SUPPLEMENTARY APPENDIX

Efficacy of bortezomib, cyclophosphamide and dexamethasone in treatment-naïve patients with high-risk cardiac AL amyloidosis (Mayo Clinic stage III)

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Supplementary Appendix

Population: The 4 central referral centers were: the Tufts Medical Center, Boston, United States of America, the National Amyloidosis Center, University College London Medical School, United Kingdom, the Medical College of Wisconsin, Milwaukee, United States of America and 7 centers of the French network for amyloidosis. Patients with underlying IgM monoclonal gammopathy were excluded.

Evaluation:

Complete patient characteristics are presented in Table 1. The data were analyzed retrospectively for all patients from each site. Hematologic response [17] required assessment of clonal markers in response to therapy as defined by the serum and urine protein electrophoresis as well as the serum free light chain assay. Best response to therapy was examined.

For the primary analysis, patients without immunofixation data to confirm CR but who normalized their sFLC levels and ratio were recorded as VGPR consistent with current criteria. Measurement of serum free light chains, Nterminal pro-brain natriuretic peptide (NT-proBNP) and/or BNP, and troponin T, troponin I or high sensitivity troponin (hs-cTnT); serum biochemistry; 24-hour urine protein were recorded in all patients before the initiation of treatment. Cardiac responses were analysed following consensus criteria (adapted for BNP measurements) published in 2012[15], using only biomarkers, NT-proBNP response if >30% and > 300 ng/L decrease if baseline NT-proBNP ≥ 650 ng/L and for BNP response if >30% and > 80 ng/L decrease if baseline BNP ≥ 200 ng/L.

Statistics: In the univariate analysis the following parameters were investigated: age, serum NT-proBNP or BNP values, estimated glomerular filtration rate (eGFR), initial dFLC. The most predictive factors were identified using univariate logistic regression analysis. For linear variables the best cut-off predicting outcome was identified using ROCs. Multivariate analyses were performed using a Cox proportional hazards model on all variables found to be significant at 0.1. The parameters were tested with respect to the risk of early death (< 3 months).