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Allogeneic Transplantation: Peripheral Blood versus Bone Marrow

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Abstract

Purpose of Review—Peripheral Blood Stem Cells (PBSC) have been widely adopted as a source of stem cells for allogeneic transplantation although controversy remains regarding their role compared to the use of bone marrow (BM).

Recent Findings—Ten year follow-up has been reported from several large randomized trials and a recently completed trial using unrelated donor stem cells have been reported. In addition, two meta-analyses have been reported from the findings of a number of randomized studies. Several studies indicate that PBSC confer survival advantages over BM with matched sibling donors for most disease categories except where the risks of disease recurrence within the first year are low, but with the extra risk of more chronic GVHD. Using PBSC from unrelated donors does not appear to be more beneficial than BM, but with early follow-up. New strategies for rapid mobilization of PBSC from normal donors using plerixafor have been reported. Early studies suggest that filgrastim stimulated BM may confer some of the advantages of PBSC without the risks of chronic GVHD.

Summary—PBSC are a preferred source of stem cells for many types of allogeneic transplant where matched related donors are available. Whether the same benefits accrue from unrelated donors will require further follow-up.

Keywords

allogeneic marrow transplants; allogeneic peripheral blood stem cells; leukemia; graft-versus-host disease; filgrastim

Introduction

It has been 18 years since the initial report of allogeneic transplant utilizing peripheral blood stem cells (PBSC) collected after filgrastim from a donor considered high risk for anesthesia, precluding marrow (BM) harvest [1]. The recipient had acute lymphocytic leukemia in second remission and was treated with cyclophosphamide and total body irradiation followed by unmodified PBSC and GVHD prophylaxis with cyclosporine and methotrexate. He engrafted promptly and did not develop acute or chronic GVHD. These initial observations led to the rapid application of this technology [2–16].

Results of allogeneic PBSC transplantation suggest that this technique can produce substantially more rapid engraftment than observed with unmodified BM. Rates of acute GVHD have been similar to or greater than BM, depending on the particular trial, but

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chronic GVHD in most trials has been greater than BM. The European Group for Blood and Bone Marrow Transplantation (EBMT) survey of transplant centers in 1996 found that out of 4400 allogeneic transplants, PBSC's were used in 30% [17]. By 2009, using a similar survey the number of allogeneic transplant had increased to 11,500, of which 71% utilized PBSC [18]. This large increase in the absolute numbers of allogeneic transplants using PBSC was due in part to the increased use of non-ablative regimens which constituted 39% of the transplants, but also is indicative of the popularity of PBSC.

This review will deal exclusively with patients undergoing myeloablative allografts since BM does not appear to be an option for patients who receive non-myeloablative conditioning. This is due to the unacceptably high rates of graft rejection or failure when BM has been used for nonmyeloablative allografts.

Prospective Randomized Comparisons of PBSC and BM

Results of eight randomized studies comparing mobilized PBSC and unstimulated BM for allogeneic transplantation have been reported; with several updated to 10 year follow-up (Table 1). These studies enrolled 30–329 patients each and in total contain over 1000 patients. All studies utilized the combination of cyclosporine and methotrexate for GVHD prevention [30], however, in 3 studies the day 11 methotrexate dose was omitted. Post-transplant myeloid growth factors were not used with the exception of the 329 patient European Group for Blood and Bone Marrow Transplantation (EBMT) study [24,25]. Neutrophil engraftment occurred significantly earlier with PBSC in 7 studies and all studies showed significantly earlier platelet recovery with PBSC. The risks of acute GVHD, grades II–IV were similar in all studies except for the multicenter EBMT which noted a 13% greater incidence of grade II–IV GVHD and a 12% greater incidence of grade III–IV GVHD in the PBSC group and a Nordic trial which reported 15% more acute GVHD with PBSC. An important difference in the design of the EBMT study compared to the others, was the omission of day 11 methotrexate from GVHD prophylaxis. In prior studies of BM transplant recipients, omission of day 11 methotrexate increased the risks of GVHD [31]. Although these were randomized studies, this omission may have further predisposed recipients of PBSC to develop GVHD due to the 10 fold greater number of T cells.

