153 Samarium-EDTMP in Myeloablative Dosage Followed by a Second Autotransplantation in Patients with Relapsed Multiple Myeloma

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Even though high-dose chemotherapy followed by autologous stem cell support has proven superior to conventional treatment,[1] relapse occurs in approximately 75% of patients within five years after autologous transplantation.[2] Initiating salvage treatment after high-dose therapy may be a reasonnable approach with survival time from relapse being more than two years as documented recently.[3] Reported treatment modalities comprise administration of conventional chemotherapy as well as a further high dose chemo(radio)therapy followed by (autologous or allogeneic) hematopoietic cell transplantation. In multiple myeloma, radiotherapy plays an important role both in transplantation settings[4,5] and palliation of lytic bone lesions. Recently, a study was published on the use of 166Ho-DOTMP combined with high-dose melphalan in the treatment of myeloma[6]. Application of bone-seeking radioisotopes has proven effective in palliative treatment of osteolytic lesions of both solid tumors and multiple myeloma.[7] Malignant plasma cells in myeloma predominantely are adjacent to areas of bone destruction. Thus, targeting osteolytic lesions by the means of locally delivered radiation may be a suitable approach as part of the conditioning regimen in high-dose therapy. When compared to 166Ho-DOTMP, 153 Samarium-EDTMP has some advantages: it is easier accessible in terms of production and logistics; has a longer physical half-life; and shows higher skeletal retention.[8]

We treated two patients with refractory multiple myeloma with myeloablative doses of 153 Samarium-EDTMP up to 60 GBq and high-dose melphalan. Patient 1 had relapsed from CR 39 months after one course of high-dose melphalan. Patient 2 had shown stable disease after single high-dose melphalan with symptomatic progression 9 months later. Both patients had been refractory to 2 conventional salvage regimens. They received 153 Samarium-EDTMP in myeloablative dosages with a bone marrow dose of 28 Gy (patient 1) and 35 Gy respectively. For treatment planning, test doses of 153 Samarium-EDTMP were administered 1 week before. Doses to bone marrow were derived from scan data as well as from the results of blood sampling and urine collection over 48 hours. Melphalan 140 mg/m2 was given on days –3 and –2. Both patients experienced myeloablation already prior to high-dose melphalan and received autologous stem cells 17 (patient 1) and 12 days after application of 153 Samarium-EDTMP, respectively. During aplasia, the first patient developed pulmonary infiltrates (possible invasive aspergillosis) and unfortunately died on day +8 (duration of neutropenia < 500/µL, 19 days) due to cerebral hemorrhage. The second patient experienced reversible renal failure and WHO °III liver toxicity. Renal failure was probably due to broad antimicrobial therapy including aminoglycosides and amphotericin B. No evidence of thrombotic microangiopathy was detected without signs of hemolysis, no fragmentation of erythrocytes nor elevated serum levels of lactic dehydrogenase (LDH). Following neutrophil engraftment on day +13, he recovered completely with normalization of renal function. The patient achieved partial remission that lasted for 6 months. Both patients did not suffer from hemorrhagic cystitis, a side effect that was seen in previous studies 6. Even though experience with application of 153 Samarium-EDTMP and high-dose melphalan is limited, we suppose it is an attractive treatment option in patients with relapsed multiple myeloma. The most important advantage of bone-seeking radiopharmaceutics when compared to external beam radiation is optimal lesion specific delivery 6, thus enabling the application of much higher skeletal doses. This, in combination with high-dose melphalan, may be an interesting conditioning regimen prior to autologous stem cell transplantation. Distribution kinetics are required for each given patient to avoid organ toxicities, most important of which are kidney, lung and liver toxicity.[8] Bone-seeking radionuclides are probably associated with more adverse effects in extensively pretreated patients especially with regard to renal toxicity. This is due to both myeloma-associated dysfunction and a possible contribution of radiation exposure of the kidney after administration of the radiopharmaceutic. In the series of patients treated with 166Ho-DOTMP, a significant incidence of HUS/TTP was observed.[6] Regarding haematological toxicity of 153 Samarium-EDTMP treatment, a prolonged period of aplasia has to be dealt with. This is one clear disadvantage of the regimen reported here when compared to 166Ho-DOTMP and requires close monitoring for and early treatment of infectious complications.

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