ASBMT eNews

AMERICAN SOCIETY FOR BLOOD AND MARROW TRANSPLANTATION

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CLINICAL RESEARCH

Certain Characteristics of Pediatric ALL Patients Linked to Induction Failure

After reviewing data on more than 44,000 children with newly diagnosed acute lymphoblastic leukemia, researchers identified 1,041 patients who had induction failure after four to six weeks of remission-induction therapy. According to the study results published in the *New England Journal of Medicine*, patients with an older age, T-cell leukemia, Philadelphia chromosome-positive leukemia, an 11q23 rearrangement and at least 25% blasts in the bone marrow at the conclusion of induction therapy were more likely to experience induction failure. The study also reported better outcomes for young B-cell leukemia patients treated with chemotherapy and improved survival for the T-cell leukemia patients who received an allogeneic stem cell transplant from a matched, related donor. More...

Azacitidine Increases Treg Cells in Some AML Patients

Researchers of a study appearing in *Blood* set out to determine if Azacitidine (AZA) can increase the graft-versus-leukemia (GVL) effect after allogeneic stem cell transplantation without increasing the risk of graft-versus-host disease (GVHD). Monthly doses of AZA were given to 27 patients who had received a reduced intensity allogeneic transplantation for acute myeloid leukemia. Compared to a control group, the AZA group experienced an increase in the number of T regulatory cells within the first three months and had a low incidence of GVHD and a cytotoxic CD8+ T-cell response to several tumor Ags. More...

Donor Lymphocyte Infusion May Improve Transplant Outcome

Modified donor lymphocyte infusion (DLI) given after allogeneic hematopoietic stem cell transplantation to standard-risk acute leukemia patients who are in first or second complete remission and have minimal residual disease may improve transplant results, according to a study in *Blood*. Researchers studied 814 patients. The largest group (709 patients) was MRD negative after transplantation. The MRD-positive patients received low-dose IL-2 (49 patients) or DLI with or without low dose IL-2 (56 patients). The DLI group had a lower risk of relapse compared to the IL-2-alone group. The cumulative risk of relapse was significantly less and DFS was significantly better in patients treated with DLI+/- IL-2 then in patients treated with IL-2 alone (P=.001 and P=.002, respectively) but was not different from patients who were MRD negative. More...

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A Word From President Elizabeth Shpall, MD

Stem Cell Transplantation and Personalized Medicine

What developments will drive the next paradigm shift in stem cell transplantation? Historically, stem cell transplant (SCT) preparative regimens have emphasized the use of alkylating agents in intensive doses. This class of drugs is unique in that it exhibits "target multiplicity," does not require receptor-mediated interaction to produce effects, and thus can produce increasing antitumor effects proportional to increasing doses. Many other classes of therapeutics (i.e., nucleoside analogs, etoposide and antibodies) have been added to the regimens but most require metabolic activation or receptor interaction, therefore dose escalation beyond a certain point will not produce increasing therapeutic benefits. Optimization of alkylating agent dose has largely been completed based upon extensive conceptual understanding and clinical trials.

A major addition to SCT therapy has developed from the recognition that cellular function in the graft can be manipulated to improve outcome. T-cell number and function can be altered to modulate graft-versus-host disease (GVHD), enhance engraftment and produce more favorable graft-versus-tumor effects. Natural Killer (NK) cells are increasingly being investigated for their MHC-independent ability to mediate graft-versus-tumor without producing GVHD. More sophisticated cellular engineering with chimeric antigen receptor-bearing T cells as well as tumor- and virus-specific cytotoxic T cells hold great promise for further enhancement of transplant-based immunotherapeutics against tumors and infection. With these developments will come a deeper understanding of "immunotherapeutic resistance," which, as with chemotherapy, produces newer barriers to cure. While we often think of cellular therapeutics as an area transplanters dominate, developments in, for example, immunotherapy of melanoma have significantly affected our field and improved conceptual understanding.

