Advances in Transplantation

A meeting review of critical advances in the field of hematopoietic cell transplantation

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Special BMT Tandem 2007 Edition

Welcome to a special edition of *Advances in Transplantation*, a National Marrow Donor Program® (NMDP) newsletter that summarizes the latest research in allogeneic hematopoietic cell transplantation. This edition is based on the BMT Tandem Meetings, held in Keystone, Colorado. The BMT Tandem Meetings are co-sponsored by the Center for International Blood and Marrow Transplant Research (CIBMTR) and the American Society for Blood and Marrow Transplantation (ASBMT).

In this issue:

Managing GVHD: Advances using several approaches

Graft-versus-host disease (GVHD) is a complex immune reaction with several underlying mechanisms and pathways. As a consequence, a variety of methods have been developed to treat this potential transplant complication.

Several investigators at the 2007 BMT Tandem Meetings presented research results demonstrating continuing progress in treating GVHD. Some of the successful GVHD treatment methods include methotrexate-free GVHD prophylaxis, high-dose cyclophosphamide as GVHD prophylaxis, a simple test to predict the development of acute GVHD, and using mesenchymal stromal cells to treat severe acute GVHD.

Sirolimus and tacrolimus as GVHD prophylaxis

Methotrexate has been part of the standard GVHD prophylactic regimen for more than 20 years, but methotrexate can delay engraftment and injure epithelial tissues, which in turn increases the risk of infection and organ toxicity in transplant recipients.

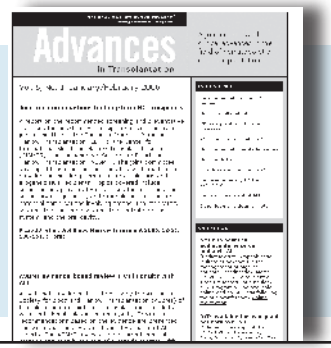
GVHD prophylaxis using sirolimus and tacrolimus instead of methotrexate has yielded "excellent control of GVHD" according to the lead author of a study presented at a BMT Tandem oral session.

Dr. Corey Cutler and his colleagues at the Dana-Farber Cancer Institute studied the outcomes of myeloablative peripheral blood cell transplantation from related (n=53) and unrelated (n=30) donors HLA-matched at -A, -B, -C, and -DRB1 using sirolimus and tacrolimus alone, without methotrexate, as prophylaxis for acute GVHD.

Transplants were performed on adult patients between 2002 and 2005, and the conditioning regimen used fractionated total body irradiation (14 Gy) and cyclophosphamide (1800 mg/m^2 x 2).

Tacrolimus was administered at 0.02 mg/kg/day intravenously with a target serum concentration of 5-10 ng/mL. Sirolimus was administered as a 12 mg oral loading dose with a target serum concentration of 3-12 ng/mL. If needed, post-transplant G-CSF was administered beginning on day 12 until neutrophil engraftment was achieved.

Managing GVHD: continued on page 2



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At a median follow-up of 32 months, the cumulative incidence of grade II-IV GVHD was 20.5% and three patients (3.6%) developed grade III-IV acute GVHD. The cumulative incidence of chronic GVHD was 52.4%, with no significant difference between related and unrelated donor cohorts. There were two deaths (2.4%) due to GVHD, which occurred among the related donor graft recipients.

One-year and two-year relapse-free survival was 72.3% and 68.5%, respectively. Non-relapse mortality at 100-days post-transplant was 4.8%

Dr. Cutler concluded that sirolimus instead of methotrexate with tacrolimus for GVHD prophylaxis can result in low transplant-related toxicity, low rates of acute GVHD and excellent outcomes equivalent between related and unrelated donors. Dr. Cutler noted that historic differences between these two groups could be eliminated with effective GVHD prophylaxis.[1]

Post-transplantation high-dose cyclophosphamide as GVHD prophylaxis

High-dose cyclophosphamide alone can also be an effective prophylaxis against both acute and chronic GVHD while permitting effective immune reconstitution, according to results present by Dr. Leo Luznik, whose research was awarded a Center for International Blood and Marrow Transplant Research (CIBMTR) Best Abstract Award for Clinical Research.