All studies showed a trend toward more chronic GVHD with PBSC, and in 3 studies the trend became statistically significant. It is interesting that the day 11 dose of methotrexate was omitted in the three studies that reported a statistically higher incidence of chronic GVHD with PBSC. While this observation does not directly explain a higher incidence of chronic GVHD, patients who have acute GVHD are more likely to develop chronic GVHD.

Two large studies of 172 and 228 patients had statistically better survival or disease free survival among patients who were randomized to receive PBSC. In the U.S. study, disease-free survival was better but overall survival was not. The survival differences were greatest among patients with more advanced hematologic malignancies, and this was due to both reduced transplant-related mortality and relapse [28,29]. These observations continue to hold up with 10 year follow-up. In comparison to the other published, randomized clinical trials, the U.S. study enrolled a larger number of patients with more advanced hematological malignancies, the patients in whom the benefit of PBSC was most apparent. The study was not large enough to determine whether the use of peripheral blood cells improved survival for patients with less advanced hematologic malignancies. The Canadian intergroup trial was mainly composed of patients with less advanced leukemias but due to larger patient numbers the survival differences were significant [27]. This trial, interestingly, showed that overall survival was better with PBSC primarily due to reduced non-relapse mortality without significant differences in relapse. In contrast the larger EBMT trial which was also

composed almost exclusively of less advanced patients showed no differences in disease-free survival or overall survival [24,25]. This trial had important differences from the Canadian study including omission of the day 11 methotrexate and the use of post transplant filgrastim. In a large meta-analysis of all the randomized trials, survival was improved in recipients of PBSC who received 4 doses of methotrexate compared to recipients of BM and 4 doses of methotrexate, due primarily to lower rates of relapse [32]. It was hypothesized that the extra dose of methotrexate suppressed antileukemic effects of the BM graft but did not affect the PBSC graft.

Ten year follow-up has been reported for both the EBMT and US trials [25,29]. Ten year follow-up in the US trial showed continued protection against relapse; 22% with PBSC v. 32% with BM, p=0.01. Transplant mortality was similar between PBSC and BM as well as chronic GVHD, 48% with PBSC v. 37% with BM, p=0.55. Overall survival was similar between PBSC and BM in the US trial, but in the subgroup analysis patients with more advanced hematologic malignancies had superior survival with PBSC. Ten year follow-up of the EBMT trial continue to show similar overall survival and leukemia free survival with both PBSC and BM. There is more chronic GVHD with PBSC but this does not impact overall outcomes, including survival.

Two meta-analyses have been reported, 1 using individual patient data supplied by the original authors [33] and another more recent paper using time-to-event data reported from the original manuscripts [34]. The individual patient analyses reported faster engraftment with PBSC but more acute GVHD grades 2–4, and chronic GVHD. Nonrelapse mortality was similar but rates of relapse were lower in both early and late stage disease. Overall survival and relapse free survival were only improved with PBSC in patients with late stage disease. In the more recent publication findings were similar to the prior meta-analysis with the exception of a greater risk of severe (grades 3–4) acute GVHD.

Experience with Unrelated Donors

Due in part to concerns about exposure of normal volunteer donors to filgrastim during the mobilization process, allogeneic transplants performed using unrelated donor PBSC have been more slowly adopted. In a limited study of the experience from 4 European centers, 45 patients received unmanipulated, filgrastim mobilized PBSC from volunteer unrelated donors, and the results retrospectively compared to those who received BM [35]. Engraftment with neutrophils and platelets was more rapid with PBSC, with similar incidences of acute and chronic GVHD transplant-related mortality and overall survival. A large, recently completed trial conducted by the US Clinical Trials Network has been reported with 551 patients from the US and Canada randomized to allogeneic PBSC or BM from matched unrelated donors [36]. By intent to treat analysis there were no differences in 2 year overall survival; 51% with PBSC, 46% with BM, p=0.25. Disease free survival, relapse, non-relapse mortality, neutrophil engraftment, and acute GVHD, grades 2–4 and 3–4 were similar. Chronic GVHD, however, was higher with PBSC 53% v. 40% with BM, p=0.02. Two year survival is a relatively early outcome and further follow-up is needed to assure equivalence. In addition only 28% of patients in this trial had high risk disease; the group that seems to derive greatest benefit from PBSC.

