Supplementary Information 1

Stem cell mobilization and peripheral blood stem cell collection

Peripheral blood stem cell (PBSC) collection was performed following cytotoxic chemotherapy either with ifosfamide/epirubicin/etoposide (IEV), cyclophosphamide/adriamycin (CA), or cyclophosphamide alone (C) followed by granulocyte colony-stimulating factor (G-CSF; 5 µg/kg/d subcutaneously, s.c.). In case chemotherapy was not indicated for stem cell harvest, steady-state mobilization was performed using stimulation with G-CSF alone (5 µg/kg/d for 5 days s.c.).

Melphalan HDCT and ASCT

For HDCT, patients obtained single agent melphalan 200 mg/m^2 fractionated on day -2 and -1, or reduced dosage of 140 mg/m^2 on day -1 before stem cell reinfusion, the latter preferentially for patients of >65 years of age with decreased renal function and elevated serum creatinine (including patients under dialysis). All patients received standard supportive care as well as prophylactic antibiotics during chemotherapy-induced neutropenia. G-CSF was administered daily starting 24 hours after ASCT (day +1) until neutrophil engraftment (defined as neutrophil counts (ANC) ≥500/µl). Platelet engraftment was considered from a platelet count of ≥50x10^9/l without transfusion support.

Supplementary Information 2

Comparison of single versus tandem melphalan HDCT/ASCT

In total, 286 patients received single ASCT (170 males; 116 females; male: female ratio 1.5). Tandem HDCT-ASCT was applied to 34 patients (21 males; 13 females; male: female ratio 1.6). Median interval between the first and second part of tandem ASCT was 3.3 months (range 1.8-9.0 months). A proportion of 75% of the patients

received the second part of the tandem ASCT within 4.41 months after the first part of tandem ASCT.

In the single ASCT group median OS was 68 months (95% CI 58.3-77.7), and median PFS 31 months (95% CI 25.7-36.4), whereas in the tandem ASCT group median OS was 43 months (95% CI 23.0-63.0) and median PFS 41 months (95% CI 28.6-53.4).

Complications

Types and rates of complications noted in the single and tandem group are presented in Suppl. Table 1. Frequent complications were: mucositis WHO grade III-IV, bacteremia, and febrile neutropenia. The rate of TRD was with 3% comparable after single and tandem ASCT, respectively (P = 0.603; Suppl. Table 1). There were no remarkable differences in time to neutrophil regeneration between the single and tandem group (P = 0.903; Suppl. Table 1). Platelet engraftment, though, has not been reached after tandem ASCT in >80% of the patients (N=26) in comparison to single ASCT with around 53% (N=118).

Haematological response

Haematological response rates are depicted in Suppl. Table 2. At day +100 post-ASCT, 51% of the patients in the single ASCT cohort (N=115) responded with VGPR or better, whereas in the tandem ASCT cohort, it was 45% (N=15). In the single ASCT group, 39% (N=88) of the patients reached PR; in the tandem ASCT cohort, it was 46%. (N=15; Suppl. Table 2).