperfractionated model similar to what Memorial Sloan-Kettering was using back in the mid-80s, we saw an unacceptable incidence of fatal pneumonitis, often without an organism cultured. We used attenuation blocks of 50% and went up to 60%, but we left the electron boosting the same," Dr. Lawton said.

"With that maneuver, we subsequently treated 107 patients and saw a total of 24 cases of fatal
pneumonia—14 cases in which an organism was cultured and 10 in which it was not—for a rate of fatal pulmonary events of 22%. Our initial group of patients had a 64% fatal pulmonary event rate, so we were quite pleased with that decrease, she reported.

“One wonders why a difference of only 10% in the dose to the lung would make what appears to be a relatively big difference in practice. It clearly depends on where you are on the dose response curve. If you are in the steeper portion, then a difference of 10% potentially could make a significant difference in outcome,” Dr. Lawton pointed out.

For patients who survive more than 6 months after transplantation, will there be long-term sequelae to the lungs from the radiation or from the transplant maneuver? For a long time this was a difficult question to answer, but a large pulmonary function study performed at Dr. Lawton’s institution several years ago found that forced expiratory volume in 1 second (FEV1), forced expiratory capacity (FEC), and total lung capacity initially declined but then recovered to some degree. Diffusing capacity of the lung for carbon monoxide (DLCO) showed an initial dip, also with some incomplete recovery.

Incomplete recovery of pulmonary function at Dr. Lawton’s institution was associated with certain factors, especially graft-vs-host disease and post-transplant pulmonary infections. A mid-lung dose of more than 6 Gy (measured centrally behind the lung shield), also was associated with a higher incidence of long-term problems. That’s part of the reason that, even at 12 Gy in six fractions, I’m more inclined to use some sort of lung shielding, Dr. Lawton explained.

A recent study from Italy focused on 90 patients undergoing mismatched transplants, 36 of whom were treated with single-dose TBI (8 Gy) and 54 of whom received 14.4 Gy delivered according to a hyperfractionated schedule. This study found that the probability of patients developing interstitial pneumonitis was higher when single-dose TBI was used, even though the dose was much lower than with fractionated delivery. Again, this demonstrates the beneficial effects of fractionation and, importantly, hyperfractionation, Dr. Lawton said.

**Veno-Occlusive Disease of the Liver**

Veno-occlusive disease of the liver occurs in approximately 10% to 15% of BMT patients. Such patients present with hepatomegaly and ascites, sudden weight gain, and high bilirubin levels. As with pneumonitis, mortality is very high (ie, approximately 50%).

Veno-occlusive disease is more likely to occur in the presence of certain risk factors, including pre-BMT liver function abnormalities, multiple transplants, and more intense conditioning regimens, especially those containing busulfan (Myleran). Interestingly, veno-occlusive disease does not appear to be related to graft-vs-host disease.

Veno-occlusive disease also is more likely with higher doses of TBI and with single-dose vs fractionated TBI. We use a 10% attenuation liver block at our institution because 3 of our first 20 patients developed fatal veno-occlusive disease. After instituting this block we had only a 5% incidence of fatal disease, Dr. Lawton reported.

Any time you add this selective organ shielding, you have to be careful that you are not influencing your engraftment rates or your relapse rates. These have been evaluated for all the measures we’ve instituted, and fortunately they have not been negatively affected, she added.

**The Kidneys**

Renal damage is an important aspect of transplant-related morbidity, simply because it can be very insidious and is not easily or quickly diagnosed. Five types of radiation renal syndromes have been described: asymptomatic proteinuria, acute radiation nephritis, chronic radiation nephritis, benign hypertension, and malignant hypertension. It is important to note that acute radiation nephritis has a short latency period of 6 to 13 months, and patients who survive the acute stage are left with chronic radiation nephritis.

Nephritis, which is being seen increasingly in transplant patients, appears to be clinically and histologically similar to radiation nephrosclerosis. Clinical features include proteinuria, hypertension, anemia, and azotemia. Overall, the kidneys shrink in size. This condition can be compatible with many years of life but is fatal in some cases.

Post-transplantation, patients must be carefully monitored for hypertension. Patients who show even mild elevations in blood pressure should be monitored aggressively. Likewise, careful monitoring of blood pressure is extremely important in the pediatric population, who also are susceptible to renal toxicity from BMT.

Radiation renal damage occurs more often to the glomerulus than to the tubules. To complicate the renal damage, there are many nephrotoxins associated with transplantation. Chemotherapy prior to and/or during the transplant, the TBI itself, antifungal agents, graft-vs-host disease, and infections in
general all can affect the kidney. In a rodent model, busulfan appeared to augment radiation nephrotoxicity. Certainly, the total dose of TBI and, possibly, fractionation or fraction size also play roles, Dr. Lawton said, adding, "I don't think it's clear that the renal damage seen following BMT is just a radiation phenomenon, although certainly radiation is playing a role."

A 1996 European study, in which the TBI doses were 10, 12, and 13.5 Gy, showed that the lowest radiation dose was associated with the best chance of remaining free of renal damage, and the highest dose was associated with highest risk of damage. However, the results were complicated by the fact that, as dose increased, so did fraction size, Dr. Lawton said.

