Long-term outcomes and renal responses following autologous hematopoietic stem cell transplantation for light chain deposition disease: a retrospective study on behalf of the Chronic Malignancies Working Party of the European Society for Blood and Marrow Transplantation

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Supplemental file

Methods

Study design and patient selection

This was a retrospective, multicenter, registry-based analysis approved by the Chronic Malignancies Working Party of the EBMT. The EBMT is a non-profit, scientific society representing more than 600 transplant centres mainly in Europe. Data are entered, managed, and maintained in a central database with internet access. Each EBMT centre is represented in this database. All centers commit to obtain informed consent according to the local regulations applicable at the time in order to report pseudonymized data to the EBMT. For patients with a verified LCDD diagnosis additional data on treatment before ASCT, disease involvement, renal related variables (serum creatinine, eGFR, serum albumin, proteinuria) at LCDD diagnosis, at ASCT and at 3, 6 and 12 months post-ASCT, hemodialysis treatment before and after ASCT were requested through a data request questionnaire.

LCDD hematological response criteria

Disease response to treatment was defined according to the new criteria for response to treatment in immunoglobulin light chain amyloidosis based on free light chain measurement as progressive disease (PD), stable disease (SD), partial response (PR), very good partial response (VGPR) or complete response (CR). If patients had non measurable FLC, hematological response could not be assessed. Hematological response was assessed at the time of transplant, on day +100, month +6, and month +12 post-transplant.

Evaluation of renal fonction

Based on the criteria proposed by the International Myeloma Working group, renal response was defined as follows: (a) Complete response (CRenal): baseline eGFR ≤50 ml/min/1.73m^2 and improvement to ≥60 ml/min/1.73m^2 (b) Partial response (PRenal): baseline eGFR <15

ml/min/1.73m^2 and improvement to 30–59 ml/min/1.73m^2 (c) Minimal response (MRenal): baseline eGFR <15ml/min/1.73m^2 and improvement to 15–29 ml/min/1.73m^2, or baseline 15–29 ml/min/1.73m^2 and improvement to 30–59 ml/min/1.73m^2, (d) progression if eGFR was lower than baseline eGFR (>25% decrease in eGFR), no response for patients who were on dialysis and remained on dialysis and (e) not assessable (eGFR >50 ml/mn). Renal function was assessed at the time of transplant, on day +100, month +6, and month +12 post-transplant.

Statistical analysis

Groups considered were divided according to sex, Karnofsky performance score (KPS, ≤80, >80), age at ASCT (<60, ≥60 years), RRT status at ASCT, disease stage at ASCT (VGPR or better, other) and calendar year of ASCT (<2011, ≥2011). Longitudinal eGFR (measured at ASCT, and at the date nearest to 3, 6, and 12 months post-ASCT) was modeled using linear mixed effect models with a random intercept and slope for each patient. Measurements obtained after renal transplantation were not used and eGFR was assumed to change in a linear manner over time after ASCT. We also excluded implausible high eGFR values in patients on RRT as these measurements were thought to have been obtained just after the patient had been on the dialysis procedure. Apart from time, the model included RRT status at ASCT and an interaction between RRT status and time after ASCT as fixed covariates.

A multistate model was used to give an overview of the probability of events or states (haematological relapse, renal transplantation and death) after ASCT. We used a non-parametric time inhomogenous Markov model stratified for RRT status at ASCT meaning that the hazard of transition to a next state may vary over time[17]. All patients started in an event-free state which could be followed by intermediate states ‘hematological relapse’, ’renal transplantation’, ‘hematological relapse after renal transplantation’, ’renal transplantation after hematological relapse’, and finally an absorbing state ‘death’. All p-values shown were from

two-sided tests and the reported confidence intervals (CI) refer to 95% boundaries, a p-value <0.05 was regarded as statistically significant.

Supplemental Figure 1: Probability of **a)** overall survival (OS), **b)** progression-free survival (PFS) according to RRT status at ASCT. Numbers below the graphs show the number at risk. Shaded areas show the 95% confidence intervals.