



IBMTR/ABMTR newsletter

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special millennium edition

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Mary M Horowitz, MD, MS

*IBMTR/ABMTR Scientific Director,
Professor of Medicine,
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The first 21st-century issue of the IBMTR/ABMTR Newsletter brings you our annual report on the “State of the Art” in blood and marrow transplantation. The report summarizes current use and outcome of transplants, and documents important decreases in transplant-related mortality and improved post-transplant survival. It also identifies the key problems (graft-versus-host disease, infection, disease control) that challenge us as the new century begins. The report is written by Dr Christopher Bredeson, who recently joined the Statistical Center as an Assistant Scientific Director. Dr Bredeson is a hematologist and transplant physician formerly at the University of Ottawa; he also holds a Master’s degree in Clinical Epidemiology from the same institution. He brings considerable experience in clinical trials and data analysis to the IBMTR/ABMTR, and we welcome him.

These summary analyses are done yearly and made available (thanks, in part, to our sponsors) through this newsletter, through our Website (www.ibmtr.org) and through a set of slides distributed free of charge to

participating centers. They represent part of the Statistical Center’s effort to share with the transplant community and others, in a meaningful way, the data voluntarily contributed by IBMTR/ABMTR centers. This is consistent with our philosophy of providing maximum access to the IBMTR/ABMTR database within the constraints of limited personnel resources. In addition to this report, the Statistical Center provides data to many users on a daily basis. Physicians search our database for guidance in making clinical decisions regarding individual patients. Investigators planning clinical trials use it to aid study design and assess feasibility. Healthcare institutions and agencies use it to better inform policy decisions. Scientific studies of the database are proposed and conducted through our 13 Working Committees. We at the Statistical Center see our role as helping the scientific and healthcare community use the database effectively to address important clinical, policy and scientific questions. We welcome proposals for novel uses of the database and encourage our participants and others to contact us with questions which might be effectively addressed by IBMTR/ABMTR data; we will do our best to help.



Armand Keating, MD

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As we enter this new decade and, to reiterate an overused but apt term, the new millennium, I believe we have extraordinary opportunities to further enhance the vitality and relevance of the ABMTR. Of course, there is every indication that the ABMTR is thriving, such as the productivity of our Working Committees with increasing involvement of junior investigators. Numbers of IBMTR/ABMTR publications continue to increase, with studies appearing in excellent biomedical journals. Moreover, there is no shortage of important clinical issues to be addressed. One being actively pursued is long-term consequences of stem cell transplants. IBMTR/ABMTR research efforts in this area are now extensive, as described in some detail by Dr Mary Horowitz in the 1999 Fall issue of this Newsletter. Of particular importance will be the results of the NCI/ABMTR study of 18,000 autotransplants to determine the incidence of and risk factors for AML/MDS after autotransplants for lymphoma.

While these activities indicate a healthy and vigorous organization, it is precisely in these circumstances that we must prepare ourselves to meet

continued on page 2

Report on state of the art in blood and marrow transplantation

– the IBMTR/ABMTR Summary Slides with guide

see page 3

The IBMTR/ABMTR Millennium Slide Issue Newsletter is supported by an unrestricted educational grant from

SangStat Medical Corporation

Messages from the Executive Committee Chairs



John M Goldman, DM

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Few could doubt that the practice of medicine has seen amazing advances in the last century, and few would doubt that even greater advances will occur in the years to come. Clearly one of the most dramatic contributions of the last thirty or so years has been the demonstration that hematopoietic stem cells collected from the bone marrow, or even from the peripheral blood, can engraft in human beings and cure a series of diseases, both malignant and non-malignant, that were regarded previously as incurable. Thus progress in the realm of allogeneic stem cell transplantation has been made on two allied but closely interdependent fronts – by individual researchers and research groups that have pioneered new concepts and new techniques and by the systematic collection, analysis and publication of prospective and retrospective clinical data. In the second realm the IBMTR has stood

and stands pre-eminent for more than thirty years. The indications are that this leading position can be maintained for the foreseeable future. It is very much to the credit of the IBMTR that it now receives clinical data from more than three hundred teams in more than forty countries around the world. This number increases annually.

Nonetheless indications for allograft procedures need constant attention and frequent revision. Nowhere is this more closely demonstrated than in the treatment of CML. During the last year the advent of signal transduction inhibitor (STI571) directed against the kinase activity of the BCR-ABL protein has fundamentally altered our thinking about treatment for CML. It is too early to estimate duration of response or the nature of long-term toxicity, but in the short term the drug has great efficacy.

From the transplant standpoint it has, on the one hand, reintroduced the notion that for certain patients a trial of non-transplant therapy should be seriously considered before proceeding to an allograft that may carry a high risk of mortality. On the other hand, STI571 may be a valuable adjunct to therapy before transplant for patients with accelerated phase or blastic phase disease. Moreover, it may usefully induce Philadelphia negativity before autografting. It may be useful for treating patients who relapse after allografting. One can think of other transplant-related indications. The IBMTR will, we hope, play an important role in addressing these issues as it has in previous changes in transplantation medicine, allowing the observational database to continue to make a fundamental contribution to medical progress.

Professor Armand Keating – continued from page 1

future challenges. And there are many such challenges on the horizon. I would like to identify and discuss two.

The ABMTR has responded well to recognizing emerging indications for transplants – establishment of a Working Committee for autoimmune diseases is an example – but how should we handle emerging technologies that do not fit conventional definitions of hematopoietic stem cell transplants? As an example, consider the nascent field of cell therapy, a good deal of which is autologous. Is intensive or myeloablative therapy an essential prerequisite to qualify a procedure as an autotransplant? Preliminary data on non-myeloablative allotransplants and donor leukocyte infusions challenge that assumption and make us re-examine the role of dose intensity with its attendant toxicity.

Many different cell populations are under investigation as possible therapeutic agents, including LAK cells, NK cells, gamma-delta cells, bone marrow stromal cells (so-called mesenchymal stem cells) and dendritic cells. These therapies target many of the same diseases treated with hematopoietic stem cell transplants, and many of the end-points measured after transplant are also

applicable. It is not surprising that established investigators in transplantation are developing cell therapy protocols – expertise in hematopoiesis, cell manipulation and clinical research are useful for both endeavors. Some of the investigators working on cell therapy protocols are also active in the ABMTR. It would seem that the unique contributions to the transplant field made by the ABMTR could also be applied to these efforts, currently conducted at widely dispersed centers each studying small numbers of subjects.

It is recognized that, while careful analysis of large databases such as ours has numerous, and indeed unique, strengths, it also has its limitations, limitations needing prospective clinical trials to address. It would seem that the ABMTR, with its expertise in statistical analysis, clinical data abstraction and wide network of accomplished transplant investigators, is remarkably well-positioned to facilitate such trials. There is a growing sense that a new approach is required to increase institutional participation and patient accrual in this field.

