

## [Abstract 16]

### IMMUNOPHENOTYPIC AND CYTOGENETIC COMPARISON OF WALDENSTRÖM'S MACROGLOBULINEMIA AND MARGINAL ZONE LYMPHOMA

San Miguel JF<sup>1,2</sup>, Ocio EM<sup>1</sup>, Mateo G<sup>1</sup>, Sánchez ML<sup>3</sup>, González B<sup>2</sup>, Vidriales B<sup>1</sup>, Gutiérrez N<sup>1,2</sup>, Orfao A<sup>2,3</sup>, Hernández JM<sup>1,2</sup> <sup>1</sup>Servicio de Hematología. Hospital Universitario de Salamanca. <sup>2</sup>Centro de Investigación del Cáncer. Salamanca. <sup>3</sup>Servicio de Citometría. Universidad de Salamanca, SPAIN.

**Introduction:** Although the clinico-pathological characterization of Waldenström's Macroglobulinemia (WM) was well defined at the last workshop held in Athens (2002), it has been recognized that WM has heterogeneous morphological, phenotypical and cytogenetic features and may overlap somewhat with marginal zone lymphoma (MZL).

We report on the immunophenotypic characterization of a series of 80 WM patients, and the molecular cytogenetic analysis performed in 40 of them. Results were compared with those obtained in a series of 29 patients with a splenic MZL.

As far as immunophenotyping is concerned, both WM and MZL constantly expressed pan B markers (CD19, CD22, and slg) although CD22 expression was significantly stronger in MZL while slg expression was dimmer with a  $\kappa:\lambda$  ratio of 1:1 (5:1 in WM). MZL and WM lymphocytes lacked CD10. FMC7 was positive in both WM and MZL (83% and 86% patients respectively) but with a different pattern of expression as it was more homogeneous and stronger in MZL than in WM (coefficient of variation of  $65\pm 12$  vs  $128\pm 7$  ( $p=0.01$ ), and mean channel  $345\pm 80$  vs  $155\pm 26$ , ( $p=0.006$ ) for MZL and WM respectively). CD25 was positive in only 20% of MZL patients while it was present in 86% of WM. Most MZL express CD11c (75% of cases) as compared to only 30% of WM patients. Finally CD103 is weak positive in 43% of MZL while it is constantly negative in WM. Upon combining CD25 and CD11c expression, only 1 out of 14 MZL patients (8%) had a CD25+ CD11c- phenotype whereas it was present in 80% of WM patients. CD5 and CD23 expression is almost identical in MZL and WM, with only a small proportion of dim positive cases (20%-35%).

Regarding cytogenetics, the main molecular abnormality found in WM, is a partial loss on the long arm of chromosome 6 (23% in our series). By contrast, extranodal MZL is characterised by a rearrangement of MLT/MALT1 gene (on 18q21) that may be translocated either to a API1 gene,  $t(11;18)$  or to IGH,  $t(14;18)$ . The first type of translocation usually corresponds to gastrointestinal MALT lymphomas, while the second is associated with MALT lymphomas from parotid gland, conjunctiva, and skin. Splenic marginal zone lymphomas frequently show a loss or rearrangements on 7q while lymphoplasmocytic lymphoma are characterised by a  $t(9;14)$ , with involvement of PAX5 gene, which prevents the expression of high levels of IgM. Interestingly, the incidence of IgH rearrangements is low in WM (10% in our experience).

In summary, immunophenotypic and molecular cytogenetic studies could contribute to differentiate WM from MZL.