Bone marrow and stem cell supported therapies

1189 POSTER

High-dose chemotherapy (HDC) and peripheral blood stem cells transplantation (PBSCT) for breast cancer: A joint EBMT-EORTC survey of their use in Europe

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Purpose: HDC with PBSCT is increasingly used as a treatment option for patients with breast cancer. This survey aims to provide an overview of the characteristics of the institutions providing this treatment and to describe their clinical practice and the techniques commonly used.

Methods: A questionnaire was sent to 200 European centers known to treat breast carcinoma with PBSCT supported HDC.

Results: 162 institutions (80%) responded, primarily from Italy, Spain, France, Germany and Belgium. 60% are university hospitals and 26% district general hospitals, the large majority public or private non-profit centers. 4/5 of them have several years experience with HDC programs (started prior to or in 1995) and treat more than 20 patients per year (all diseases included). For breast carcinoma, 90% use an age limit of 60–65 years. 94% are in favor of an accreditation system, and most prefer this to be institutionalized on a European level. More than 80% use chemotherapy plus hematopoietic growth factors (HGF) for mobilization of progenitors, and for two thirds the minimum number of CD34+ cells is 2×10^6/kg. There is a large variation with regard to the HDC regimens used: 22 different combinations (ignoring variations in the precise doses) are used in the adjuvant setting and 25 for metastatic disease. In both settings, cyclophosphamide, thiotepa and carboplatin is the most common combination, preferred by one third. HGF are given routinely by 80%, while 70% use primary antibiotic prophylaxis; 59% do both. Purging of the apheresis product to eliminate minimal residual disease is still controversial. 62% perform purging of CD34+ cells, but only 7% of these do so routinely. 16% of the centers operate outpatient HDC programs, varying with respect to the specific steps taken, and 40% believe that it will eventually become possible to perform all PBSCT procedures on an outpatient basis.

Conclusions: HDC for breast cancer is becoming widely diffused, but there are huge variations between the protocols used by different investigators. Almost all support an accreditation system, preferably supranational. HDC as an outpatient procedure is becoming a reality, and this may reduce the costs of the treatment.

1190 POSTER

Epoetin alfa administered prior to high-dose chemotherapy (HDCT) and autologous stem-cell rescue

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Purpose: HDCT is associated with severe anemia that often necessitates red blood cell (RBC) transfusions (TFs). Studies have shown that epoetin alfa therapy following HDCT generally improves anemia and decreases TF requirements in patients (pts) who received allogeneic bone marrow (BM) or peripheral blood stem-cell (PBSC) transplants. However, comparable results have not been obtained in the autologous transplant setting. The difference in outcome may be related to the greater sensitivity to erythropoietin of engrafted BM cells from healthy donors compared with those from already compromised pts. A study was therefore conducted to assess the effectiveness of epoetin alfa administered to autologous transplant pts before HDCT, when BM cells are still sensitive to erythropoietin.

Methods: Twenty-one patients with solid tumors or lymphomas who were to undergo HDCT and autologous PBSC rescue received 10,000 IU epoetin alfa SQ daily for 14 days prior to HDCT, and 10 μg/kg G-CSF SQ daily for 5 days prior to PBSC harvest. Pts also received supplementary oral iron. Controls were 9 matched, previously treated pts who had not received epoetin alfa.

Results: Mean hemoglobin (Hb) levels at the time of HDCT were 12.0 g/dL for pts treated with epoetin alfa vs 9.7 g/dL for the untreated controls. For epoetin alfa-treated and control pts combined (n = 30), the number of RBC units transfused was associated with Hb level at the time of HDCT. More pts with Hb levels of 11 g/dL or less (7/15 or 46.7%) required more than 2 units of transfused RBCs than pts with Hb levels greater than 11 g/dL (1/15 or 6.7%).

Conclusion: The preliminary findings of this study suggest that administration of epoetin alfa prior to HDCT may be an effective strategy for decreasing post-HDCT anemia and TF requirements in pts who undergo autologous BM or PBSC transplantation.

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Treatment of documented deep fungal infections in patients with sibling or unrelated stem cell transplantation: A study comparing safety and efficacy of conventional amphotericin B to liposomal amphotericin B (ambisome®)

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Deep fungal infections are still an important cause of morbidity and mortality in immune compromised patients. Patients undergoing allogeneic sibling or unrelated donor stem cell transplantation are at high risk if these patients experience acute and/or chronic graft versus host disease. Between Mai 1994 and December 1998 we treated 9 patients with documented fungal infections by either conventional amphotericin B or a liposomal formulation of amphotericin B (ambisome®). Fungal infections have been documented by CT scan, material obtained by bronchioalveolar lavage or by transbronchial biopsy. Patients on amphotericin B received 1–2 mg/kg/d, liposomal amphotericin B was also given in a dose of 2 mg/kg/d. Patients on antifungal therapy were assessed and followed by repeated CT scans. The response rate to amphotericin B is equal effective as for liposomal amphotericin B in this cohort of patients (4/5 patients responded to amphotericin B and 4/4 patients to liposomal amphotericin B). Toxicity was seen in all patients, however, with liposomal amphotericin B significantly lower ($p < 0.001$). We conclude that conventional and liposomal amphotericin B might be effective in the treatment of documented deep fungal infections in particular in patients undergoing stem cell transplantation experiencing acute and/or chronic graft versus host disease.

1192 POSTER

Hematological and immunological recovery after high dose chemotherapy (HDC) and reinfusion of cd34+ selected peripheral blood progenitor cells (PBPC) in patients with breast cancer (BC)

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Purpose: To evaluate the effect of autograft with CD34+ selected PBPC on hematological and immunological recovery post transplant, we initiated a HDC program for the treatment of poor prognosis BC.

Methods: 11 pts (6 metastatic and 5 > 10 axillary nodes positive) with BC are entered into the study. PBPC were collected after HD-FEC chemotherapy and G-CSF, 30 aphereses and 15 positive selection were performed. Six pts received tandem and 5 single autograft consisting in ICE (ifosfamide, carboplatin and VP16) protocol (4 tandem received also HD-melphalan) with CD34+ PBPC reinfusion. All pts received G-CSF post-HDC.

Results: A median of 3.3 x 10e6/kg CD34+ cells were reinfused. Median time to recovery WBC 1000/ul, PMN 500/ul and plts > 20000/ul was respectively 11.5, 11.5 and 14.5 days. A significant correlation between CD34+ cells reinfused and plts engraftment was observed ($p < 0.005$). In most of pts CD8 cytotoxic and NK cells early increased starting 4 weeks post-HDC and slowly decreased with CD4/CD8 ratio < 1 after 6 months. B cells recovered slowly starting from 8 weeks post-HDC. No significant extrahematologic toxicity and no viral infections were observed post-HDC. Two pts relapsed and died after 6 and 15 months, the other 9 pts are alive (7 CR and 2 PR) from 3 to 37 months post-transplant.

Conclusions: Our study shows that in BC pts single and tandem autograft with CD34+ selected PBPC did not affect the engraftment kinetics. The immunological recovery was slow and although no severe infections occurred, a longer follow-up is necessary for a correct evaluation.