The sense of betrayal and disappointment that many of us felt by the discovery of scientific fraud in the Bezwoda breast cancer

autotransplant data might best be transmuted into a resolve to continue to conduct clinical research at the highest level. We need to emphasize that authoritative, scientifically impeccable and efficient delivery and analysis of clinical studies can, and are, being conducted in transplantation. In this regard, the ABMTR is in a position not only to contribute, but to provide a leadership role. It is, I believe, equal to this formidable challenge. The addition of prospective clinical studies to our research armamentarium, already successfully accomplished by our colleagues in the EBMTG, will inject the ABMTR with added vitality for decades to come.

As for what is in store for transplants in the new millennium, predictions are a hazardous venture. We must inevitably extrapolate from current knowledge. Those who have seen drawings from previous decades representing the future, may be mildly amused by visions of 21st-century cities consisting of extremely tall buildings linked by numerous skywalks and a sky thick with aircraft that look like 1957 Chevrolets. A safer and more modest prediction is that the Registry will continue to be an important force in the biomedical community, especially if we position ourselves to meet these challenges.

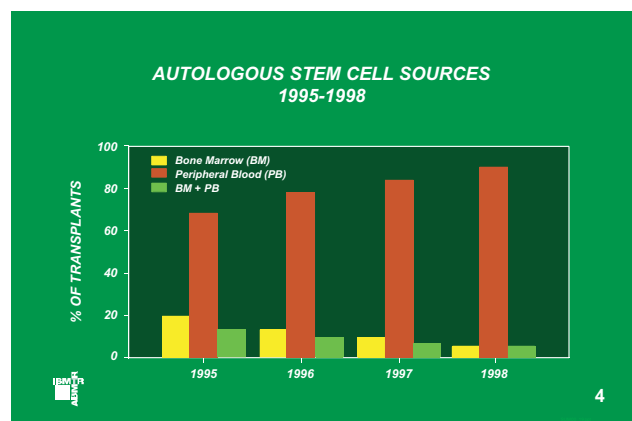
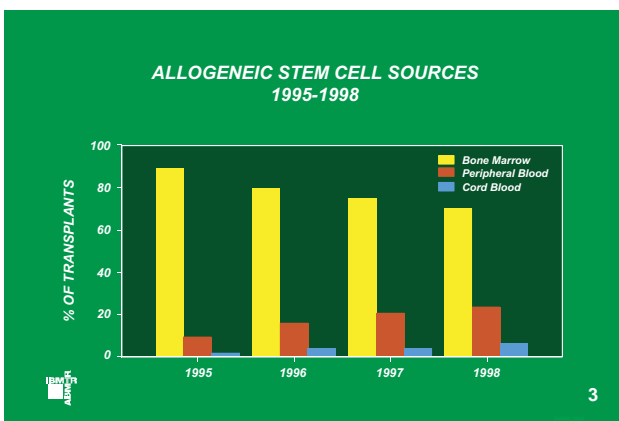
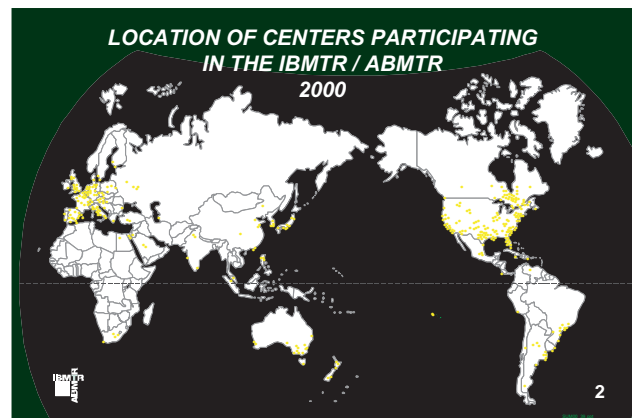
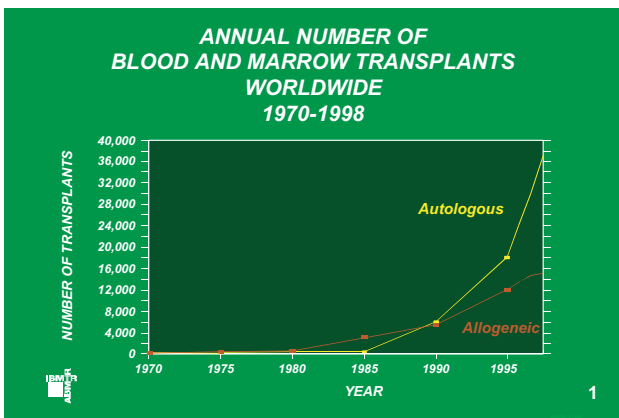
Summary Slides 2000

Report on state of the art in blood and marrow transplantation – the IBMTR/ABMTR Summary Slides with guide

Since 1972 the International Bone Marrow Transplant Registry (IBMTR) has collected and reported outcome data from blood and marrow transplant centers worldwide. More than three hundred centers now participate in the IBMTR. The IBMTR database includes information for about 40% of allogeneic bone marrow transplants done between 1970 and 1998. In 1991, the Autologous Blood & Marrow Transplant Registry (ABMTR) began collecting outcome data on autotransplants from centers in North and South America. More than two hundred autotransplant centers now participate,