Dr. Luznik's study followed 46 consecutive patients (median age 41, range 1-64) at Johns Hopkins University with advanced hematologic malignancies who underwent HLA-matched related donor (n=28) or unrelated donor (n=18) bone marrow transplantation.

The conditioning regimen was busulfan on days -7 to -3 and cyclophosphamide (50 mg/kg/day) administered on days -2, -1, +3, and +4, and was the sole agent used as GVHD prophylaxis.

The cumulative incidence of acute grade II-IV GVHD was 41%, and the cumulative incidence of grade III-IV GVHD was 9%. Thirty-six of 46 patients were alive after day 100, and of these, only four developed chronic GVHD, an "unexpectedly low incidence of chronic GVHD," according to Dr. Luznik.

Dr. Luznik suggested that the low incidence of chronic GVHD may have been due to the rapid recovery of regulatory T cells in transplant recipients. Patients with grade II-IV acute GVHD had significantly fewer regulatory T cells than patients who had no GVHD or those with minimal (grade I) GVHD.[2]

Mesenchymal stromal cells to treat GVHD

Allogeneic transplant recipients with severe acute GVHD can effectively be treated with mesenchymal stromal cells, according to several research results presented at the BMT Tandem Meetings.

In a Plenary Session on mesenchymal stromal cells, Dr. Francesco Frassoni noted that mesenchymal stromal cells obtained from adult bone marrow can inhibit T-cell alloreactivity in vitro. Dr. Frassoni, from the San Martino Hospital in Genoa, Italy, described results from a European Group for Blood and Marrow Transplantation (EBMT) study of 40 patients with grade III-IV acute GVHD who were resistant to second-line GVHD therapy.

Patients in this study were infused with mesenchymal stromal cells obtained from HLA-identical sibling donors (n=5), haploidentical donors (n=19) and unrelated HLA-mismatched donors (n=41). Median cell dose was 1.0 x 10^6 cells/kg recipient body weight (range 0.4-9). Patients received one dose (n=19), two doses (n=19), three doses (n=1) or five doses (n=1) of mesenchymal stromal cells.

Nineteen patients had complete responses, nine had incomplete responses and seven did not respond. Nine patients developed extensive chronic GVHD. Twenty-one of the 40 patients (52.5%) are alive at six weeks to 3.5 years post-transplant and showed evidence that the infused mesenchymal stromal cells repaired tissues in the gut, liver, and skin damaged by GVHD.

However, the optimal strategy for treating GVHD with mesenchymal stromal cells is not yet known, according to Dr. Frassoni, although it's clear that they do have tissue-repairing effects and should therefore be tested in randomized clinical trials.[3]

In a poster presentation, Dr. Partow Kebriaei reported results from a phase II study of mesenchymal stromal cells in combination with steroids used to treat 31 patients who developed acute GVHD after related or unrelated donor hematopoietic cell transplantation.

Dr. Kebriaei, from the M.D. Anderson Cancer Center, reported that 21 of the 31 patients achieved a complete response (no evidence of GVHD) and seven patients achieved a partial response with an improvement in one or more affected organs. All of the patients initially diagnosed with GVHD of the skin had a response, and 83% of the patients with gastrointestinal GVHD had a response.[4]

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Choosing the best cell source for patients

Physicians can select from three hematopoietic cell sources for their transplant patients—marrow, peripheral blood stem cells (PBSC) and umbilical cord blood (UCB). Although comparable outcomes have been achieved with all three sources, thoughtful selection of one type of stem cell over another may lead to better transplant outcomes.

In the opening Plenary Session of the BMT Tandem Meetings, three speakers outlined state-of-the-science criteria for stem cell source selection.

PBSC or bone marrow?

Dr. Richard Champlin from the M.D. Anderson Cancer Center noted that when PBSC transplantation was first being developed, many transplant physicians quickly began to choose PBSC over bone marrow because of more rapid engraftment.

The resulting shorter time of neutropenia seen after PBSC transplantation did indeed lead to better short-term survival, according to Dr. Champlin. However, as longer follow-up data emerged, it became clear that an increased incidence of chronic GVHD after PBSC transplantation was leading to higher rates of late transplant-related mortality in these patients.

