The most common sarcoma for which HDT and AuSCT has been investigated is the Primitive Neuroectodermal Ectodermal Tumor (PNET) family of tumours which includes Ewing's sarcoma (ES). Indeed, the median age at diagnosis of PNET is14 years with 90% of patients being under the age of 20 years.[4] In adults with PNET, the 5-year overall survival (OS) following conventional-dose therapy is between 38–60% while the progression-free survival (PFS) is 27–59%. [5-7] Conversely, adult and paediatric patients who fail to achieve a complete response following surgery and conventional-dose chemotherapy are considered incurable and those with distant metastases have only 9% – 33% long term survival.[8] With respect to the role of HDT with AuSCT, no randomized studies have been performed and most published studies have included predominantly paediatric patients. [9-16]

Similarly, there is limited data on the role of HDT and AuSCT for osteosarcoma.[17] Again, studies to date have predominantly involved paediatric patients.[1,18,19]

The most common soft tissue sarcoma (STS) in children is rhabdomyosarcoma (RMS). Rare in adults, the disease free survival at 5 years of adult STS (different histologies) is approximately 10%. [20-25] In general, aggressive local therapy consisting of maximum tumor bulk reduction with surgery, with or without radiotherapy, is the cornerstone of initial management and patients with STS who are rendered disease free after surgery have a superior DFS than those who are inoperable.[26] However, many patients with STS are diagnosed with advanced-stage of the disease and/or complete surgical resection of the tumor is not feasible. Moreover, 40 to 60% of patients, even after a primarily curative local therapy, will develop metastases most frequently occurring within 2 to 3 years, and they will ultimately die of the disease.[27] Adult patients with RMS treated with conventional-dose therapy have an even worse prognosis than children.[28] The role of HDT and AuSCT for RMS remains unclear.[11,29]

Given the results with conventional-dose therapy, the role of HDT with AuSCT for sarcomas has largely been explored for patients with relapsed disease or those at high-risk of relapse. Patients with adult STS generally are poorly responsive to conventional-dose chemotherapy, with doxorubicin and ifosfamide being the only available agents showing response rates of greater than 20%. Combination regimens generally do not add efficacy, but do add toxicity.[21,24,27] For both agents, a dose-response relationship has been shown. Despite this theoretical rationale, the benefit of HDT is far from established in paediatric population, let alone for adult patients with sarcomas, with only a few studies reported and with small patient numbers.[9-11,17,18,27,30]

Of the studies reported to date, improved survival rates appear to be achieved for patients who achieve a complete remission (CR) prior to HDT or for those where total resection of tumor is feasible either before or after HDT. [10-12,26,30] Conversely, HDT with AuSCT appears not to improve outcome for PNET patients with metastatic disease at presentation.[13-16,31] Here we report our experience in treating *adult* patients with PNET, osteosarcoma and RMS.

Materials and methods

A retrospective review of adult patients who underwent HDT with AuSCT for sarcoma since 1992 at our institute was performed. Toxicity was assessed according to the World Health Organisation scale. Survival curves were generated according to the Kaplan-Meier method with OS and PFS calculated from the date of first stem cell infusion.

Results

A total of 17 patients underwent HDT and AuSCT and their characteristics are presented in Table 1 and included ES (9), PNET (1), osteosarcoma (5) and RMS (2). There were 14 males and 3 females with the median age at time of AuSCT of 24 years (range 20–41 years). HDT was administered as part of initial treatment (8), of which only one was in CR, five in PR, one with progressive disease (ProD) and one with stable disease (SD); in first relapse (7), of which four were in CR, one in PR and two with ProD; fourth relapse (1) who was in CR. Disease status immediately prior to HDT (following conventional-dose chemotherapy and/or surgery and/or radiotherapy) was CR (6), partial remission (PR) (6), stable disease (SD) (1) and ProD (4). The source of autologous stem cells was peripheral blood for 15 patients and bone marrow for two patients. Eleven patients underwent a planned tandem transplant.

HDT regimens were selected depending on prior therapy or involvement in specific clinical trials. Patients with osteosarcoma received carboplatin (700 mg/m^2) and etoposide (750 mg/m^2)[a]. Four patients subsequently received a second HDT and AuSCT with the same regimen (2) or melphalan (180 mg/m^2) and etoposide (60 mg/kg)[b] (2). Patients with PNET/ES received a single course of melphalan (180 mg/m^2)[c](2) or radionuclide Samarium^{153} EDTMP[d](1) or carboplatin (700 mg/m^2) and etoposide (750 mg/m^2)[e](1) or carboplatin (AUC = 21), thiotepa (900 mg/m^2) and etoposide (750 mg/m^2)[f] (1) or tandem cycles with ifosfamide (12 g/m^2), carboplatin (AUC = 20) and etoposide (60 mg/kg)[g] followed by and melphalan (180 mg/m^2) and etoposide (60 mg/kg)[b] (3);or tandem cycles with two cycles of carboplatin (700 mg/m^2) and etoposide (750 mg/m2)[a] (1); or tandem cycles with carboplatin (AUC = 21), thiotepa (900 mg/