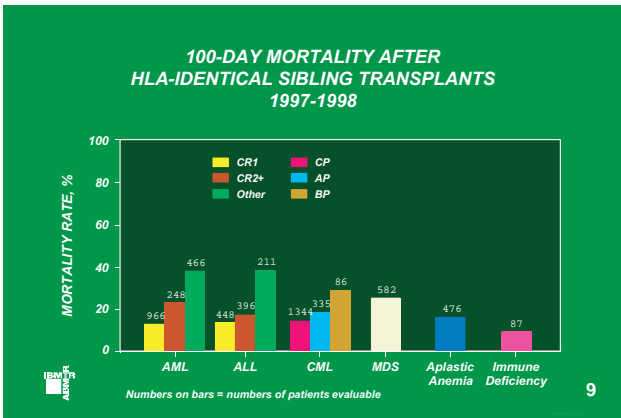
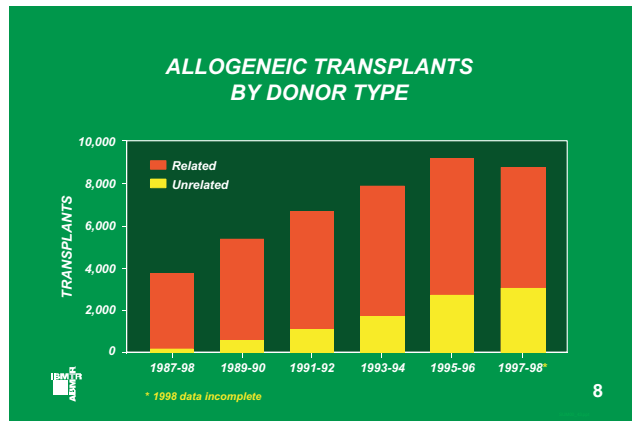
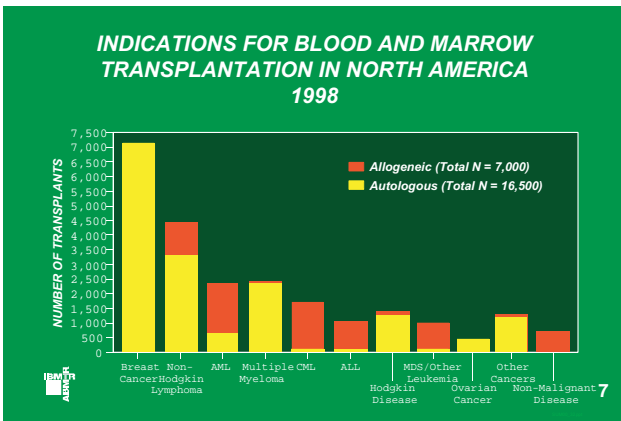
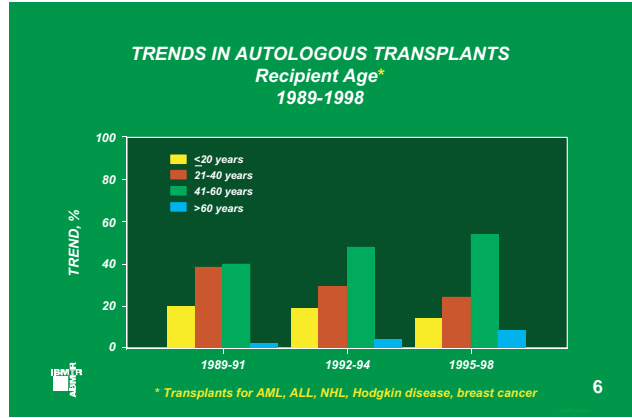
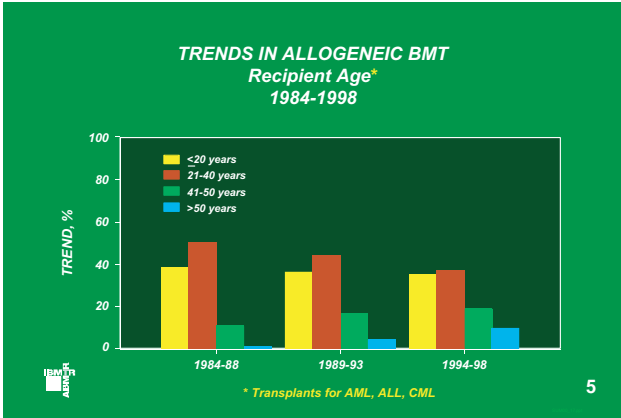
including centers from other regions of the world. The ABMTR database includes information for about 50% of autotransplants done in North and South America between 1989 and 1998.

Using these data, the Statistical Center periodically prepares and distributes slides summarizing current use and outcome of allogeneic and autologous hematopoietic stem cell transplants (SCT). This year's Summary Slides are reproduced below. Descriptive text for the slides runs along the bottom of each page.



Slide 1: Use of blood and marrow transplants continues to increase. While the rate of growth for autologous transplants did not appear to be slowing at the end of 1998, there was some leveling off for allogeneic transplants. The continually increasing numbers of autologous transplants are likely due to several factors, including

new disease indications, application to older patient populations and increased penetration of the standard target population. Leveling off of allogeneic transplants may represent the limited availability of HLA-matched donors (related or unrelated), limited success to date with more disparate donors and a slower expansion into new



Slide 4: Approximately 90% of autotransplants use only hematopoietic progenitor cells collected from blood. The remainder use bone marrow alone or in combination with cells collected from blood.

Slides 5 & 6: For both allogeneic and autologous transplants, the proportion of patients over the age of 40 years at the time of transplant continues to increase. This may reflect advances in supportive care with resultant decrease in transplant-related toxicity and the application of transplantation to diseases affecting older patients (e.g. multiple myeloma). Patients over 50 years of age now account for 10% of allogeneic transplants and 28% of autografts.

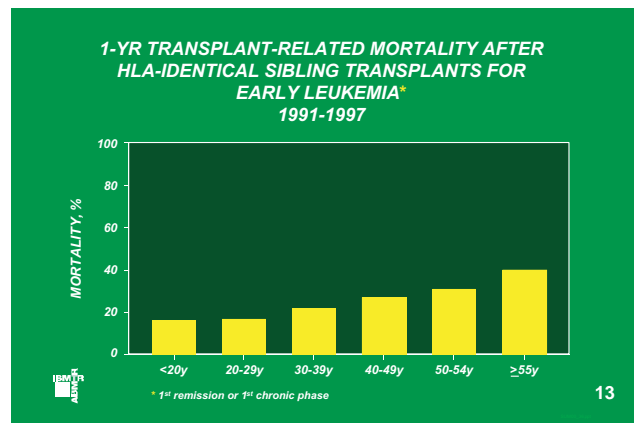
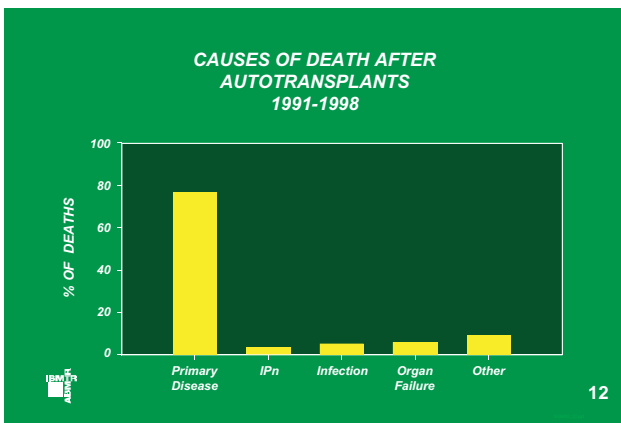
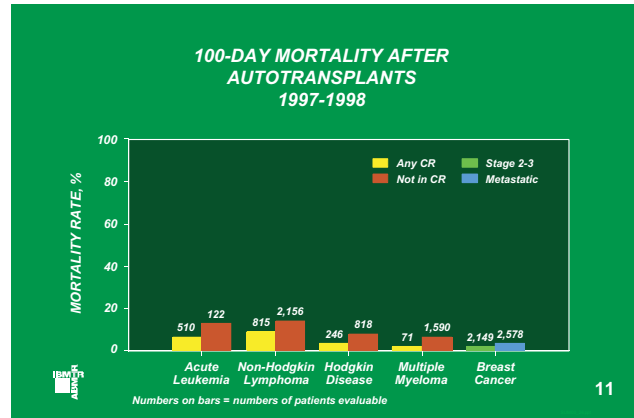
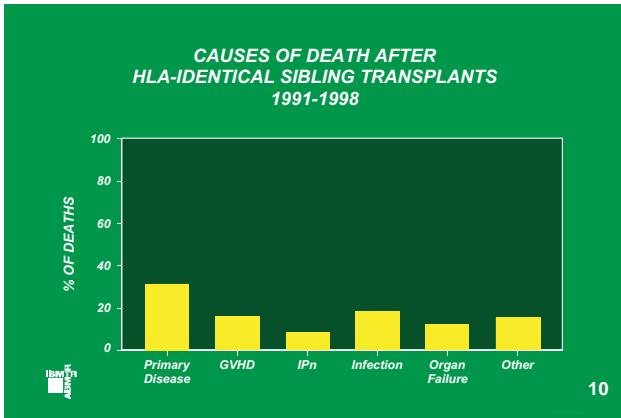
Slide 7: This slide illustrates indications for allogeneic and autologous stem cell transplants in North America. The most common indications for allogeneic and autologous transplants differ. For acute and chronic leukemias, myelodysplasia (MDS) and non-malignant diseases (aplastic anemia, immune deficiencies, inherited metabolic disorders), allogeneic transplant is the predominant approach. Autotransplants are generally used for breast, ovarian and other solid malignancies, as well as Hodgkin and non-Hodgkin lymphomas and multiple myeloma. In 1998, breast cancer was the most common indication for transplant in North America, accounting for nearly one third of all transplants. Non-Hodgkin lymphoma was the second most common indication, followed by acute myelogenous leukemia (AML), multiple myeloma and chronic myelogenous leukemia (CML).