Therefore, current data suggests that there is no general survival advantage for PBSC as compared to bone marrow as a source of stem cells for allogeneic transplantation in adults, according to Dr. Champlin. He noted, however, that there are some studies that suggest a slight advantage for one cell source over another depending on disease and disease stage.

That point was made by Dr. Mary Eapen, of the Center for International Blood and Marrow Transplant Research (CIBMTR), who presented data from two large-scale studies of patients transplanted for hematological malignancies. Both studies examined outcomes after allogeneic donor transplantation, using either related or unrelated donors.

The first study was of 413 patients transplanted using sibling donors at 20 North American and European transplant centers using marrow (n=272) or PBSC (n=141). In this study, PBSC transplantation for advanced chronic myelogenous leukemia (CML) resulted in significantly lower mortality (RR=0.45, p=0.03) and higher leukemia-free survival (LFS) than bone marrow transplantation.

However, in early CML, mortality was significantly higher (RR=0.70, p=0.01) and LFS lower following PBSC transplantation than after bone marrow transplantation. In patients transplanted for acute leukemias, however, survival was not significantly affected by stem cell source.

Thus, although patients with advanced CML may benefit from PBSC transplantation, patients with acute leukemia or early CML may not, said Dr. Eapen.[5]

The second study presented by Dr. Eapen examined the outcomes of 1,232 leukemia and myelodysplastic syndrome patients transplanted using unrelated donors. PBSC recipients (n=451) had significantly more chronic GVHD than patients receiving bone marrow grafts (n=781); 54% vs. 40%, respectively (p<0.001). However, this study found no significant difference survival in the two groups based on disease type or stage.[6]

Dr. Eapen concluded her presentation by noting that a Phase III randomized multicenter trial comparing unrelated donor marrow and PBSC transplant outcomes is being conducted by the Blood and Marrow Transplant Clinical Trials Network (Protocol 0201).

When is cord blood the best graft source?

Dr. Juliet Barker addressed the Plenary Session with a talk entitled "Who should get cord blood transplants?"

The question is not a simple one to answer, according to Dr. Barker. Although UCB has several advantages over marrow or PBSC (HLA mismatch is better tolerated in UCB transplantation, UCB can be more rapidly obtained, and UCB leads to less GVHD), it has a significant limitation: low cell dose.

Although an adequate cell dose can usually be obtained for a pediatric transplant patient, it can often be problematic in adult patients or in large adolescent patients. Transplant physicians must often chose between a small UCB unit with a high degree of HLA match and a larger UCB unit with a lower HLA match.

While no consensus has emerged on this issue, Dr. Barker offered the guidelines used at her institution, the Memorial Sloan-Kettering Cancer Center: minimum cell doses of 5.0 x 10^7 cells/kg for 4/6 matches, 2.5 x 10^7 cells/kg for 5/6 matches, and 2.0 x 10^7 cells/kg for 6/6 matches.

Recent research has also revealed the importance of HLA match in UCB transplantation, said Dr. Barker. She highlighted a 2006 study by the CIBMTR and the New York Blood Center that compared outcomes of 503 UCB transplants and 116 marrow transplants in pediatric patients with acute leukemia. All marrow grafts were allele-level matched at HLA-A, -B, -C, and -DRB1. UCB grafts were antigen-level typed at HLA-A and -B, and allele-level typed at HLA-DRB1.

In this study, the best five-year LFS was observed after transplantation with HLA-matched cord blood (60%), which was significantly higher than the LFS after transplantation with matched bone marrow (38%) (p=0.04).

Most notably, according to Dr. Barker, the transplant-related mortality (TRM) in 5/6 matched UCB transplantation was comparable to the TRM of 8/8 matched bone marrow recipients (29% vs. 19%, respectively) provided UCB cell dose was greater than 3 x 10^7 cells/kg. Fully matched UCB (6/6) transplants, regardless of cell dose, had the lowest TRM, at 6%.[7]

The best results so far to extend UCB transplantation to more adults has been the use of double-cord blood transplants, said Dr. Barker. (See double cord blood article in the "In Brief" section, page 6.)

