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POSTER ABSTRACTS

654.MGUS, AMYLOIDOSIS AND OTHER NON-MYELOMA PLASMA CELL DYSCRASIAS: CLINICAL AND EPIDEMIOLOGICAL

Orthotopic Heart Transplantation Followed By Autologous Stem Cell Transplantation in Patients with Cardiac AL Amyloidosis: Results from a Single Centre Prospective Study

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Background: Patients with advanced cardiac AL amyloidosis have a dismal prognosis, with an overall survival (OS) of only 5 months for Stage IIIb patients (Palladini et al, 2023). Induction chemotherapy followed by high dose chemotherapy and autologous stem cell transplantation (HDT and ASCT) has been widely used as treatment for AL amyloidosis. However, patients with advanced cardiac AL amyloidosis are often not suitable for HDT and ASCT due to high transplant related mortality (TRM). Orthotopic cardiac transplantation (OHT) following induction treatment may improve patient fitness and thus allow HDT and ASCT to deepen and prolong responses. We present our single centre, prospective study of patients with Stage IIIa and Stage IIIb cardiac AL amyloidosis who received OHT followed by sequential HDT and ASCT.
Aims: The primary outcomes were 3 year OS and progression-free survival (PFS). Efficacy and safety were assessed as secondary outcomes. Efficacy was evaluated by light chain and cardiac response after ASCT. Safety was assessed by rate of TRM, cardiac rejection, opportunistic infections, and cytopenia related complications.
Methods: During 2015 to 2021, patients with Stage IIIa or Stage IIIb AL amyloidosis aged under 65 years underwent OHT followed by HDT and ASCT. Patients with multiple myeloma were excluded. At approximately 6 months following OHT, patients underwent stem cell mobilization with granulocyte colony-stimulating factor alone followed by peripheral blood apheresis stem cell collection. Mycophenolate immunosuppression was temporarily withheld during stem cell mobilization and collection. Patients then received a high dose melphalan ASCT followed by 3-6 monthly assessments.
Results: Nine patients (median age of 53 years, range 47-60 years) completed both OHT and ASCT. Seven other patients were screened but did not proceed with OHT. The cohort included both stage IIIa (55%) and stage IIIb (44%) patients. Most patients received cyclophosphamide-bortezomib-dexamethasone induction therapy (89%) and one patient received lenalidomide-bortezomib-dexamethasone. The median time from diagnosis of AL amyloidosis to OHT was 11 months (range 5-57 months) and median time from OHT to ASCT was 7 months (range 5-8 months). 3 year OS was 83% and PFS was 56% (Figure 1). At a median follow up of 37 months (range 17-69 months), 89% of patients remain alive. One patient with Stage IIIa disease who underwent HDT and ASCT with progressive disease (PD) died 28 months following ASCT due to PD.
Subgroup analysis demonstrated 3 year OS in Stage IIIa patients of 75% compared to 100% in Stage IIIb (p=0.48). 3 year PFS was 53% in Stage IIIa patients and 66% in Stage IIIb (p=0.8). Patients in complete remission (CR) prior to ASCT had an improved 3 year OS of 100% compared to 66% for those in partial remission (PR) or with PD (p=0.32). 3 year PFS was significantly improved at 100% when ASCT occurred in CR compared to 0% in those in PR or with PD (p=0.01) (Figure 2).

All patients either maintained a CR or achieved an improved haematological response following HDT and ASCT, with 89% of patients in CR at 6 months post ASCT. At the median follow up of 37 months, 78% were in CR and 22% had PD. At last follow up, there has been no documented amyloid recurrence in a cardiac allograft.
There was no TRM noted in this study. All patients had cardiac rejection with 66% developing Grade 3A/2R rejection requiring methylprednisone. The most common infective complication was CMV reactivation (44%). Other infective complications included cryptococcal infection (11%), aspergillus and MAC infection (11%) and HSV reactivation requiring hospitalization (11%). During admission for HDT and ASCT, 89% had febrile neutropenia and there were no bleeding complications.
Conclusions: We have demonstrated, in a prospective design, that sequential OHT/ASCT following induction therapy is safe in patients with Stage IIIa/b cardiac AL amyloidosis without an increase in TRM. This approach was associated with excellent survival outcomes compared with historical cohorts. Given the deep and prolonged responses seen with daratumumab based induction, a risk adapted strategy may be more appropriate moving forward, with only those not achieving a haematological CR undergoing consolidation ASCT following OHT.

Disclosures McCaughan: *Janssen:* Honoraria; *BMS:* Honoraria.

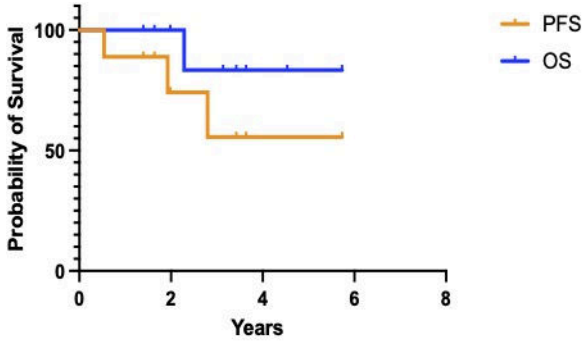

Figure 1: Survival following ASCT

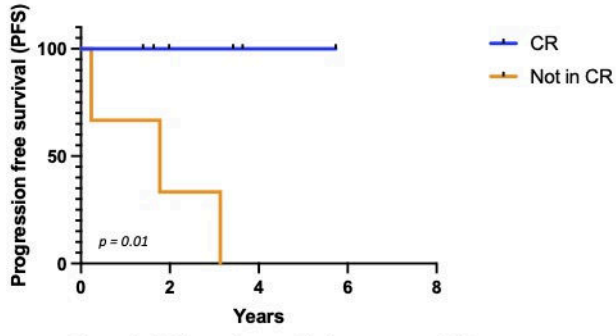

Figure 2: PFS based on remission status at ASCT

Figure 1

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