Slide 8: Most allogeneic transplants are from HLA-identical sibling donors. However, only about 30% of transplant candidates have such a donor. Increasing availability of HLA-typed volunteer donors through large national and international registries has enabled increasing use of unrelated donors for bone marrow transplants.

diagnoses. We estimate that seventeen thousand allogeneic and over thirty thousand autologous transplants were done in 1998. Whether disappointment with the preliminary results of several recent autologous trials in breast cancer will affect 1999 numbers is unknown but seems likely.

Slide 2: Currently, more than four hundred centers participate in the IBMTR/ABMTR. The number of participating centers continues to increase.

Slide 3: Most allogeneic transplants use bone marrow grafts. There has been, however, a steady increase in the number of allogeneic transplants using cells collected from blood. Though use is increasing, there are still relatively few transplants using umbilical cord blood cells.

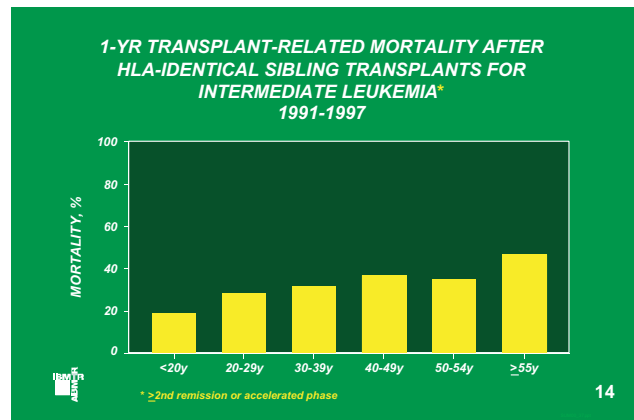


Transplants from unrelated donors now account for approximately 25% of allogeneic transplants.

Slides 9 & 10: 100-day mortality is often used as a gauge of procedure-related toxicity. Allogeneic transplants are associated with relatively high risks of graft-versus-host disease (GVHD), infections and liver toxicity, resulting in high early mortality. Among HLA-identical sibling transplants done in 1997–8 and reported to the IBMTR, 100-day mortality rates ranged from about 10% for persons with acute leukemia in first remission to almost 40% for those with advanced leukemia. 100-day mortality rates after transplants for aplastic anemia and immune diseases ranged between 10% and 15%. Recurrence or progression of the primary disease is responsible for over 30% of all deaths following HLA-identical sibling transplants, with GVHD and infection each responsible for approximately 20% of deaths.

Slides 11 & 12: Early mortality is generally lower following auto- than following allotransplants. Among patients receiving autotransplants in 1997–8, patients transplanted for Hodgkin lymphoma, multiple myeloma or breast cancer while in a remission had 100-day mortality < 5%, while patients treated for non-Hodgkin lymphoma or acute leukemia not in remission had > 15% early mortality. Primary disease recurrence continues to account for the overwhelming majority of deaths in autotransplant recipients.

Slides 13, 14 & 15: The effects of both age and disease state on transplant-related mortality (TRM) with HLA-matched sibling transplants are depicted in these slides. When analyzed by decade, increasing age is associated with increased 1-year TRM after allografts. Additionally, patients with more-advanced disease

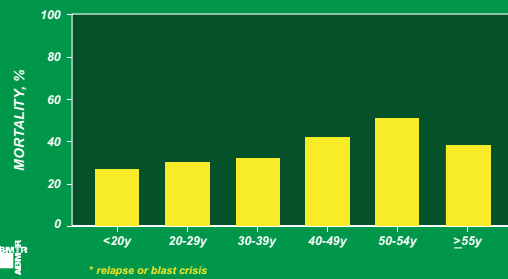


generally have higher mortality compared with those with less-advanced disease. TRM remains a significant problem, being higher than 30% for all patients over 50 years of age and for patients with intermediate and advanced disease who are over 30 years of age.

Slide 16: The effect of age on 1-year transplant-related mortality after unrelated transplants is similar but less dramatic than that seen with matched sibling transplants (slide 13). TRM after unrelated transplants remains a significant problem at 35–50% even for good-risk leukemia patients.

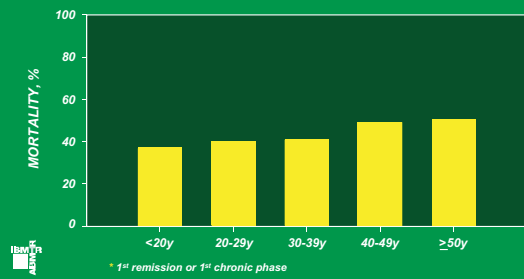
Slide 17: Less-intense preparative regimens and absence of GVHD result in significantly less 1-year transplant-related mortality in

1-YR TRANSPLANT-RELATED MORTALITY AFTER HLA-IDENTICAL SIBLING TRANSPLANTS FOR ADVANCED LEUKEMIA* 1991-1997



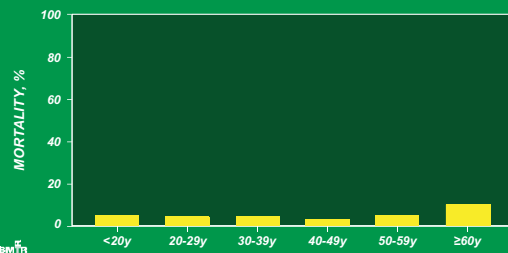
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1-YR TRANSPLANT-RELATED MORTALITY AFTER UNRELATED TRANSPLANTS FOR EARLY LEUKEMIA* 1991-1997