T- Cell Depletion Studies

As in BM, investigators have been interested in T-cell depletion approaches as a means of reducing GVHD. The main advantage of T depletion in PBSC is that larger numbers of stem and progenitor cells can be harvested to offset their inevitable losses when cells are manipulated. One multicenter study enrolled 62 patients who had allogeneic PBSC from HLA matched sibling donors, which were CD34 enriched using immunomagnetic beads or

avidin-biotin [37]. In that study engraftment was rapid and GVHD was virtually eliminated with cyclosporine prophylaxis. Only short-term outcomes were available making the questions of relapse and chronic GVHD in further follow-up important. One theoretical advantage of CD34+ cell enrichment over complement lysis techniques is that a second stage selection technique could be utilized to select other cell populations such as CD56+ or CD8+ cells that could be added back to the graft. This engineering technique would potentially allow the selective infusion of cells able to enhance immune reconstitution against infectious agents or anti-leukemic effects without the development of GVHD. Two more recent studies reported outcomes of small numbers of patients with hematologoic malignancies receiving T depleted PBSC after myeloablative conditioning with TBI. In one study patients with AML in remission received sibling grafts that were CD34 selected without additional GVHD prophylaxis [38]. Acute GVHD grades 2–4 was seen in 23% with chronic GVHD in 7%. Relapse rates were 17% with 58% surviving disease free at 36 months. In the second trial 35 patients with mostly acute leukemia received PBSC from unrelated donors after CD34 selected/E-rosetting with additional ATG post transplant. The four year disease free survival was 57% with acute GVHD grades 2–4 of 9% and chronic GVHD of 29%. Rates of relapse were low at 6% [39]. The outcomes of these 2 studies are similar to T replete transplants but with lower rates of chronic GVHD making this a potentially attractive strategy. A randomized trial of T cell depletion by means of CD34 selection was performed comparing selected PBSC vs. selected BM and the results were strikingly different [40]. In this trial PBSC recipients were given 50% higher numbers of residual T cells than BM recipients, 3.0×10^5/kg vs. 2.0×10^5/kg, but 4 times the number of CD34 cells. Engraftment of both neutrophils and platelets was significantly faster but acute GVHD was significantly higher with PBSC and correlated with the number of residual T cells. Transplant mortality was strongly linked to GVHD. Survival at 3 years was significantly better for BM than PBSC, 60% v. 45%, p=0.04. Higher mortality in the PBSC group was linked to more acute GVHD among recipients of $>2.0 \times 10^5$ residual T cells/kg. This trial had a majority of good risk patients but found a threshold effect of the dose of T cells on the development of GVHD which suggests that CD34 selection results in too many residual T cells to be a stand alone method for T depletion of PBSC.

