ELSEVIER

Blood 142 (2023) 537–538

The 65th ASH Annual Meeting Abstracts

ORAL ABSTRACTS

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

Limited Utility of Mayo 2012 Cardiac Staging System for Risk Stratification of Patients with Advanced Cardiac AL Amyloidosis - Analysis of a Uniformly Treated Cohort of 1275 Patients

Jahanzaib Khwaja[1], Sriram Ravichandran[1], Joshua Bomsztyk[2], Oliver Charles Cohen, MBBS, BSc, FRCPath[2], Darren Foard[2], Ana Martinez - Naharro[2], Lucia Venneri[2], Marianna Fontana[2], Philip N Hawkins[2], Julian Gillmore[2], Helen J Lachmann[2], Shameem Mahmood[2], Carol Whelan[2], Ashutosh D. Wechalekar, MBBS,DM,FRCP,FRCPath[2,3]

[1] University College London Hospitals, London, United Kingdom
[2] Royal Free London Hospital, National Amyloid Centre, London, United Kingdom
[3] Clinical Haematology, Cancer Division, University College London Hospital, London, United Kingdom

Introduction:
Systemic light chain (AL) amyloidosis is a rare incurable disorder caused by extracellular deposition of misfolded light chain protein fibrils causing organ dysfunction. Cardiac involvement is present in approximately two thirds of cases at diagnosis. Survival depends largely on the severity of cardiac involvement as well as haematological response to treatment. Two validated cardiac staging systems, Mayo 2012 (stage I-IV) (Kumar, Dispenzieri et al. 2012) and European modification of the standard Mayo staging system 2004 (stage I-IIIb) (Wechalekar, Schonland et al. 2013, Palladini, Sachchithanantham et al. 2015), stratify patients according to different thresholds of biomarkers markers of disease involvement (NTproBNP, troponin T and, additionally for Mayo 2012, difference between involved and uninvolved free light chain [dFLC]). Patients included in these original models were not treated with a uniform induction protocol and treated with regimens such as oral melphalan dexamethasone, which are now rarely used. There is a need to re-assess the predictive performance and robustness of these staging systems with current treatment approaches.
We report here the comparison of cardiac staging in a large cohort of patients with AL amyloidosis uniformly treated bortezomib-containing regimens in the first-line setting from the ALChemy study.
Methods:
Patients enrolled in a prospective observational study at the United Kingdom National Amyloidosis Centre from 2010-2019 treated with bortezomib-based regimens were analysed. Outcomes were stratified according to Mayo 2012 and the European modified Mayo classification. Written consent was obtained from all patients in accordance with the Declaration of Helsinki.
Results:
1275 patients (755 male, 520 female) were included. Median age at presentation was 67 years (range 29-89), with a median of two involved organs (range 1-5); 812 (64%) had cardiac involvement, 892 (70%) had renal and 154 (12%) liver involvement. All patients were treated with first-line bortezomib-based therapy: bortezomib-cyclophosphamide-dexamethasone in 1190 [93%]; bortezomib-dexamethasone in 48 [4%]; bortezomib-thalidomide-dexamethasone in 21 [2%] and 16 others. None were treated with a daratumumab based combination or autologous stem cell transplant (ASCT) upfront; 95 (7%) had ASCT at a subsequent line of therapy. Patients were classified by Mayo 2012 staging as: stage I, II, III, IV in 199 (16%), 329 (26%), 413 (32%) and 334 (26%) cases, respectively and by European modified staging as: stages I, II, IIIa and IIIb in 219 (17%), 436 (34%), 424 (33%) and 196 (15%), respectively.
The median follow-up was 47 months (95% CI 45-50), median overall survival (OS) was 59 months (95% CI 51-67) and 3-year OS was 59% (95% CI 56-61). Whilst both Mayo 2012 and European modification models were predictive of overall survival, the European modification discernibly discriminated those with the poorest and best outcomes. Median OS by European staging for stage I, II, IIIa, IIIb was: not reached (NR), 76, 34 and 8 months respectively, compared with Mayo 2012 stage I, II, III, IV: NR, 74, 36, and 26 months respectively. European stage II, IIIa, IIIb had a hazard ratio (HR) for death of: 2.42 (95% CI 1.69-3.49), 4.65 (95% CI 3.27-6.61) and 9.18 (95% CI 6.36-13.25), respectively. Mayo stage II, III, IV had a HR of: 2.54 (95% CI 1.72-3.76), 4.66 (95% CI 3.21-6.76) and 5.99 (95% CI 4.12-8.71), respectively.
Conclusion:

Advanced stage cardiac involvement remains a prognostic predictor of adverse outcomes. In a cohort of bortezomib-treated patients, the European modification has a stronger predictive value for poorer outcome. The Mayo 2012 staging, utilising additional dFLC, did not discriminate the most advanced disease as well suggesting that treatment markedly impacts the predictive capability of cardiac staging systems. Daratumumab-based treatments may have an even greater impact in ameliorating the adverse prognostic significance of high presenting dFLC. Until cardiac staging is revalidated for the modern treatment era of AL amyloidosis, our data should be taken into consideration when using cardiac staging systems in the clinic as well as for clinical trial design.

Disclosures Wechalekar: *Takeda:* Other: Travel support; *GSK:* Honoraria; *Janssen:* Honoraria; *Attralus:* Honoraria; *Alexion:* Honoraria; *Alexion, Attralus, Janssen, Prothena.:* Consultancy.

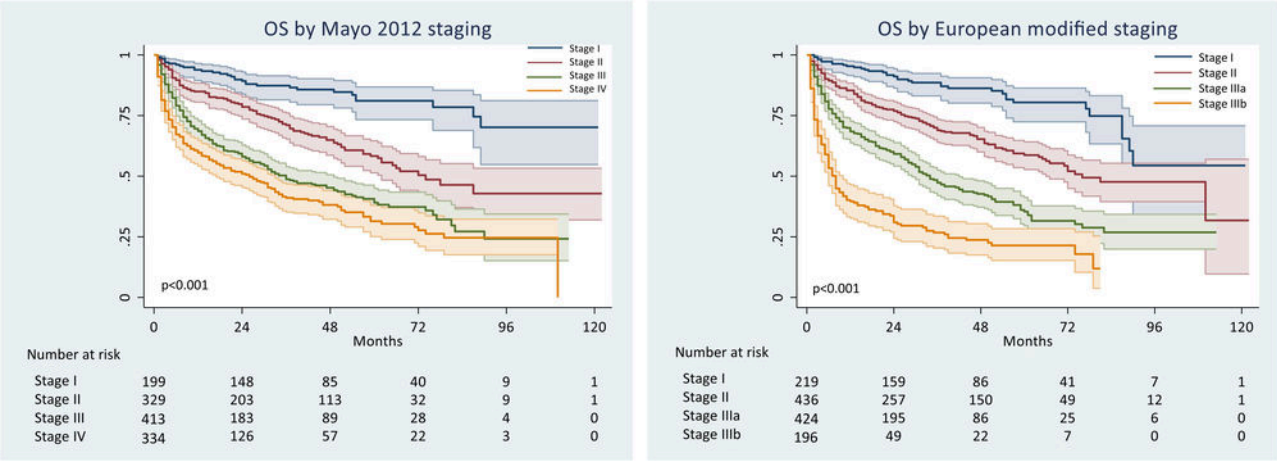

Figure 1

https://doi.org/10.1182/blood-2023-178243