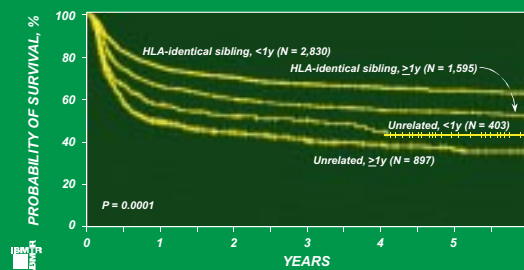
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1-YR TRANSPLANT-RELATED MORTALITY AFTER AUTOTRANSPLANTS FOR NON-HODGKIN LYMPHOMA / HODGKIN DISEASE IN 2ND REMISSION OR 1ST RELAPSE 1991-1997



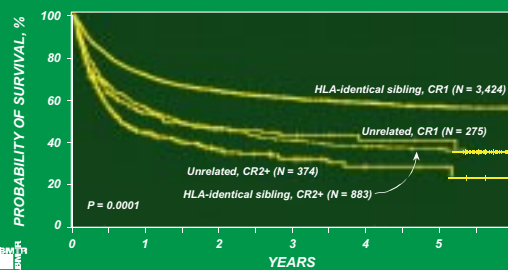
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PROBABILITY OF SURVIVAL AFTER 5,725 ALLOGENEIC BMTs FOR CML IN CHRONIC PHASE BY DONOR TYPE AND DISEASE DURATION, 1991-1997



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PROBABILITY OF SURVIVAL AFTER 4,956 ALLOGENEIC BMTs FOR AML BY DONOR TYPE AND REMISSION STATUS, 1991-1997



19

autologous transplant recipients. For good-risk Hodgkin and non-Hodgkin lymphoma patients, older age is not associated with higher TRM except in the oldest cohort of patients, those ≥ 60 years of age.

Slide 18: CML is the most frequent indication for allogeneic bone marrow transplantation worldwide. Among 5,725 recipients of HLA-identical sibling transplants done between 1991 and 1997 and reported to the IBMTR, 3-year probabilities of survival were $67\% \pm 2\%$ for 2,830 transplants performed within 1 year of diagnosis and $57\% \pm 3\%$ for 1,595 patients transplanted more than 1 year after diagnosis.

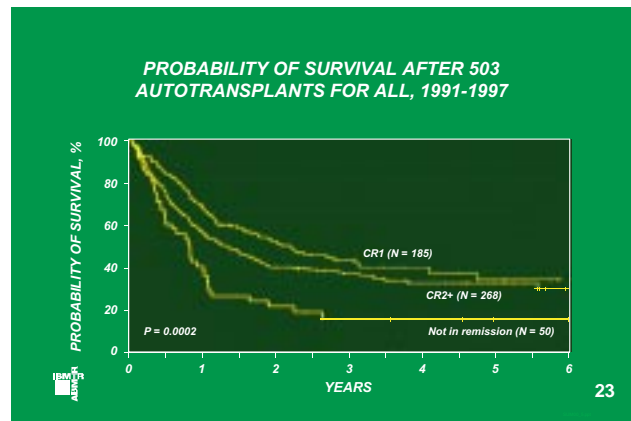
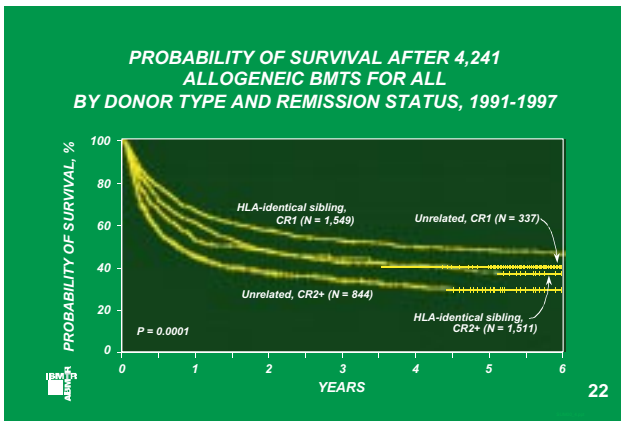
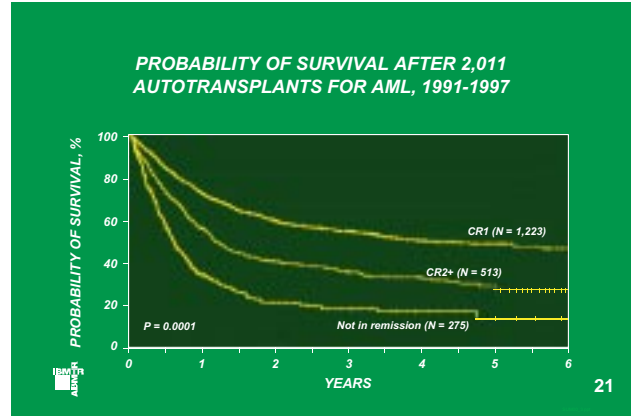
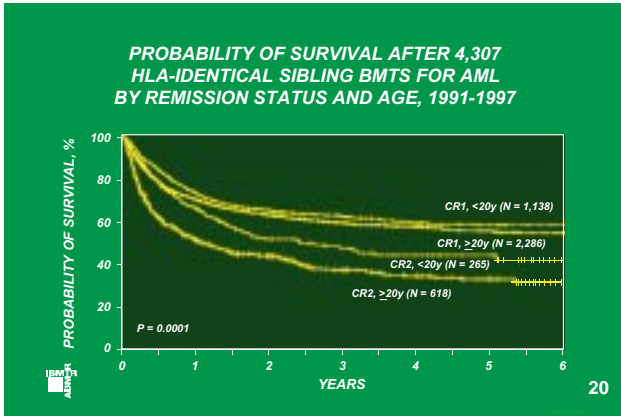
Only about 30% of persons with CML have an HLA-identical sibling donor. Unrelated donor transplants can cure CML but are associated with higher risks of GVHD and transplant-related mortality. Additionally,

unrelated donor transplants are often delayed because of the time required to identify a donor and reluctance to risk the higher TRM. Delaying transplantation may adversely affect outcome. For patients receiving unrelated transplants, the 3-year probability of survival was $50\% \pm 5\%$ for 403 patients transplanted within the first year of diagnosis, and $40\% \pm 4\%$ for 897 patients transplanted beyond the first year after diagnosis of CML.

Slides 19 & 20: Results of HLA-identical sibling transplants for AML correlate with remission state. Among 4,307 recipients of HLA-identical sibling transplants for AML performed between 1991 and 1997 and reported to the IBMTR, 3-year probabilities of survival were $60\% \pm 2\%$ for 3,424 transplants in first complete remission (CR), and $40\% \pm 4\%$ for 883 patients in second or subsequent CR. Survival was generally worse in 649 patients receiving transplants from unrelated donors. Recipients of unrelated donor transplants in first CR had 3-year probabilities of overall survival of $43\% \pm 7\%$, while those in second CR or greater had 3-year probabilities of survival of $32\% \pm 6\%$. There is an additional effect of age on survival following HLA-matched sibling transplants independent of remission status. In both CR1 and CR ≥ 2 , patients younger than 20 years have superior survival to older patients.