Filgrastim Stimulated Marrow

Based on the hypothesis that filgrastim may improve yield of BM from normal donors, several small studies have examined engraftment and GVHD for patients receiving allogeneic BM from donors who received 3–4 days of filgrastim immediately prior to harvest [41–43]. When compared to filgrastim mobilized PBSC, recipients of filgrastim stimulated allogeneic BM experienced similar neutrophil engraftment, but slower platelet recovery, significantly lower incidences of acute and chronic GVHD and similar survival [42]. Two studies, which compared filgrastim stimulated BM to historical BM patients showed earlier neutrophil and platelet recovery in patients given stimulated BM with similar rates of GVHD, relapse and survival [41,43]. A small prospective randomized trial comparing filgrastim stimulated BM to PBSC found similar rates of neutrophil and platelet engraftment but greater rates of acute and chronic GVHD with PBSC, without differences in short term survival [44]. A review of this topic which included a meta-analysis of studies comparing filgrastim BM to PBSC found similar rates of engraftment, acute GVHD, relapse and OS but a greater risk of chronic GVHD with PBSC [45]. These preliminary studies provide data suggesting that filgrastim stimulated allogeneic BM may confer early engraftment similar to mobilized PBSC but possibly without the increased risk of GVHD. A large prospective randomized trial sponsored by the Canadian Blood and Marrow transplant group is currently open with the aim of comparing filgrastim mobilized PBSC with filgrastim stimulated BM. The study is designed to detect a 30% difference in the rates of chronic GVHD.

New PBSC Mobilization Strategies for Allogeneic Transplantation

A novel cytokine, plerixafor, blocks chemokine receptor-4 binding by stem cells and is approved for autologous transplant to augment mobilization with filgrastim [46,47]. This drug has the potential, however, to revolutionize PBSC harvests from normal donors as it has been shown that plerixafor alone can be used to rapidly mobilize PBSC from normal donors within 1–3 days and that these cells are capable of rapid engraftment in allogeneic recipients [48]. This would allow donors to mobilize and collect PBSC within a 24–48 hour period, a huge savings of time and effort; making PBSC donation more attractive for unrelated donors.

Conclusion

The rapid application of allogeneic PBSC for transplantation in the past 18 years has raised legitimate concerns about the relative benefits of this source of stem cells compared to BM. It is clear that engraftment is more rapid with PBSC than BM and that this can be associated with a reduced transplant related mortality. Most legitimate comparison trials using the optimum GVHD prophylaxis regimen of a calcineurin inhibitor and methotrexate have demonstrated equivalent rates of acute GVHD. Chronic GVHD can be expected to be 15–20% higher with PBSC than BM. This chronic GVHD, however, is associated with significant anti-leukemic effects which in turn confers a major survival benefit to patients with more advanced hematologic malignancies. Patients with less advanced hematologic malignancies probably do not benefit from the use of PBSC. Small studies indicate that pretreatment of BM donors with filgrastim may confer some of the benefits of mobilized PBSC. Larger, randomized comparisons are underway and will be required to be certain of this. Early phase III data using allogeneic PBSC from phenotypically matched unrelated donors indicates more rapid engraftment than BM with similar rates of acute GVHD, but more chronic GVHD and no early survival benefit. Longer follow-up will be needed to define the value of allogeneic PBSC from unrelated donors compared to BM. A recent study used decision analysis modeling to determine the best source of stem cells [49]. Using individual patient data from randomized trial they determined that PBSC was superior to BM in overall and quality adjusted life expectancy. The only situation in which BM may be preferred is when the 1 year probability of relapse is <5%.

The very large quantities of stem and progenitor cells made available from mobilized PBSC will allow future trials of graft engineering in which highly purified stem and progenitor cells will be transplanted along with purified or manipulated T cell subset capable of ensuring engraftment, immune reconstitution, and anti-leukemic effects without GVHD.

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References

1. Russell NH, Hunter A, Rogers S, et al. Peripheral blood stem cells as an alternative to marrow for allogeneic transplantation. Lancet. 1993; 341:1482. [PubMed: 8099182]
2. Goldman J. Peripheral blood stem cells for allografting. Blood. 1995; 85:1413–1415. [PubMed: 7534129]
3. Russell NH, Hunter AE. Peripheral blood stem cells for allogeneic transplantation. Bone Marrow Transplant. 1994; 13:353–355. [PubMed: 7517257]