Dr. Barker also noted that the Blood and Marrow Transplant Clinical Trials Network (BMT CTN) is conducting a randomized trial comparing single versus double cord blood transplantation in children with myelodysplasia and leukemia. ■

Data collection on transplant outcomes to expand

Patients to get increased access to information

Federal legislation in 2005 and 2006 has set the groundwork for an expanded database of transplant outcomes that will provide data on all allogeneic transplants to physicians and the public. Patients will also be able to enter their HLA tissue type into an online resource to view the number of potential matches (adult donors and cord blood units) they may have on the NMDP Registry.

Stem Cell Therapeutic Outcomes Database (SCTOD)

The challenges—and opportunities—of developing the SCTOD were outlined in a Scientific Session by Dr. Mary Horowitz, Chief Scientific Director, Center for International Blood and Marrow Transplant Research (CIBMTR); Dr. Douglas Rizzo, Associate Scientific Director, CIBMTR; and Dr. Dennis Confer, NMDP Chief Medical Officer.

> "The intent is to place more data and information in the hands of the public."
> -- Dr. Dennis Confer

Dr. Rizzo outlined the broad scope of the new database, which will be managed by the CIBMTR. The SCTOD will include for the first time the gathering of data on non-traditional uses of hematopoietic cells, such as therapy to repair damaged cardiac tissue. Other key elements of the SCTOD include:

- Required data submission for all allogeneic transplants, related and unrelated
- Creating a related donor-recipient research sample repository
- Broadened reporting of U.S. transplant center-specific survival rates
- Assessing recipient quality of life

Dr. Rizzo noted that prior to this legislation, data submission to the NMDP was required for unrelated transplantation, but reporting of related allogeneic outcomes to the CIBMTR was voluntary.

Such reporting requirements may initially prove challenging, according to Dr. Rizzo, especially maintaining follow-up on a large number of transplant recipients who have returned to local primary care centers once they return home. Transplant centers will need to carefully consider the new data management demands of the SCTOD, he said.

The CIBMTR and the NMDP are therefore working together to streamline the data collection process by creating a single system of data instruments, and are developing a standard dataset of hematopoietic cell transplantation data designed to ease the burden of data collection and submission to the SCTOD.

NMDP to offer new online patient resource

As a result of the legislation, the NMDP has developed a new online resource, MatchView[SM], which will allow patients to enter their HLA-tissue typing results and receive a real-time report showing the number of potential adult donor and cord blood unit matches on the NMDP Registry (see Figure 1). "The intent [of MatchView] is to place more data and information in the hands of the public," said Dr. Confer.

To help patients use MatchView and to properly interpret their results, the NMDP will provide patients with educational materials on the MatchView Web pages, including answers to these questions:

- What is HLA and how can I get my HLA type?
- What is a match?
- How do I get a donor or cord blood unit for my transplant?

The results returned on the Web site will not include any identifying information about the possible availability of donors or cord blood units, according to Dr. Confer. By using MatchView, a patient will also not start a search of the NMDP Registry. Instead, the MatchView results will allow patients to be more informed when discussing transplantation with their physicians. ■

Audio and visual of all speakers presenting in this session can be found on the Web at: www.asbmt.org/News/Outcomes