Slide 21: Among patients receiving autologous transplants for AML between 1991 and 1997, reported to the ABMTR, the 3-year probability of survival was $55\% \pm 3\%$ for 1,223 patients in first CR at the time of transplant, $35\% \pm 5\%$ for 513 patients in second CR, and $18\% \pm 5\%$ for 275 patients not in CR at the time of transplant.

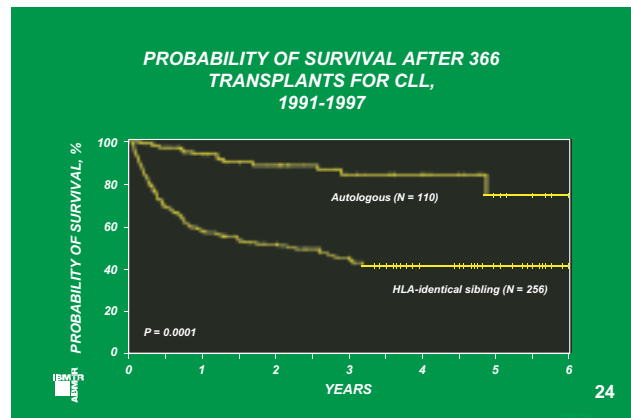
Slide 22: Most patients with ALL are cured with conventional chemotherapy. Consequently, bone marrow transplants are generally



reserved for patients failing conventional therapy, i.e., in relapse or second or subsequent remission, or patients in first remission with prognostic factors predicting a high risk of failure with conventional therapy. The most frequent indications for transplants in first remission are older age, high leukocyte count at diagnosis, Philadelphia and other chromosome abnormalities and difficulty obtaining a first remission. Among 3,060 recipients of HLA-identical sibling transplants between 1991 and 1997, reported to the IBMTR, 3-year probabilities of survival were $52\% \pm 3\%$ for 1,549 transplants done in first remission and $42\% \pm 3\%$ for 1,511 transplants in second or subsequent remission. Although associated with higher transplant-related mortality, unrelated donor transplants may be considered for patients with ALL unlikely to be cured with chemotherapy. Among 1,181 recipients of unrelated donor transplants for ALL in first remission reported to the IBMTR, 3-year probability of survival was $44\% \pm 7\%$ among 337 receiving unrelated donor transplants in first remission, and in 844 patients in second or subsequent remission it was $33\% \pm 3\%$.

Slide 23: Among 503 recipients of autotransplants for ALL between 1991 and 1997, reported to the ABMTR, 3-year probabilities of survival were $43\% \pm 9\%$ for 185 transplants done in first remission, $37\% \pm 7\%$ for 268 transplants done in second or subsequent remission, and $15\% \pm 11\%$ for 50 transplants done in relapse.

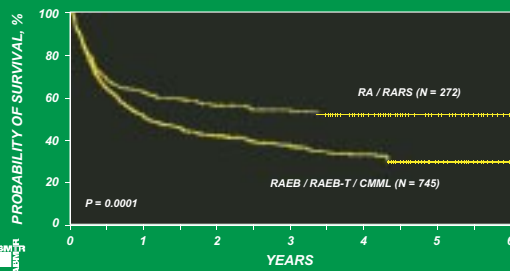
Slide 24: Interest in both allogeneic and autologous transplantation for chronic lymphocytic leukemia (CLL) is increasing. To date these transplants have primarily been performed for poor-prognosis patients, although patients earlier in the course of their disease are starting to be transplanted as well. In 256 patients with CLL undergoing matched sibling allogeneic transplants between 1991



and 1997, the 3-year probability of survival was $44\% \pm 7\%$. Although the number of patients followed beyond 3 years is small, some patients may be cured with this approach. The experience with autologous transplantation for CLL is more limited. Among 110 recipients of autotransplants for CLL between 1991 and 1997, reported to the ABMTR, the 3-year probability of survival was $84\% \pm 9\%$, but relapses are frequent.

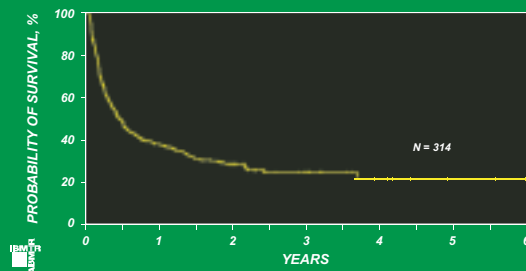
Slides 25 & 26: Allogeneic bone marrow transplantation can cure some patients with myelodysplastic syndromes. For 272 patients with refractory anemia (RA) or refractory anemia with ringed sideroblasts (RARS) receiving matched sibling allogeneic transplants between 1991 and 1997, the overall survival at 3 years was $53\% \pm 7\%$, while 745 patients with refractory anemia with excess blasts

PROBABILITY OF SURVIVAL AFTER 1,017 HLA-IDENTICAL SIBLING BMTS FOR MYELODYSPLASTIC SYNDROMES, BY FAB CLASSIFICATION, 1991-1997



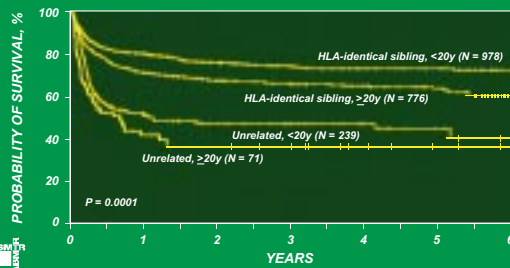
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PROBABILITY OF SURVIVAL AFTER 314 UNRELATED BMTS FOR MYELODYSPLASTIC SYNDROMES, 1991-1997



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PROBABILITY OF SURVIVAL AFTER 2,064 ALLOGENEIC BMTS FOR SEVERE APLASTIC ANEMIA BY DONOR TYPE AND AGE, 1991-1997



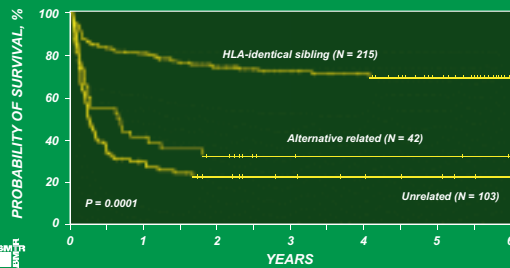
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PROBABILITY OF SURVIVAL AFTER 11,764 HLA-IDENTICAL SIBLING BMTS FOR PATIENTS SURVIVING AT LEAST 2 YRS POSTTRANSPLANT, 1973-1997



28

PROBABILITY OF SURVIVAL AFTER 360 ALLOGENEIC BMTS FOR FANCONI ANEMIA BY DONOR TYPE, 1991-1997



29

310 recipients of unrelated donor transplants: 46% ± 7% in 239 patients < 20 years and 36% ± 12% in 71 older patients.