4. Körbling M, Przepiorka D, Huh YO, et al. Allogeneic blood stem cell transplantation for refractory leukemia and lymphoma: potential advantage of blood over marrow allografts. Blood. 1995; 85:1659–1665. [PubMed: 7888684]
5. Schmitz N, Dreger P, Suttorp M, et al. Primary transplantation of allogeneic peripheral blood progenitor cells mobilized by filgrastim (granulocyte colony-stimulating factor). Blood. 1995; 85:1666–1672. [PubMed: 7534141]
6. Bensinger WI, Weaver CH, Appelbaum FR, et al. Transplantation of allogeneic peripheral blood stem cells mobilized by recombinant human granulocyte colony-stimulating factor. Blood. 1995; 85:1655–1658. [PubMed: 7534140]
7. Bensinger WI, Clift RA, Anasetti C, et al. Transplantation of allogeneic peripheral blood stem cells mobilized by recombinant human granulocyte colony-stimulating factor. Stem Cells. 1996; 14:90–105. [PubMed: 8820955]
8. Majolino I, Aversa F, Bacigalupo A, et al. Allogeneic transplants of rhG-CSF-mobilized peripheral blood stem cells (PBSC) from normal donors. Haematologica. 1995; 80:40–43. [PubMed: 7538968]
9. Bensinger WI, Clift R, Martin P, et al. Allogeneic peripheral blood stem cell transplantation in patients with advanced hematologic malignancies: A retrospective comparison with marrow transplantation. Blood. 1996; 88:2794–2800. [PubMed: 8839878]
10. Bensinger WI, Buckner CD, Shannon-Dorcy K, et al. Transplantation of allogeneic CD34+ peripheral blood stem cells in patients with advanced hematologic malignancy. Blood. 1996; 88:4132–4138. [PubMed: 8943847]
11. Russell JA, Bowen T, Brown C, et al. Allogeneic blood cell transplants for haematological malignancy: Comparison of engraftment and graft-versus-host disease with bone marrow transplantation. Bone Marrow Transplant. 1996; 17:703–708. [PubMed: 8733685]
12. Przepiorka D, Anderlini P, Ippoliti C, et al. Allogeneic blood stem cell transplantation in advanced hematologic cancers. Bone Marrow Transplant. 1997; 19:455–460. [PubMed: 9052911]
13. Azevedo WM, Aranha FJP, Gouvea JV, et al. Allogeneic transplantation with blood stem cells mobilized by rhG-CSF for hematologic malignancies. Bone Marrow Transplant. 1995; 16:647–653. [PubMed: 8547861]
14. Anderlini P, Przepiorka D, Champlin R, et al. Biologic and clinical effects of granulocyte colony-stimulating factor in normal individuals. Blood. 1996; 88:2819–2825. [PubMed: 8874177]
15. Korbling M, Champlin R. Peripheral blood progenitor cell transplantation: a replacement for marrow auto- or allografts. Stem Cells. 1996; 14:185–195. [PubMed: 8991538]
16. Champlin RE, Schmitz N, Horowitz MM, et al. Blood stem cells compared with bone marrrow as a source of hematopoietic cells for allogeneic transplantation. Blood. 2000; 95:3702–3709. [PubMed: 10845900]
17. Gratwohl A, Passweg J, Baldomero H, et al. Blood and marrow transplantation activity in Europe 1997 (Special Report). Bone Marrow Transplant. 1999; 24:231–245. [PubMed: 10456992]
18. Baldomero H, Gratwohl M, Gratwohl A, et al. The EBMT activity survey 2009: trends over the past 5 years. Bone Marrow Transplant. 2011; 46:485–501. [PubMed: 21358689]
19. Blaise D, Kuentz M, Fortanier C, et al. Randomized trial of bone marrow versus lenograstim-primed blood cell allogeneic transplantation in patients with early-stage leukemia: a report from the Société Française de Greffe de Moelle. J Clin Oncol. 2000; 18:537–571. [PubMed: 10653869]
20. Heldal D, Tjonnfjord GE, Brinch L, et al. A randomised study of allogeneic transplantation with stem cells from blood or bone marrow. Bone Marrow Transplant. 2000; 25:1129–1136. [PubMed: 10849524]
21. Vigorito AC, Azevedo WM, Marques JF, et al. A randomised, prospective comparison of allogeneic bone marrow and peripheral blood progenitor cell transplantation in the treatment of haematological malignancies. Bone Marrow Transplant. 1998; 22:1145–1151. [PubMed: 9894716]
22. Vigorito AC, Marques Junior JF, Aranha FJ, et al. A randomized, prospective comparison of allogeneic bone marrow and peripheral blood progenitor cell transplantation in the treatment of hematologic malignancies: an update. Haematologica. 2001; 86:665–666. [PubMed: 11418381]
23. Mahmoud HK, Fahmy OA, Kamel A, et al. Peripheral blood vs bone marrow as a source for allogeneic hematopoietic stem cell transplantation. Bone Marrow Transplant. 1999; 24:355–358. [PubMed: 10467322]