In a study by Dr. Lawton and co-investigators, in which dose per fraction or fraction size remained stable and selective organ shielding was used, the incidence of BMT nephropathy differed significantly by renal dose, with diminishing damage associated with diminishing doses from 14 Gy, to 11.8 Gy, to 9.8 Gy. These observations suggested that monitoring renal doses is important, she said.

Lethal Complications
Lethal complications are more likely to occur in older patients, and also depend on the patient’s disease status prior to transplantation, the type of transplant (with allogeneic being riskier than autologous BMT), and donor type (with HLA-matched sibling offering the best scenario for allogeneic transplants).

Secondary Malignancies
Secondary malignancies can be divided into two broad categories: B-cell lymphoproliferative disorders and solid tumors. B-cell lymphoproliferative disorders have been seen in cases of prolonged immunosuppression. The increased frequency in transplant patients occurs more often with mismatched and T-cell-depleted transplants. B-cell lymphoproliferative disorders appear to be related to the Epstein-Barr virus but are not thought to be causally related to the TBI in the conditioning regimen. The risk of developing B-cell lymphoproliferative disorders is very low, but when they do occur, they are usually fatal, Dr. Lawton said.

Solid tumors, on the other hand, are associated with TBI in the conditioning regimen. In the International Bone Marrow Transplant Registry (IBMTR) database, there were 166 cases of secondary malignancies among 15,000 transplants. Most were lymphomas and leukemias, while 20% were skin cancers and 30%, other solid tumors.

According to the Seattle data, age-adjusted incidence for all secondary malignancies was 6.5 times that of primary malignancies in the general population. About one-third of these secondary malignancies were solid tumors, which is similar to the IBMTR data.

Psychological Morbidity
Because of the gravity of the disease and the intensity of the transplant procedure, the psychological morbidity of undergoing transplantation is, understandably, considerable. One prospective, quantitative psychosocial evaluation of 31 BMT patients found a 54% incidence of psychological morbidity, which was still present 69 months after transplantation. While psychological morbidity was unrelated to the type of transplant, patients with CML appeared to fare the worst.

Data show that cancer patients in general—not just transplant patients—who receive adjuvant psychological therapy following their diagnosis demonstrate less psychological morbidity over the long term. Thus psychological therapy should be offered to all transplant patients.

TBI and Survival
The magnitude of risk for short- and long-term toxicity from transplant-related TBI might lead one to question its value, but I think there really are some good reasons to use it," Dr. Lawton said. Along with its immunosuppressive effects, TBI appears to improve survival.

A study from Japan involving 123 patients receiving transplants for acute leukemia, in which 81 patients received TBI and 42 did not, showed a statistically significant improvement in relapse rates and survival with TBI. In certain situations, in fact, TBI appears to be critical for good results. These include transplantation for AML and the use of either mismatched or T-cell-depleted transplants. For example, a randomized trial from France in patients with acute leukemia transplanted either with cyclophosphamide or busulfan/cyclophosphamide as the conditioning regimen found that outcome with the cyclophosphamide TBI regimen was significantly better.

One must remember that these patients are undergoing transplantation because they have what is otherwise a fatal disease, Dr. Lawton stressed. Transplantation has measurable morbidity, but this is a trade-off for extended survival. The guiding principle is to understand which factors can be altered to improve the risks, to monitor patients for toxicities, and to try to reduce toxicity by, for example, sparing normal tissues.
Outcome of BMT in Different Diseases

Updated data from the IBMTR provide information about the outcome of transplantation in certain scenarios. Patients with CML who receive a transplant from an HLA-identical sibling while in the chronic phase have a likelihood of being leukemia-free at 6 years of just over 50%. The same patient transplanted in the accelerated phase or blast crisis has a 20% to 25% chance of leukemia-free survival at 6 years. “Interestingly, it’s not zero,” Dr. Lawton said. This is important information. Patients with acute lymphocytic leukemia (ALL) who receive an HLA-identical transplant are also a favorable group. The outcome of transplantation during first remission in these patients is as good as the outcome of transplantation for CML in the chronic phase. The leukemia-free survival diminishes significantly when transplants are done in patients in subsequent remissions, not in remission, or in relapse. Acute myelogenous leukemia (AML) is very similar to ALL, in that outcome is the best with first remission, followed by second remission, not in remission, or in relapse, Dr. Lawton explained. In ALL and AML, the probability of survival depends not only on whether the patient is in first or second remission but also on the donor. The best scenario is the patient in first remission with an HLA-identical sibling donor. Unrelated-donor and mismatched-related donor transplants are riskier situations than transplants from an HLA-identical sibling. “Slowly but surely we are getting better at doing those transplants, but there still is a decrement there,” Dr. Lawton commented.

“As for breast cancer, the story has not ended yet as to whether a transplant is really better than aggressive chemotherapy up front,” she added. “For patients with metastatic breast cancer, I think we need to be cognizant of the fact that when we are putting them through therapy that could be very toxic for the remainder of their lives, that they are still likely to die of their disease. I think you have to think long and hard about this approach.”

References:

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