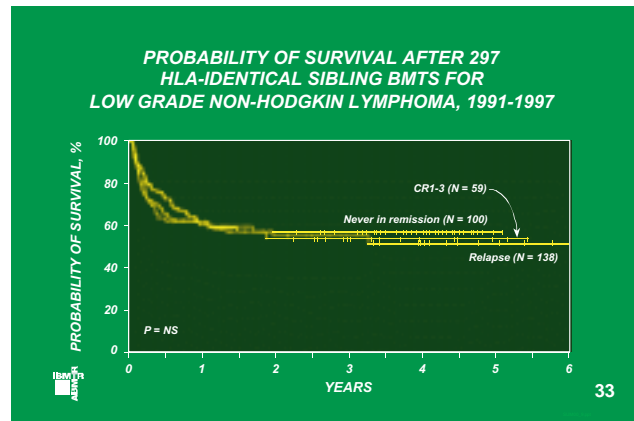
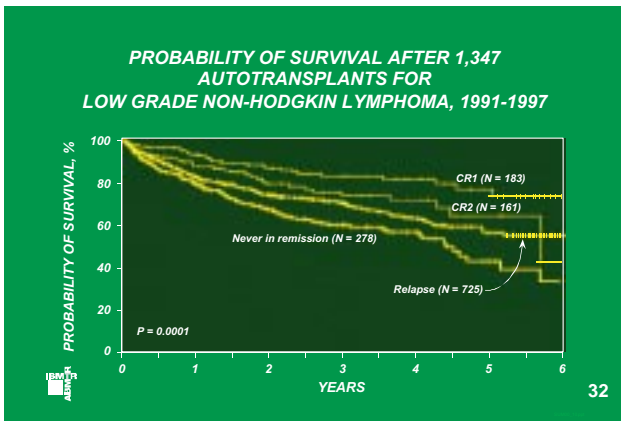
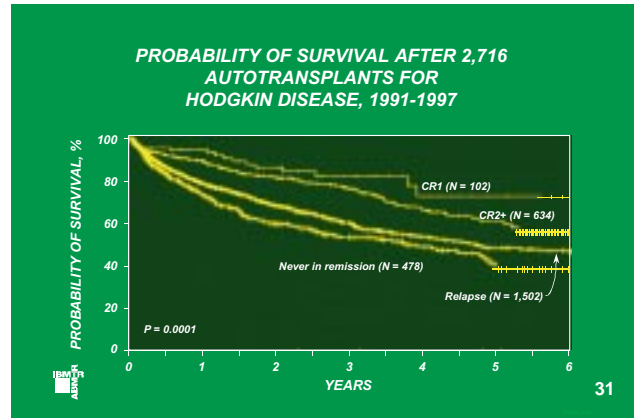
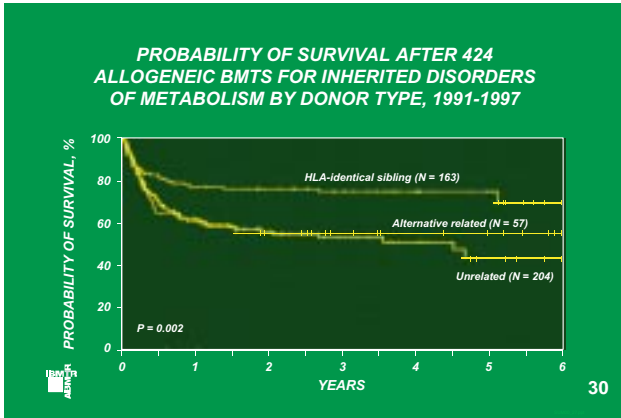
Slide 28: Data on HLA-matched sibling allogeneic transplants has been collected by the IBMTR since 1972. As the number of patients with long-term follow-up after an HLA-matched sibling allogeneic transplant increases, it becomes possible to address the issue of long-term survival for different patient populations. Analysis of 2-year survivors after a matched sibling allogeneic transplant is useful, since much of the mortality risk associated with intensive preparative regimens, GVHD and early relapse has passed. Among 11,764 patients surviving 2 years after a matched sibling transplant between 1973 and 1997, probabilities of survival at 7 years post-transplant were 94% ± 1% for 1,716 patients with severe aplastic anemia, 83% ± 1% for 3,728 patients with AML, 83% ± 1% for 3,896 patients with CML and 79% ± 2% for 2,424 patients with ALL.

Slide 29: Allogeneic transplants cure some patients with Fanconi anemia. Among 215 patients transplanted between 1991 and 1997 from matched siblings the 3-year survival was 72% ± 7%. Transplants from other donors have been less successful. Among 42 patients transplanted from related donors other than matched siblings, 3-year survival was 32% ± 15% and among 103 patients transplanted from unrelated donors the survival was 22% ± 9%.

Slide 30: Allogeneic transplantation is currently the only curative therapy for inherited disorders of metabolism. Among 424 patients transplanted for inherited disorders of metabolism between 1991 and 1997, 3-year probabilities of survival were 74% ± 7% for 163 patients receiving matched sibling transplants, 55% ± 14% for 57 patients receiving transplants from other relatives and 53% ± 9%

(RAEB), refractory anemia with excess blasts in transformation (RAEB-T), or chronic myelomonocytic leukemia (CMML) had a 3-year probability of survival of 36% ± 4%. Among 314 patients receiving unrelated transplants, the 3-year overall survival was 23% ± 6%. Differences by FAB classification were not seen. This may reflect the small numbers and poor prognosis of patients with RA/RARS undergoing unrelated donor transplants.

Slide 27: Allogeneic transplantation is the treatment of choice for young patients with aplastic anemia who have an HLA-identical sibling. Three-year probabilities of survival after 1,754 HLA-identical sibling transplants between 1991 and 1997, reported to the IBMTR, were 74% ± 3% for 978 patients < 20 years of age and 65% ± 3% for 776 patients older than 20 years. Results were not as good in

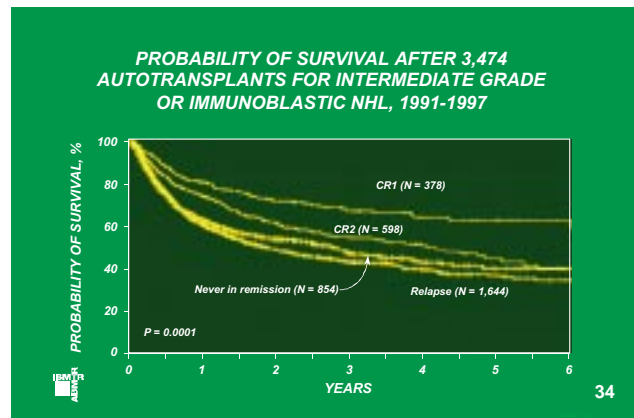


for 204 patients receiving unrelated donor transplants.

