Mannheimer Onkologie Praxis

Treatment and outcome of patients with Waldenström`s Macroglobulinemia (WM) in private oncology practices and a university hospital

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Background

- WM is a rare type of malignant B-cell lymphoma, defined as a lymphoplasmocytic lymphoma in bone marrow and a monoclonal gammopathy of immunoglobulin-M (IgM) type.
- Due to the paucity of large clinical trials, a standard treatment regimen is still controversial. The purpose of this study was to compare the standard treatment and outcome of patients (pts) treated in private oncology practices (PP) and a university hospital (UH) in a region of southern Germany (Nordbaden).

Methods

- We retrospectively reviewed the charts of all pts with WM of the last 2 decades until 31.12.2010 of 4 PP in Mannheim, Heidelberg, Karlsruhe and Speyer and the department of hematology/oncology/rheumatology of the University of Heidelberg.

Results

Patient characteristics

	all patients	Private practice	University hospital	
Number of patients (n)	170	74	96	
Practice Mannheim		39		
Practice Karlsruhe		21		
Practice Heidelberg		8		
Practice Speyer		6		
Gender				
male (%)	105 (61.8%)	52.7%	68%	
female	65 (38.2%)			
Age at diagnosis				
Median, years	63.3	65.3	62.4	p=0.01
Range, years	29.1-88.5	35.1-88.5	29.1-81.4	
CIRS-Score				
available in n Pts.		35	42	
median (range)	4.0 (0-14)	4.0 (0-13)	3.5 (0-14)	p=0.8

Symptoms at diagnosis

Splenomegaly	36 (21.2%)	29.2%	16.7%	P=0.1
Lymph node enlargement	27 (15.9%)	10.8%	18.6%	P=0.1
Previous MGUS IgM	22 (12.9%)		no data	
Polyneurapathy	19 (11.2%)	12.5%	9.8%	P=0.7
Raynaud	2 (1.2)	1 (1.5%)	1 (1%)	p=0.1
Hyperviscosity syndrome	27 (15.9%)	2 (3%)	26 (25.5%)	p<0.001
Visus impairment	9 (5.3%)	8 (12.3%)	1 (1%)	P=0.005
Bleeding	18 (10.6%)	8 (12.1%)	10 (9.8%)	P=0.9
Amyloidosis	6 (3.5%)	2 (3.1%)	4 (3.9%)	P=0.6

Activity parameters at diagnosis

IgM (mg/dl)				
mean (SD)	2332 (2078)	2261 (1921)	2422 (2274)	p=0.67
Hb (g/dl)				
mean (SD)	11.8 (2.3)	12.2 (2.0)	11.4 (2.5)	p=0.04
ß2-microglobulin (mg/l)				
mean (SD)	3.0 (2.5)	2.52 (1,1)	3.57 (3.2)	p=0.11
Platelets (/nl)				
mean (SD)	263 (104)	274 (106)	249 (100)	p=0.18
Hb < 11.5 g/dl		23/68 (33.8%)	26/57 (45.6%)	p=0.17
Platetelts< 100/nl		0/65	4/55 (7.2%)	p=0.027
IPSSWM risc category				
data avail. from n pts.	115	63	52	
low	53.0%	55.6%	50.0%	
intermediate	40.0%	38.1%	42.3%	
high	7.0%	6.3%	7.7%	p=0.83

International Prognostic Scoring System for WM (IPSSWM): 5 adverse covariates: age >65 years, hemoglobin <11.5 g/dL, platelet count <100x10⁹/L, β2-microglobulin >3 mg/L,monoclonal protein concentration >70 g/L. Low risk:1 adverse variable except age; high risk:>2 adverse characteristics;intermediate risk:2 adverse characteristics or age >65 years.Morel P et al.,Haematologica 2007;92 6 suppl 2: 1-229.