24 ••. Friedrichs B, Tichelli A, Bacigalupo A, et al. Long-term outcome and late effects in patients transplanted with mobilised blood or bone marrow: a randomised trial. Lancet Oncol. 2010; 11:331–338. [PubMed: 20117965] Ten year follow-up of EBMT study shows more GVHD but no adverse effects of disease-free or overall survival.

25. Schmitz N, Beksac M, Hasenclever D, et al. Transplantation of mobilized peripheral blood cells to HLA-identical siblings with standard-risk leukemia. Blood. 2002; 100:761–767. [PubMed: 12130483]

26. Powles R, Mehta J, Kulkarni S, et al. Allogeneic blood and bone-marrow stem-cell transplantation in haematological malignant diseases: a randomised trial. Lancet. 2000; 355:1231–1237. [PubMed: 10770306]

27. Couban S, Simpson DR, Barnett MJ, et al. A randomized multicenter comparison of bone marrow and peripheral blood in recipients of matched sibling allogeneic transplants for myeloid malignancies. Blood. 2002; 100:1525–1531. [PubMed: 12176866]

28. Bensinger WI, Martin PJ, Storer B, et al. Transplantation of bone marrow as compared with peripheral-blood cells from HLA-identical relatives in patients with hematologic cancers. N Engl J Med. 2001; 344:175–181. [PubMed: 11172139]

29 ••. Mielcarek M, Storer BE, Martin PJ, et al. Transplantation of peripheral blood cells as compared with bone marrow from HLA-identical related donors is associated with superior long-term outcomes. Blood. 2011 In Press. Ten year follow-up from the large US trial showing continued protection against relapse with PBSC, still no differences in overall survival but better outcomes in patient with more advanced disease.

30. Storb R, Deeg HJ, Whitehead J, et al. Marrow transplantation for leukemia and aplastic anemia: Two controlled trials of a combination of methotrexate and cyclosporine versus cyclosporine alone or methotrexate alone for prophylaxis of acute graft-versus-host disease. Transplant Proc. 1987; 19:2608–2613. [PubMed: 3547942]

31. Nash RA, Pepe MS, Storb R, et al. Acute graft-versus-host disease: analysis of risk factors after allogeneic marrow transplantation and prophylaxis with cyclosporine and methotrexate. Blood. 1992; 80:1838–1845. [PubMed: 1391947]

32. Bensinger W. Individual patient data meta-analysis of allogeneic peripheral blood stem cell transplant vs bone marrow transplant in the management of hematological malignancies: indirect assessment of the effect of day 11 methotrexate administration. Bone Marrow Transplant. 2006; 38:539–546. [PubMed: 16953207]

33. Stem Cell Trialists' Collaborative Group. Allogeneic peripheral blood stem-cell compared with bone marrow transplantation in the management of hematologic malignancies: an individual patient data meta-analysis of nine randomized trials. J Clin Oncol. 2005; 23:5074–5087. [PubMed: 16051954]

34 ••. Chang YJ, Weng CL, Sun LX, et al. Allogeneic bone marrow transplantation compared to peripheral blood stem cell transplantation for the treatment of hematologic malignancies: a meta-analysis based on time-to-event data from randomized controlled trials. Ann Hematol. 9999; prepublished online July 26, 2011; doi:10.1007/s00277-011-1299-8. A meta analysis using reported time-to-event results finding faster engraftment, lower rates of relapse, more chronic GVHD but similar leukemia free and overall survival.