Patients can view number of potential matches

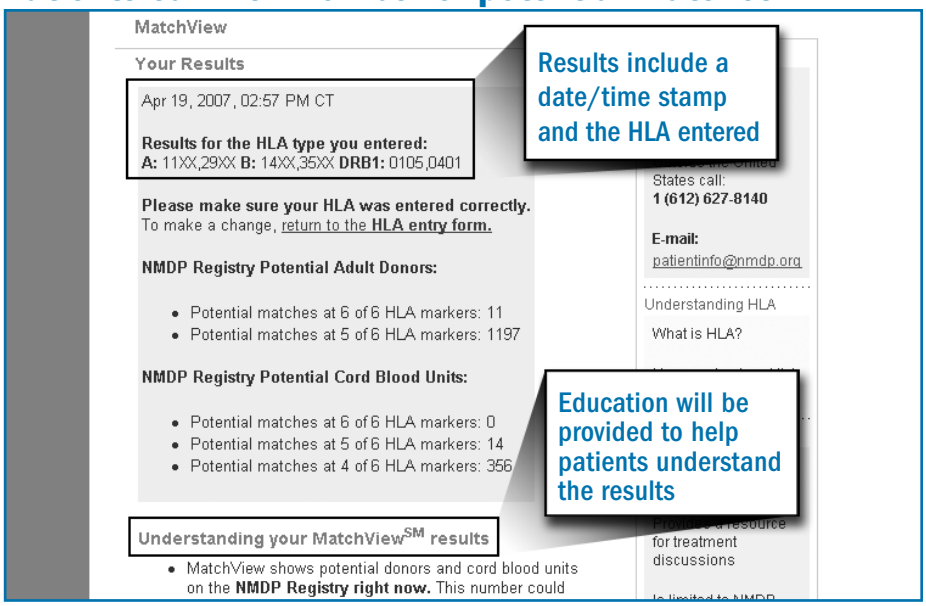


Figure 1. Sample of MatchView results.

Non-myeloablative transplantation to treat solid tumors

Transplantation of tumor-reactive T cells can yield partial and complete responses

The graft-versus-tumor (GVT) effect that eradicates residual disease after allogeneic transplantation for hematologic diseases may also effectively treat patients with solid tumors, according to research presented at the BMT Tandem Meetings.

Speaking at a Plenary Session, Dr. Richard Childs of the National Heart, Lung, and Blood Institute noted that conventional chemotherapy has generally had limited success in treating metastatic cancers. Thus, beginning in the 1990s, researchers began using allogeneic transplantation to treat several types of solid tumors, including:

- Metastatic pancreatic cancer
- Colon cancer
- Breast cancer
- Ovarian cancer
- Renal cell carcinoma
- Sarcomas

Metastasized renal cell carcinoma (RCC) has been studied the most, according to Dr. Childs, and non-myeloablative conditioning regimens are generally used because of their lower transplant-related mortality (TRM).

Dr. Childs highlighted a 2006 study of the pooled results from 21 different European transplant centers having protocols to treat metastatic RCC with non-myeloablative allogeneic transplantation.[8] In this study, 124 patients underwent allogeneic transplantation after conditioning regimens that included combinations of lowered doses of busulfan, fludarabine, cyclophosphamide, TBI, or melphalan.

Of the 98 evaluable patients, 28 experienced a tumor response (32%), and of these patients, four experienced a complete response. A multivariate analysis revealed that tumor responses were significantly associated with use of a partially mismatched donor, development of acute graft-versus-host disease (GVHD), and a time from disease diagnosis to transplantation of less than a year.

Overall survival (OS) was also significantly associated with receiving donor lymphocyte infusions, developing chronic GVHD, and having fewer than three metastatic sites.

Tumor response rates in studies of allogeneic transplantation for RCC are "extremely variable," according to Dr. Childs. The 32% tumor response rate seen in this pooled study fits in the middle of the range observed in studies of non-myeloablative transplantation for RCC published to date, which range from 8%-57%, according to Dr. Childs.

Patient selection factors

Attention in the field is now turning to discovering which patient factors might lead to better survival, said Dr. Childs, who cited a 2005 study that identified C-reactive protein and lactate dehydrogenase levels as useful predictors of improved survival after non-myeloablative allogeneic transplantation.[9] Such prognostic tools can help clinicians select RCC patients who might benefit most from allogeneic transplantation, according to Dr. Childs.

In allogeneic transplantation for hematologic diseases, the GVT effect is most effective when patients are transplanted with minimal residual disease, noted Dr. Childs.

When transplanting patients with solid tumors, clinicians should be aware that the GVT effect is often somewhat delayed, according to Dr. Childs. Therefore, transplant physicians must select patients "with sufficient pre-transplantation life expectancy."

Unfortunately, the majority of transplants for solid tumors to date are for advanced, treatment-refractory diseases, according to Dr. Childs, and patients often have life expectancies too short to benefit from a delayed GVT effect.

