

Late treatment mortality and secondary cancers after autologous stem cell transplant for relapsed or refractory Hodgkin lymphoma (HL)

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Background: Late treatment-related mortality and second cancers have an important influence on the long-term outcome of patients (pts) with HL. The incidence of treatment failure and causes of death were evaluated in pts with advanced HL receiving high-dose therapy and ASCT, to understand the impact of late events on overall survival (OS).

Methods: From Dec 1986 to Nov 2005, 323 pts with relapsed/refractory HL after primary chemotherapy (plus radiation [RT]: 32%) received salvage chemotherapy to best response, followed by etoposide 60 mg/kg day -4 and melphalan 160-180 mg/m² day -3 supported by autologous bone marrow (46%), mobilized peripheral blood stem cells (49%) or both (5%) on day 0; 24% received involved field RT post-ASCT. Risk of treatment failure and second cancer was estimated using competing risks methods.

Results: Patient Characteristics: male: 61%; median age 33 years (range 16-67). Number of salvage regimens pre-ASCT: 1: 72%; 2: 25%. Disease status post-salvage chemotherapy: CR 28%, PR 66%. After a median follow-up of 4.7 years post-ASCT (range 1-17), 174 pts (54%) have experienced treatment failure (relapse or treatment related death) and 154 pts (48%) have died, 75% following relapse and 20% from toxicity without relapse. Of the 30 deaths without relapse, 30% occurred >5 years post-ASCT. Failure free survival at 3 and 10 years is 50% (95% CI, 44-55%) and 40% (33-46), and overall survival is 68% (63-73) and 39% (33-46), respectively. There have been 29 second cancers (17 AML/MDS, 12 solid tumors) in pts alive without relapsed HL. The probability of a second cancer is 4.9% (2.8-7.8) at 3 years and 12% (8-17%) at 10 years. The hazard rates for second malignancy, leukemia and solid tumors for each 10-year age increment are 1.9 (p=0.0001), 1.9 (0.001) and 1.8 (0.03), respectively. Only 4 pts have relapsed beyond 5 years post-ASCT but the cumulative incidence of treatment-related death (from toxicity or second cancers) continues to increase from 9% (6-13) at 3 years to 15% (11-20) 10 yrs post-ASCT.

Conclusions: In this single-institution series of uniformly treated patients with relapsed/refractory HL, late relapse of disease is uncommon, but late toxicities have a significant and ongoing impact on failure-free survival.