35. Ringden O, Remberger M, Runde V, et al. Peripheral blood stem cell transplantation from unrelated donors: a comparison with marrow transplantation. Blood. 1999; 94:455–464. [PubMed: 10397713]

36 ••. Anasetti C, Logan B, Lee SJ, et al. Increased incidence of chronic graft-versus-host disease (GVHD) and no survival advantage with filgastrim-mobilized peripheral blood stem cells (PBSC) compared to bone marrow (BM) transplants from unrelated donors: results of Blood and Marrow Transplant Clinical Trials Network (BMT CTN) protocol 0201, a phase III prospective randomized trial. Blood. 2011 In Press. Early results of a large N. American trial comparing unrelated donor PBSC with BM showed more GVHD with PBSC and no differences in overall survival. Relatively short follow-up of this trial limits these conclusions.

37. Urbano-Ispizua A, Solano C, Brunet S, et al. Allogeneic transplantation of selected CD34+ cells from peripheral blood: experience of 62 cases using immunoadsorption or immunomagnetic

technique. Spanish Group of Allo-PBT. Bone Marrow Transplant. 1998; 22:519–525. [PubMed: 9758337]

38. Devine SM, Carter S, Soiffer RJ, et al. Low risk of chronic graft-versus-host disease and relapse associated with T cell-depleted peripheral blood stem cell transplantation for acute myelogenous leukemia in first remission: results of the Blood and Marrow Transplant Clinical Trials Network protocol 0303. Biol Blood Marrow Transplant. 2011; 17:1343–1351. [PubMed: 21320619]
39. Jakubowski AA, Small TN, Kernan NA, et al. T cell-depleted unrelated donor stem cell transplantation provides favorable disease-free survival for adults with hematologic malignancies. Biol Blood Marrow Transplant. 2011; 17:1335–1342. [PubMed: 21232623]
40. Cornelissen JJ, van der HB, Petersen EJ, et al. A randomized multicenter comparison of CD34(+)-selected progenitor cells from blood vs from bone marrow in recipients of HLA-identical allogeneic transplants for hematological malignancies. Exp Hematol. 2003; 31:855–864. [PubMed: 14550800]
41. Isola L, Scigliano E, Fruchtman S. Long-term follow-up after allogeneic granulocyte colony-stimulating factor-primed bone marrow transplantation. Biol Blood Marrow Transplant. 2000; 6:428–433. [PubMed: 10975511]
42. Serody JS, Sparks SD, Lin Y, et al. Comparison of granulocyte colony-stimulating factor (GCSF)-mobilized peripheral blood progenitor cells and G-CSF-stimulated bone marrow as a source of stem cells in HLA-matched sibling transplantation. Biol Blood Marrow Transplant. 2000; 6:434–440. [PubMed: 10975512]
43. Couban S, Messner HA, Andreou P, et al. Bone marrow mobilized with granulocyte colony-stimulating factor in related allogeneic transplant recipients: a study of 29 patients. Biol Blood Marrow Transplant. 2000; 6:422–427. [PubMed: 10975510]
44. Morton J, Hutchins C, Durrant S. Granulocyte-colony-stimulating factor (G-CSF)-primed allogeneic bone marrow: significantly less graft-versus-host disease and comparable engraftment to G-CSF-mobilized peripheral blood stem cells. Blood. 2001; 98:3186–3191. [PubMed: 11719353]
45 •. Chang YJ, Huang XJ. Use of G-CSF-stimulated marrow in allogeneic hematopoietic stem cell transplantation settings: a comprehensive review (Review). Clin Transplant. 2011; 25:13–23. [PubMed: 20626760] A review of studies comparing filgrastim stimulated BM with unstimulated BM or PBSC in both HLA identical and haploidentical studies. Faster engraftment with stimulated BM, apparently less GVHD but study did not address the comparative rates of relapse.
46. DiPersio JF, Micallef IN, Stiff PJ, et al. Phase III prospective randomized double-blind placebo-controlled trial of plerixafor plus granulocyte colony-stimulating factor compared with placebo plus granulocyte colony-stimulating factor for autologous stem-cell mobilization and transplantation for patients with non-Hodgkin's lymphoma. J Clin Oncol. 2009; 27:4767–4773. [PubMed: 19720922]
47. DiPersio JF, Stadtmauer EA, Nademanee A, et al. Plerixafor and G-CSF versus placebo and G-CSF to mobilize hematopoietic stem cells for autologous stem cell transplantation in patients with multiple myeloma. Blood. 2009; 113:5720–5726. [PubMed: 19363221]
48. Devine SM, Vij R, Rettig M, et al. Rapid mobilization of functional donor hematopoietic cells without G-CSF using AMD3100, an antagonist of the CXCR4/SDF-1 interaction. Blood. 2008; 112:990–998. [PubMed: 18426988]
49 ••. Pidala J, Anasetti C, Kharfan-Dabaja MA, et al. Decision analysis of peripheral blood versus bone marrow hematopoietic stem cells for allogeneic hematopoietic cell transplantation. Biol Blood Marrow Transplant. 2009; 15:1415–1421. [PubMed: 19822301] An interesting article integrating data on the risks and benefits of PBSC compared to BM to arrive at recommendations for treatment decisions

