Outcome for patients with Monoclonal B-cell Lymphocytosis (MBL), a pre-cursor state for Chronic Lymphocytic Leukaemia (CLL).

Fiona Bennett, Andy C. Rawstron, Sheila J. M. O'Connor, Marwan Kwok, James A.L. Fenton, Marieth Plummer, Ruth de Tute, Stephen J. Richards, Andrew S. Jack and Peter Hillmen.

From HMDS, Leeds Teaching Hospitals, U.K.

Monoclonal B-lymphocytes (MBL) are detectable in over 3% of adults. In most cases the cells have a phenotype consistent with Chronic Lymphocytic Leukemia (CLL). The aim of this study is to compare the biological features of MBL and CLL cells and to determine whether individuals with MBL are at risk of progression to CLL. MBL/CLL cells were identified using flow cytometry in 1520 individuals with normal blood counts and 2228 patients referred for investigation of a lymphocytosis. Monoclonal B-cells were further characterised by cytogenetic and molecular analysis. MBL cells were indistinguishable from indolent CLL cells on the basis of protein expression, chromosomal abnormalities, V_H gene family usage and mutation status. After a median 6.7 years follow-up (range 0.2 – 11.8), 15% of MBL cases had progressed to a lymphocyte count above 30 x 10^9/L with 8% of cases (14/185) requiring treatment. The absolute B-cell count was the only independent risk factor for progressive CLL. During follow-up 33% died, predominantly due to unrelated causes; age above 70, haemoglobin concentration below 11 g/dL and T-lymphopenia were the only independent prognostic factors. MBL is biologically equivalent to CLL and approximately 1-2% of cases will show disease progression per year. The incidence of individuals with MBL at risk of disease progression is approximately 2 per 100,000 per year. The absolute B-cell and T-cell counts are predictors of progression-free and overall survival respectively but V_H mutation status, CD38 expression and total lymphocyte count are uninformative. The relationship between MBL and CLL is very similar to that between MGUS and myeloma.