POPULATION-BASED STUDY OF PATIENTS WITH MANTLE CELL LYMPHOMA; ERA-BY-ERA IMPROVEMENT IN SURVIVAL MEDIATED BY FIRST-LINE RITUXIMAB AND AUTOLOGOUS STEM CELL TRANSPLANTATION.

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Introduction:

Mantle cell lymphoma is associated with a poor prognosis, however recent reports suggest a median overall survival (OS) for patients enrolled in clinical studies to be approximately five years; an improvement on the 2.5 year OS from the mid 1990s. This has been attributed to the improvement in treatment over the years. This study was done to assess the validity of these claims. In addition, an assessment of the impact on survival of novel agents, namely Rituximab and autologous transplantation was done.

Objectives:

The primary objective was to assess whether era-by-era survival for MCL patients has improved over the years. The secondary aim was to analyse if different treatment regimes impacted on OS.

Methods:

Patients with a mantle cell lymphoma diagnosis made between 1994 and 2015 in Nottingham University Hospitals Trust were identified using a SNOMED search of histological samples.

Baseline clinical parameters were captured for each patient, and the OS and progression free survival for first to fourth line treatments were calculated. The MIPI score was calculated for each patient.

Using this data Cox regression was performed for univariate and multivariate analysis of the baseline clinical readings.

Thereafter Cox regression analysis was used to look at the impact of the use of Rituximab first line, autologous transplantation in first remission as well as the impact of era of diagnosis.

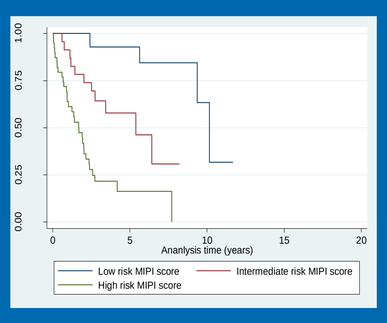

Figure 1: Overall survival by MIPI score

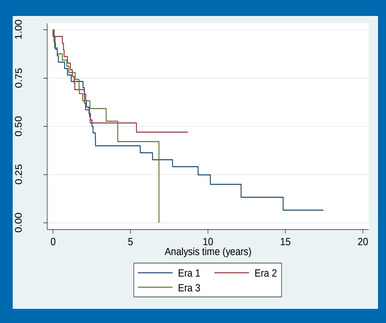

Figure 2: Overall survival by Rituximab

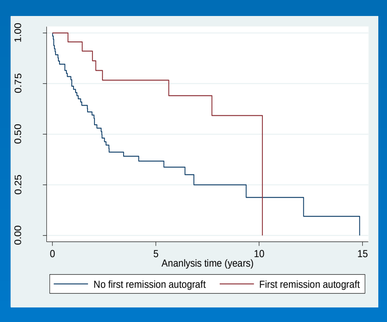

Figure 3: Overall survival by autograft

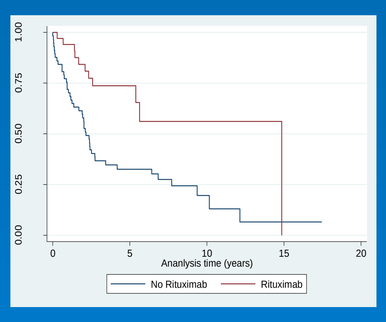

Figure 4: Overall survival by era

Results:

104 patients, 71 male; 33 female, median age 73 years were identified. Median 5-year OS was 46.8%. By univariate analysis, MIPI predicted 5-year OS (low risk 81.3%, medium risk 70.6%, high risk 21.9%)(p=<0.0001). When OS was analysed by 5- or 10-year era of diagnosis, there was no significant improvement over time, although 5-year OS improved in patients <70 years from 54.5% in 1996-2005 to 85.9% in 2006-2015 (p=0.0373). First-line rituximab (1996-2005 n=4, and 2006-2015 n=31), improved outcomes; 5-year OS of 32.1% and 81.7% +/- rituximab, respectively (p=0.0004). ASCT in first remission (1996-2005 n=12, and 2006-2015 n=29) also improved outcomes; 5-year OS of 32.6% and 79.7% +/- first-line ASCT, respectively (p=<0.0001). Patients who received neither rituximab nor ASCT first line had a median 5-year OS of 21% (neither), compared to 76.2% first-line rituximab without ASCT, 69.2% ASCT without rituximab, and 88.1% (rituximab and ASCT first-line) (p=<0.0001).

Multivariate analysis was performed using the variables age, era of diagnosis, MIPI score, first remission autograft and rituximab. Only the MIPI score and first line rituximab independently predicted OS, P=0.01 and <0.05 respectively. Conversely, first remission autograft had no impact on OS, with a Hazard ratio of 0.99 and p-value of 0.99, and era of diagnosis also failed to predict OS.

Variable		Hazard ratio	P-value	95% confidence interval	
Age group (years)	45-59	Comparison group			
	60-69	0.81	0.76	0.22	2.97
	70-79	1.94	0.36	0.47	8.04
	80-92	1.97	0.38	0.43	8.95
Era	1994-2005	Comparison group			
	2006-2010	0.81	0.58	0.39	1.67
	2011-2015	0.60	0.21	0.27	1.33
First remission autograft	No	Comparison group			
	Yes	0.99	0.99	0.37	2.70
MIPI score	<5.7	Comparison group			
	5.7-6.2	2.50	0.09	0.83	14.28
	≥6.2	5.51	0.01	1.65	32.08
Rituximab	No	Comparison group			
	Yes	0.44	0.05	0.20	0.99

Table one: Results of multivariate analysis adjusting for age, era of diagnosis, autograft at first remission, MIPI and first line Rituximab.

Conclusion:

In conclusion, for this unselected population-based cohort, by univariate analysis, significant improvements in OS were observed for patients <70 years and first-line treatment incorporating rituximab and/or ASCT significantly improved OS.

In the multivariate analysis, only MIPI and first line rituximab independently predicted OS, and surprisingly no association was found between first line autologous transplantation and OS. This data supports proposed studies examining the omission of first line autologous transplantation in MCL.

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