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Influence of stem cell mobilization after cyclophosphamide, thalidomide and dexamethasone regimen in patients with newly diagnosed multiple myeloma

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Backgrounds: CTD regimen has been known as an effective induction therapy in patients with newly diagnosed MM. But, there were inconsistent results for the autologous stem cell yield for transplantation. The aim of present study was to identify the influence of CTD therapy on outcome of peripheral blood stem cell (PBSC) collection. **Methods:** Forty-eight patients received 4 cycles of CTD therapy. Stem cells were mobilized with cyclophosphamide (3.0 g/m^2) and G-CSF (10 g/kg, daily) or G-CSF alone. Patients failing to collect $\leq 4.0\times10^6$ CD34+ cells/kg received a second mobilization courses. **Results:** The median age at diagnosis was 56 years (range, 39-69). Median duration from start of CTD therapy to first collection was 4.6 months (range, 3.3-8.7). Forty-four patients were mobilized with cyclophosphamide following with G-CSF and 4 patients with G-CSF alone. The median day of apheresis was 3 days (range, 2-7). The response rate for CTD regimen at mobilization was 10% (5/48) of CR, 25% (12/48) of VGPR and 63% (30/48) of PR. A median number of harvested CD34+ cells was 8.6×10^6 cells/kg. At the first mobilization, 83% (40/48) of patients had been reached the minimal PBSC collection target of $\geq 2.0\times10^6$ CD34+ cells/kg and 71% (34/48) of patients achieved the collection $\geq$ 4.0 x 10^6 CD34+ cells/kg. At the end of second mobilization, 90%(43/48) of patients had yields of at least $\geq 2.0\times10^6$ CD34+ cells/kg and 77% (37/48) of patients had yields of $\geq 4.0\times10^6$ CD34+ cells/kg. During mobilization period, three patients were developed grade 3/4 non-hematologic adverse events. **Conclusion:** CTD regimen is an effective induction therapy in patients with newly diagnosed MM showing high response rate and acceptable rate of autologuos stem cell yield without any detrimental effect for the following stem cell collection.

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Cyclophosphamide-containing regimen (TCD) is superior to melphalan-containing regimen (MPT) in elderly MM patients with renal impairment

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Background: Renal impairment (RI) is frequent complication in patients with multiple myeloma (MM). Severe RI is important prognostic factor for survival. Melphalan clearance is renal function dependent whereas cyclophosphamide is renal function independent. Therefore, it is important theme which combination regimen should be selected between melphalan-combining regimen (MPT) or cyclophosphamide-combining regimen (TCD) in elderly MM patients with RI **Patients and methods:** Between 2005 and 2009, 139 newly diagnosed MM patients with RI were included comparing MPT with TCD therapy as initial treatment. Sixty-two patients were given MPT regimen and 77 patients were given TCD regimen. The doses of Melphalan and cyclophosphamide were not adjusted. **Results:** Baseline characteristics were similar between MPT and TCD group. For determine adequate cut-off level, analysis of different cut-off levels between the 25% and 75% quartile using log-rank test determined that glomerular filtration rate (GFR), 45ml/min/1.73m2 as the cut-off point yielded the highest difference in event-free survival (EFS) and overall survival (OS). MPT subgroup with low GFR (GFR<45ml/min/1.73m2) had poorer response rates than any other subgroups. The incidence of neutropenia was higher in MPT subgroup with low GFR than others (p=0.027). Infection with febrile neutropenia was higher in MTP subgroup with low GFR. Furthermore, mortality due to the infection was higher in MPT subgroup with low GFR than others (p=0.002, Figure 2). Event-free survival (EFS) was lower in MPT subgroup with low GFR than any other groups (p<0.001). Moreover, the survival in TCD subgroup with GFR $\geq$ 45ml/min/1.73m2 was higher than TCD group with low GFR. Overall survival was lower in MPT subgroup with low GFR than others (p=0.001). **Conclusion:** In newly diagnosed elderly MM patients with RI, MPT regimen would be more toxic and less effective to RI. In contrast, TCD regimen would be effective and tolerable treatment option due to combination of cyclophosphamide independent to renal function and dexamethasone effective for RI