Slide 31: Most patients with Hodgkin disease are cured with conventional chemotherapy. However, for the 20–30% failing conventional therapy, autotransplants are effective salvage therapy. Among 2,716 autotransplants between 1991 and 1997, reported to the ABMTR, 3-year probabilities of survival were 53% ± 5% for 478 patients never in remission, 82% ± 9% for 102 patients transplanted in first remission, 59% ± 3% for 1,502 patients transplanted in relapse and 76% ± 4% for 634 patients transplanted in second or subsequent remission.

Slides 32 & 33: Autotransplants are also commonly used for non-Hodgkin lymphoma. Among 1,347 patients receiving autotransplants for low-grade lymphoma between 1991 and 1997, 3-year probabilities of survival were 83% ± 6% for 183 patients in first remission, 74% ± 9% for 161 in second remission, 70% ± 4% for 725 in relapse, and 60% ± 7% for 278 never achieving remission with standard chemotherapy. Relapse is less frequent but treatment-related mortality is higher with HLA-identical sibling transplants. Among 297 patients with low-grade non-Hodgkin lymphoma, the 3-year probability of survival was approximately 50% regardless of stage.

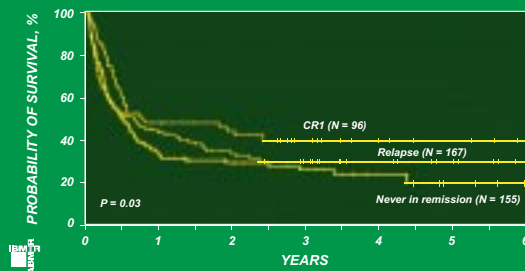
Slides 34 & 35: Among 3,474 patients receiving autotransplants for intermediate grade or immunoblastic lymphoma, 3-year probabilities of survival were 67% ± 6% for 378 patients in first remission, 55% ± 5% for 598 in second remission, 42% ± 3% for 1,644 in relapse and 46% ± 4% for 854 never achieving remission with conventional chemotherapy. Most failures after autotransplants for non-Hodgkin lymphoma are due to relapse. Higher transplant-related mortality more than offsets the lower relapse rate seen with



HLA-identical sibling transplants for these lymphomas, resulting in poorer survival than with autotransplants. The 3-year survival rates among 418 patients transplanted between 1991 and 1997 from HLA-identical siblings for intermediate and immunoblastic lymphoma were 39% ± 11% in 96 patients in first remission, 25% ± 8% for 155 patients not achieving remission and 29% ± 8% for 167 patients in relapse.

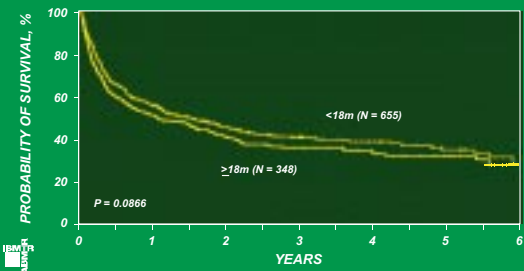
Slides 36 & 37: Stem cell transplantation is now considered standard therapy for multiple myeloma, a disease incurable with conventional therapy. The 3-year survival after 1,003 HLA-identical sibling transplants reported to the IBMTR between 1991 and 1997 was 39% ± 3% regardless of duration of myeloma at the time of transplant. For those patients receiving autologous transplants for

PROBABILITY OF SURVIVAL AFTER 418 HLA-IDENTICAL SIBLING BMTs FOR INTERMEDIATE GRADE OR IMMUNOBLASTIC NHL, 1991-1997



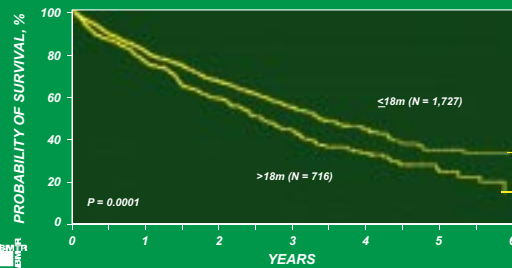
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PROBABILITY OF SURVIVAL AFTER 1,003 HLA-IDENTICAL SIBLING BMTs FOR MULTIPLE MYELOMA BY DISEASE DURATION, 1991-1997



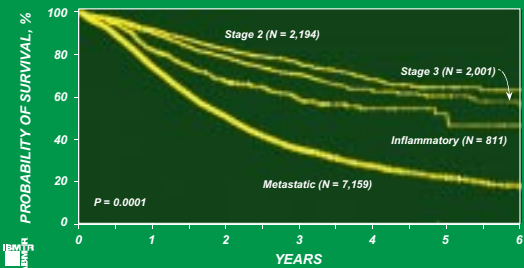
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PROBABILITY OF SURVIVAL AFTER 2,443 AUTOTRANSPLANTS FOR MULTIPLE MYELOMA BY DISEASE DURATION, 1991-1997



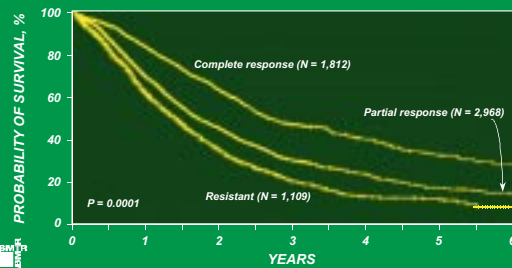
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PROBABILITY OF SURVIVAL AFTER 12,165 AUTOTRANSPLANTS FOR BREAST CANCER, 1991-1997



38

PROBABILITY OF SURVIVAL AFTER 5,889 AUTOTRANSPLANTS FOR METASTATIC BREAST CANCER BY PRETRANSPLANT CHEMOSENSITIVITY, 1991-1997



39

year survival was $55\% \pm 4\%$, while it was $43\% \pm 5\%$ for 716 patients having myeloma longer than 18 months. We do not have adequate long-term data to establish whether either strategy is truly curative for multiple myeloma.

Slides 38 & 39: Breast cancer was the most frequent indication for autotransplant in North America in 1998. Among 12,165 women receiving autotransplants for breast cancer between 1991 and 1997 and reported to the ABMTR, 3-year probabilities of survival were $74\% \pm 3\%$ in 2,194 women with Stage 2 disease, $70\% \pm 3\%$ in 2,001 women with Stage 3 disease, $57\% \pm 5\%$ in 811 women with inflammatory breast cancer and $34\% \pm 1\%$ in 7,159 women with metastatic breast cancer. Outcome in metastatic breast cancer is significantly better for women who achieve a complete remission with conventional therapy prior to transplant. Among the 5,889 women transplanted for metastatic disease in whom pretransplant response to chemotherapy was known, 3-year probability of survival was $47\% \pm 3\%$ in 1,812 with a complete response, $30\% \pm 2\%$ in 2,968 with a partial response and $20\% \pm 3\%$ in 1,109 women with resistant disease.

multiple myeloma, the 3-year survivals are higher, largely due to lower transplant-related mortality. For 1,727 patients receiving an autotransplant within 18 months of diagnosis of myeloma, the 3-

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