Treatment

	all patients	Private practice	University hospital	
Treatment lines				
median (range)	1 (0-8)	1 (0-8)	2 (0-7)	
>2 treatment lines	41 (24.4%)	12/74 (16.2%)	30/96 (31.3%)	p=0.03
First line treatment				
Chlorambucil		17/40 (42.5%)	13/75 (17.3%)	
Bendamustin		7 (17.5%)	0	
R-Bendamustin		7 (17.5%)	2 (2.7%)	
Fludarabine		3 (7.5%)	4 (5.3%)	
FC		1 (2.5%)	2 (2.7%)	
R-PC		1 (2.5%)	21 (28%)	
COP		1 2.5%)	12 (16%)	
CHOP/R-CHOP		0	4 (5.4%)	
Rituximab in any line (% of treated pts)	61 (53%)	14/40 (35%)	47/75 (62.6%)	p<0.001
Bendamustin in any line (% of treated pts)	30 (26%)	24/40 (60%)	6/75 (8%)	p<0.001
Rituximab-Bendamustin (% of treated pts)	19 (16.5%)	14/40 (35%)	5/75 (6.6%)	p<0.001

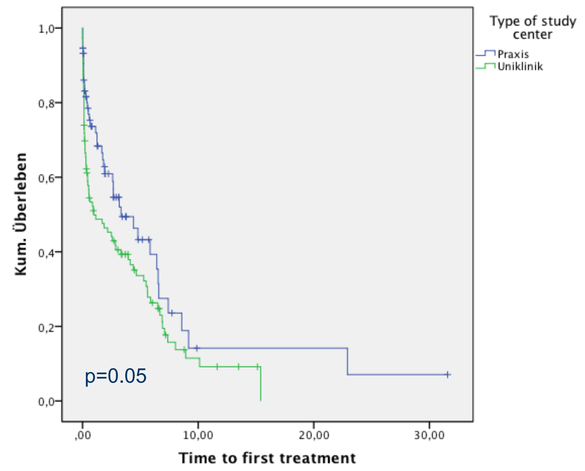
Survival

	all patients	Private practice	University hospital	
Time to first treatment (Median (month))	31.9	52.9	13,7	p=0.05
Overall survival (median, years)	25,07	25,00	not reached	p=0.1
Overall survival (median, years) (only patients with documented initial bone marrow infiltration, n=127)	16,30	25,00	16,3	p=0.47

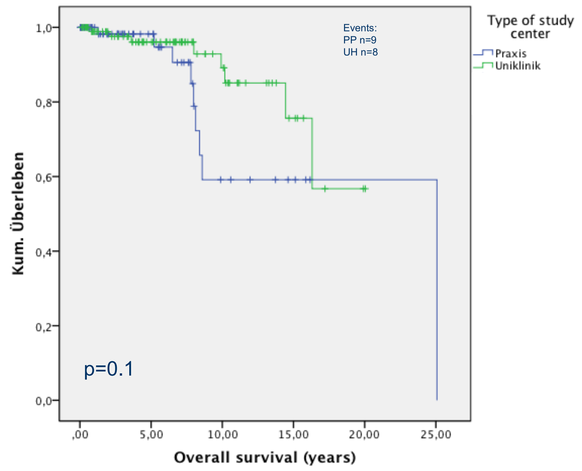
Key results

- Patients from PP were older (median 65.3 vs. 62.4, p=0.01).
- No significant difference in CIRS-Score (comorbidity) between PP and UH.
- No significant difference in International Prognostic Scoring System for WM (IPSSWM) between PP and UH.
- Mean hemoglobine level at diagnosis was lower in pts from UH (11.4 vs. 12.2, p=0.04).
- There was no significant difference in mean platelet count, IgM and ß2-microglobuline level at diagnosis.
- 54% of pts from PP have received treatment during the observation time, as compared to 78.1% of the UH (p<0.001).
- The most common first line treatment protocols of PP were Chlorambucil (17/40, 42.5%), Bendamustin (17.5%) and Rituximab(R)-Bendamustin (17.5%).
- The UH most commonly administered R-Pentostatin-Cyclophosphamide (28%), Chlorambucil (17.3%) and COP (16%) in first line .
- 35% of the treated pts of PP have received R, as compared to 62.6% of the pts of the UH (p<0.001)
- 60% of the treated pts of PP have received Bendamustin, as compared to 8% of the pts of the UH (p<0.001).
- The time to first treatment was significantly shorter in pts from the UH (median 13.7 mo.) as compared to PP (52.9 mo.) (p=0.05).
- Median overall survival of all pts was 25.0 years and did not differ between PP and UH.
- IPSSWM had significant prognostic value