Research results to date have already demonstrated clear evidence of the GVT effect in several types of solid tumors, said Dr. Childs. And because non-myeloablative conditioning regimens have successfully reduced transplant-related toxicities, Dr. Childs predicted that allogeneic transplantation will be offered in an increasing number of solid tumor patients who are in better condition to benefit from it. ■

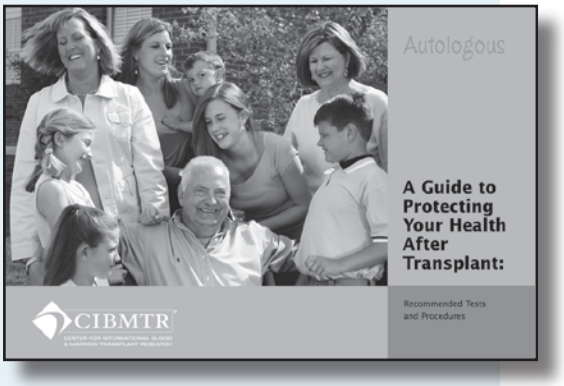
Post-Transplant Guidelines for Patients and Physicians

A Guide to Protecting Your Health after Transplant: Recommended Tests and Procedures.

These new guides — in an autologous version and an allogeneic version — provide checklists for patients and physicians regarding proper long-term follow-up care after a marrow, peripheral blood stem cell (PBSC) or cord blood transplant.

Both guides can be downloaded from: www.cibmtr.org/posttransplant

(These guides were produced by the NMDP for its research partner, the Center for International Blood and Marrow Transplant Research (CIBMTR).)



IN BRIEF:

Double-unit cord blood transplantation in adults

Although umbilical cord blood is an acceptable source of graft cells for patients without HLA-matched blood or marrow donors, transplantation with single units of cord blood can have unacceptable rates of transplant-related mortality (TRM) due to graft failure, delayed engraftment, and infection. To overcome the cell dose limitations of single cord blood transplants, several research groups transplanted patients using two cord blood units.

A poster presentation by Dr. Corey Cutler from the Dana-Farber Cancer Institute reported on 18 adults (median age 48.5 years) undergoing reduced-intensity transplantation using two cord blood units matched with each other and the recipient at 4/6, 5/6, or 6/6 (HLA -A, -B, -DRB1). Patients had non-Hodgkin's lymphoma (n=6), acute myelogenous leukemia (n=5), Hodgkin's lymphoma (n=3), myelodysplastic syndrome (n=3) and chronic myelogenous leukemia (n=1).

The minimum combined nucleated cell dose was 3.7 x 10^7 cells/kg, measured pre-cryopreservation. The reduced-intensity regimen used fludarabine, melphalan, and rabbit ATG, and tacrolimus and sirolimus were used for GVHD prophylaxis.

Overall survival (OS) at one year was 64.3%, which Dr. Cutler noted was comparable to other unrelated donor cohorts. Three patients developed grade II-IV acute GVHD, and two patients developed chronic GVHD, which Dr. Cutler characterized as low compared to historical rates when using cyclosporine and mycophenolate mofetil for GVHD prophylaxis.[10]

In a second BMT Tandem oral presentation by Dr. Margaret MacMillan, compared 169 double cord blood transplants with 210 single cord transplants performed between 1994-2005 at the University of Minnesota.

Although rates of grade III-IV acute GVHD were significantly higher in double-cord than in single-cord recipients (21% vs. 11%, respectively; p=0.01), the one-year TRM was significantly lower after double-cord transplants versus single-cord transplants (17% vs. 47%, respectively; p=0.02).

In addition, one-year OS was also significantly higher in double versus single cord blood transplant recipients (67% vs. 41%, respectively; p=0.04).[11] ■

Cord blood transplantation in Hurler's syndrome

Cord blood transplantation in Hurler's syndrome patients before the age of two can result in sustained engraftment, full-donor chimerism, and normal enzyme levels that halt disease progression, according to research presented in a BMT Tandem poster.

Dr. Jaap Boelens of the University Hospital for Children, Utrecht, Netherlands, studied the outcomes of 40 patients with Hurler's syndrome registered with the EUROCORD database and the EBMT-Hurler syndrome database between 1991 and 2004.