Further improvements in therapy will undoubtedly come from study of newer alkylating compounds, DNA damage-repair modulation, graft selection and modification, and other related areas in which investigators already involved in our field have great expertise. It is always important, however, to evaluate developments largely outside our field that are changing the face of cancer treatment. One such conceptual framework is personalized therapy, which is often defined as the use of genomic information to inform treatment choice. Dissection of apoptotic signaling pathways in cancer cells have resulted in the development of newer, less toxic-targeted therapies. These treatments are already producing major improvements in the therapy of tumors such as lung cancer and melanoma. In hematologic malignancies, inhibitors of Bruton's tyrosine kinase (Btk) are already showing great promise in the treatment of B-cell malignancies. This is just one of a number of emerging examples where targeted therapies will change our field.

These targeted therapies are not only minimally toxic but are also target-specific molecules that can be measured in tumor cells. It seems likely that less toxic-targeted therapy could be added to more conventional transplant regimens based on individual patient (personalized) measurement of the target. Because of minimal toxicity from these agents, selecting an appropriate drug or drugs from a larger array of available targeted agents for the tumor in question and adding it to a "standard" transplant regimen would seem possible. This paradigm is also attractive because of the increasingly obvious heterogeneity of tumor

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A WORD FROM THE PRESIDENT (CONTINUED FROM PAGE 2)

cell clones in most malignancies. The use of targeted therapy in association with high-dose alkylating agent therapy might overcome tumor resistance, thus improving the cure fraction for many hematologic malignancies. Hypothetically, this approach might also reopen the investigation of transplant for a variety of tumors in which transplant is known to produce substantial (but mostly subcurative) effects and for which targeted therapies are rapidly developing. Breast cancer, melanoma, colorectal cancer and several others come quickly to mind. It is an exciting time to be involved in SCT medicine!

-Elizabeth

BASIC SCIENCE STUDIES

Lineage of Tissue Macrophages That are Unrelated to Hematopoietic Stem Cells

The transcription factor Myb is necessary for hematopoietic stem cells (HSCs) and CD11bhigh monocytes and macrophages to develop, but is not needed for the creation of yolk sac macrophages and YS-derived F4/80bright macrophages in mouse tissue that can survive without HSCs. This finding led authors of the study published in *Science* to conclude that there is a lineage of tissue macrophages that come from the yolk sac that are genetically different from and, therefore, do not develop from HSCs. More...

Moment That T Cell Lineage Transfers from Bone Marrow to Thymus

A study from *Nature Immunology* examined the earliest thymic progenitors. According to the researchers, the earliest progenitors in the neonatal thymus had combined granulocyte-monocyte, T lymphocyte and B lymphocyte lineage potential but did not show signs of megakaryocyte-erythroid lineage potential. These potentials were the same as the potentials for candidate thymus-seeding progenitors in bone marrow. More...

Purified Hematopoietic Stem Cells Combined With Specific Cells Provide Antiviral Protection

Transplanting purified allogeneic hematopoietic stem cells may help prevent impaired immunity in transplant patients, according to a study appearing in *Proceedings of the National Academy of Science*. Researchers discovered that mice given allogeneic purified HSCs experienced better antiviral responses to murine cytomegalovirus (MCMV) than the mice that received HSC and unselected bulk T cells. In addition, supplementing purified HSCs with CD8+ memory or MCMV-specific T cells also improved protective viral immunity. More...

ASSOCIATION NEWS

FACT Accreditation Report

Two new blood and marrow transplant programs earned accreditation and four additional organizations received accreditation renewal during the first quarter of 2012, according to the Foundation for the Accreditation of Cellular Therapy. More...

BMT Transplant Research Fund

Recently, you received a mailing about *The ASBMT Transplant Research Fund*. Post-transplant complications continue to be a major challenge for patients. Since 1987, Be The Match Foundation and the National Marrow Donor Program have supported investigators and their promising research through the Amy Strelzer Manasevit Research Program. Given current funding levels, typically only one Amy Scholar is selected each year. *The ASBMT Transplant Research Fund*, over time and with your help, can support one or more awards in the future. More...