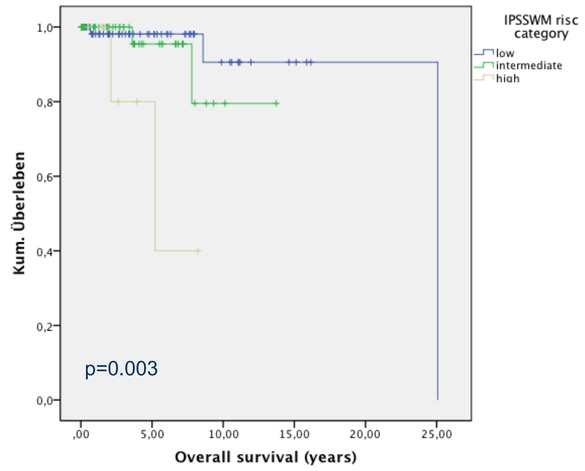
Time to first treatment



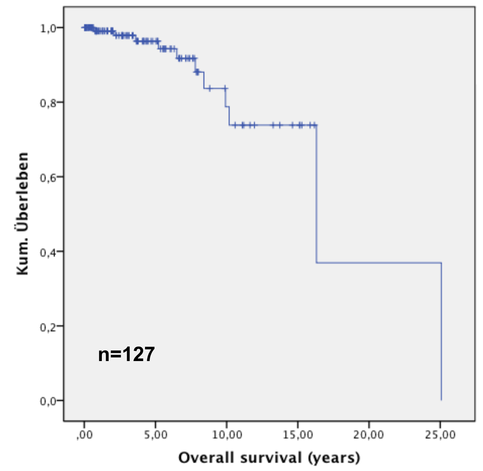
Overall survival



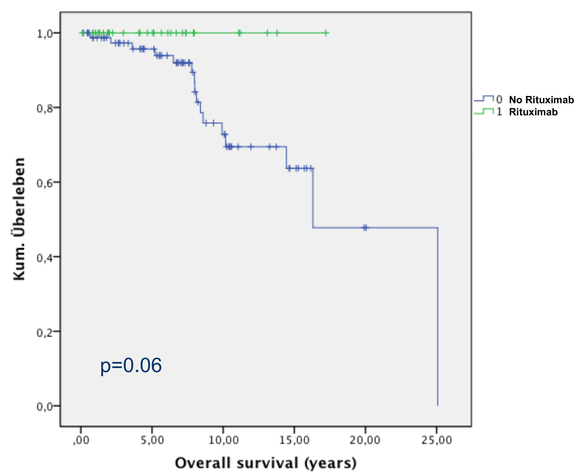
Overall survival according to IPSSWM



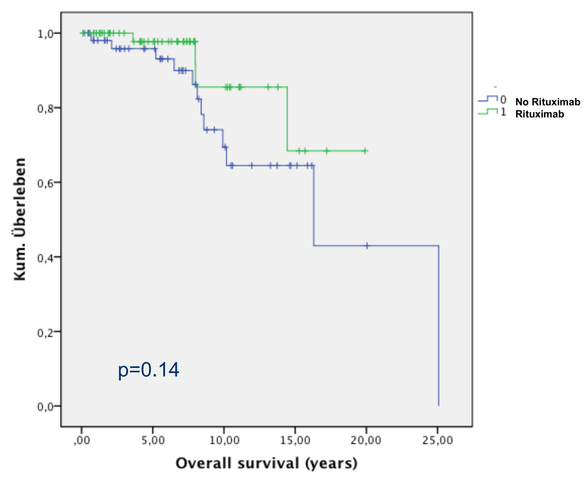
Overall survival (only patients with documented initial bone marrow infiltration)



Overall survival according to use of Rituximab-containing first line regimen



Overall survival according to use of Rituximab-containing regimen in any treatment line



Conclusions

- Pts characteristics were comparable in PP and UH with regard to CIRS-Score and IPSSWM.
- Pts with WM treated in PP were older and had higher initial hemoglobin levels as compared to pts from the UH.
- Treatment differs significantly between PP and UH.
- Time to first treatment was shorter in pts from UH.
- Overall survival was excellent, and better than reported previously.