Key Points

- PBSC result in faster engraftment than unstimulated BM, and reduce rates of relapse, especially in patients with more advanced hematologic malignancies, but with more chronic GVHD.
- In randomized trials compared with BM, progression free survival is superior with PBSC but overall survival is superior in only 1 trial.
- Filgrastim stimulated BM may provide similar rates of engraftment to PBSC but without the greater risk of chronic GVHD and likely without the benefits of lower rates of relapse, due to fewer T cells.

Table 1

Randomized Comparisons of Allogeneic PBSC v. BM

	Total No. Pts	% Patients with Advanced Disease[4]	Stem Cell Source	Engraftment: Median Day to:		Acute GVHD %		Chronic GVHD %	DFS[3] %	Survival %
				Neutrophils5 00/ul	Platelets 20,000/ul	Grade II–IV	Grade III–IV			
[19]	101	5	PBSC BM	15* 21	13* 21	44 42	17 23	50* 28	58 62	61 61
[20]	61[1]	28	PBSC BM	17* 23	13* 21	25 10	NR	55 26	85 65	82 75
[21] [22]	56	32	PBSC BM	15* 18	12* 18	26 23	13 13	77* 61	60 50	56 48
[23]	30	NR[2]	PBSC BM	9* 25	10* 30	7 40	7 40	NR	NR	NR
[24] [25]	329	14	PBSC BM	12* 15	15* 20	52* 39*	28* 16	74* 53	42[5] 45	49[5] 57
[26]	39	46	PBSC BM	17* 23	11* 19	50 47	NR	44 40	NR	70 63
[27]	228[1]	27	PBSC BM	19* 22	16* 22	40 40	NR	71 55	NR	68* 60
[28] [29]	172	47	PBSC BM	16* 21	13* 19	64 57	15 12	48 38	65[5]* 45	58[5] 56

[1] 6 donor-recipients were 5/6 antigen matches

[2] NR = not reported

[3] DFS = disease -free survival

[4] Advanced disease = CML >CP, Acute leukemias >1st CR, Lymphomas >2nd CR, RAEB(T), multiple myeloma

[5] 10 year outcomes

* = statistically significant