Medicare Coverage and Reimbursement for Hematopoietic Cell Transplant

The number of hematopoietic cell transplants (HCT) for Medicare beneficiaries has increased substantially in recent years, a trend that is expected to continue in the future. This increase has heightened the need to address Medicare coverage and reimbursement issues that present significant barriers for HCT centers. Rectifying these issues will be critical to maximizing reimbursement and ensuring the future financial solvency of transplant programs with significant and/or growing Medicare case volume. The National Marrow Donor Program and the American Society for Blood and Marrow Transplantation have undertaken a series of analyses to understand and begin to impact the primary Medicare coverage and reimbursement issues for HCT. This document will define these activities and highlight progress in the chosen action strategies. More...

BMT Tandem Meetings Abstracts

All accepted abstracts for the 2012 BMT Tandem Meetings were published in the February issue of *Biology of Blood and Marrow Transplantation* (Vol. 18, No. 2, Supplement 2). Abstracts are also available online at http://www.abstracts2view.com/bmt/.

Audio and Slide Recordings

Order your copy of audio and slide recordings from the 2012 BMT Tandem Meetings by completing and submitted this form.

Calendar of Events

•May

7th International Symposium on Neuroprotection and Neurorepair
May 2-5
Potsdam, Germany

Oncology Nursing Society
37th Annual Congress
May 3-6
New Orleans, Louisiana

The American Association of Immunologists
Immunology 2012
May 4-8
Boston, Massachusetts

American Society of Pediatric Hematology Oncology
25th Annual Meeting
May 9-12
New Orleans, Louisiana

American Society of Gene & Cell Therapy
15th Annual Meeting
May 16-19
Philadelphia, Pennsylvania

•June

American Society of Clinical Oncology
Annual Meeting
June 1-5
Chicago, Illinois

American Transplant Congress
American Society of Transplant Surgeons/American Society of Transplantation
June 2-6
Boston, Massachusetts

CRYO 2012
Society for Cryobiology, 49th Annual Meeting
June 3-6
Rosario, Argentina

•June (cont.)

International Society for Cellular Therapy
18th Annual Meeting
June 5-8
Seattle, Washington

Foundation for the Accreditation of Cellular Therapy
Cord Blood Inspection and Accreditation Workshop
June 10
San Francisco, California

International Society for Stem Cell Research
10th Annual Meeting
June 13-16
Yokohama, Japan

Federation of Clinical Immunology Societies
Annual Meeting
June 21-24
Vancouver, British Columbia, Canada

•July

Radiation Injury Treatment Network
2012 Advance Training: Radiation Medical Emergency Course
July 16-17
Oak Ridge, Tennessee

2012 Pan Pacific Lymphoma Conference
July 17-20
Maui, Hawaii

•August

The 30th World Congress of Biomedical Laboratory Sciences
August 18-22
Berlin, Germany

Society for Hematology and Stem Cells
41st Annual Scientific Meeting
August 23-26
Amsterdam, Netherlands

•September

World Cord Blood Congress
September 20-21
Boston, Massachusetts

ESH-iCMLf 14th International Conference
Chronic Myeloid Leukemia: Biology and Therapy
14th International Conference
September 20-23
Baltimore, Maryland

European Society for Medical Oncology
37th Congress
September 28-October 2
Vienna, Austria

•October

2nd World Congress on Controversies in Hematology
October 4-7
Istanbul, Turkey

American Association of Blood Banks
2012 Annual Meeting
October 6-9
Boston, Massachusetts

American Society for Histocompatibility and Immunogenetics
38th Annual Meeting
October 8-12
San Juan, Puerto Rico

European Society of Gene & Cell Therapy
20th Anniversary Congress
October 26-29
Versailles, France

• 2013

BMT Tandem Meetings
Combined ASBMT and CIBMTR Annual Meetings
February 13-17
Salt Lake City, Utah

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Do you have news, responses or opinions to share with us?
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