Thirty-six patients received unrelated donor cord blood (13 matched 6/6, 18 matched 5/6, and five matched 4/6), and four patients received HLA-identical family cords. All but two patients received myeloablative conditioning regimens.

The median cell dose used was 7.9 x 10^7 nucleated cells/kg (range 1.5-32). Grade II-IV acute GVHD developed in 15% of recipients, and chronic GVHD was seen in 19%. Eight percent of recipients had extensive chronic GVHD.

At a median follow-up time of 14 months (range 7-84 months), 27 patients (69%) were alive and engrafted.

The researchers concluded that unrelated donor cord blood "is a good alternative stem cell source and might even be preferential since cord blood appeared to increase the likelihood of sustained engraftment resulting in full-donor chimerism and normal enzyme levels."[12] ■

Transplantation in relapsed AML

Allogeneic transplant is superior to chemotherapy in acute myeloid leukemia (AML) patients in second remission or after failed first salvage, according to research presented in a BMT Tandem poster.

Dr. Paul Armistead presented results of a retrospective review of 600 consecutive AML patients treated at first relapse at the M.D. Anderson Cancer Center between 1995-2004. Outcomes were compared between patients achieving second complete remission who received transplants and those who did not, either due to patient preference or the lack of a suitable donor.

The median age of all patients was 58 (range 15-85), and 23% had poor risk cytogenetics (-5 or -7 deletions). Patients who achieved second complete remission (n=102) were evaluated for transplant. Of these, 72 underwent allogeneic transplantation and 30 did not.

Two-year relapse-free survival was significantly better in the 72 transplanted patients compared to the 30 untransplanted patients (46% vs. 13%, p=0.007). Two-year overall survival was also better in the transplanted patients, but this trend was not statistically significant (44% vs. 23%, p=0.105).

Two-year overall survival was also significantly better in the 105 patients resistant to their first salvage regimen who underwent allogeneic transplantation compared to 71 patients who did not due to lack of an available donor (13% vs. 0%, p<0.001). In patients >50 years, two-year survival was also significantly better after allogeneic transplantation than with chemotherapy (12% vs. 0%, p<0.001).

Because of the superiority of allogeneic transplantation in this patient cohort, Dr. Armistead concluded that physicians should make greater efforts to identify potential donors (related or unrelated) prior to first relapse.[13] ■

continued from page 2

TNFR1 levels predict for GVHD

Acute GVHD can be predicted before outward signs of the disease develop in transplant recipients, according to research presented in an oral session.

Tumor necrosis factor-alpha (TNF) is an inflammatory cytokine that is implicated in the pathogenesis of GVHD. Dr. Carrie Kitko presented research results demonstrating that by measuring levels of TNFR1 (a surrogate marker for TNF), physicians can predict which transplant recipients will likely develop acute GVHD.

Dr. Kitko and her colleagues at the University of Michigan, Ann Arbor, measured the baseline levels of TNFR1 (transplant day zero) in 82 children undergoing related (n=38) and unrelated (n=44) donor myeloablative hematopoietic cell transplantation. The level of TNFR1 in the peripheral blood was measured a second time at day seven post-transplant and compared to the baseline level.

Dr. Kitko's study, which received a CIBMTR Best Abstract Award for Clinical Research, found that the TNFR1 ratio was significantly correlated with the severity of acute GVHD, transplant-related mortality, and overall survival.

Dr. Kitko concluded that calculating TNFR1 ratios may be useful in predicting which transplant recipients may develop acute GVHD one to two weeks prior to any clinical manifestations of the disease, which may allow transplant physicians to initiate GVHD treatment as early as seven days post-transplant.[14] ■

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A meeting review of critical advances in the field of hematopoietic cell transplantation

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Special Edition:

Look inside for the latest research on hematopoietic cell transplantation.

This issue contains information presented at the 2007 BMT Tandem Meetings held in Keystone, Colorado.

The BMT Tandem Meetings are co-sponsored by the Center for International Blood and Marrow Transplant Research (CIBMTR) and the American Society for Blood and Marrow Transplantation (ASBMT).

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