

## [Abstract 04]

### DNA CELL CONTENT ANALYSIS AND CELL CYCLE DISTRIBUTION IN PATIENTS WITH IgM MONOCLONAL GAMMOPATHIES

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Little is known about the DNA cell content and the cell cycle characteristics of tumoral cells involved in IgM monoclonal gammopathies. Moreover, the malignant clone appears to be rather heterogeneous including from mature B-lymphocytes to plasma cells (PC). Accordingly, for an appropriate evaluation of the proliferating activity of these patients, DNA ploidy and the cell cycle distribution of the different cell subsets involved in the disease should be separately analysed.

In the present study, we have evaluated the DNA cell content of 29 patients with IgM monoclonal gammopathies: 20 of them had a Waldenström Macroglobulinemia (WM) and 9 were diagnosed of IgM monoclonal gammopathy of undetermined significance (IgM-MGUS). In order to specifically analyse the cell cycle of the B-lymphocytes and PC populations, we have used a flow-cytometric double-staining technique with CD19/CD20/CD22/propidium iodide for B-lymphocytes and CD38/propidium iodide for PC, respectively.

In most patients (28/29 of WM and IgM-MGUS) both subsets of tumor cells (B-lymphocytes and PC) showed a diploid DNA cell content (DNA index equal to 1). This pattern differs from that observed in Multiple Myeloma and non-IgM-MGUS in which up to 60% of cases display an aneuploid DNA PC content, mainly hyperdiploid. In one patient two cell subsets with different DNA ploidy (one diploid and the other near-tetraploid, DNA index: 1.93) coexisted. This coexistence was present both in the B-lymphocytes and the PC.

We were able to analyse the cell cycle characteristics of the B-lymphocytes in 23 cases. The median percentage of proliferating B-lymphocytes -including the synthesis (S) and G<sub>2</sub>/Mitoses (G<sub>2</sub>M) phases - was 1.8% (range: 0.4% to 4%) while the remaining B-lymphocytes were in the G<sub>0</sub>G<sub>1</sub> phase of the cell cycle (98%; range: 91% to 99%). This proliferative activity is significantly lower from that observed, in the same sample, for non-malignant cells (6%, range: 1% to 15%; p=0.004).

Upon comparing the percentage of the proliferating B-lymphocytes in WM and in IgM-MGUS, no significant differences were observed: median: 2.2%, (1.2%-4.1%) versus 1.7% (0.4%-2.4%), p=0.6.

In 9 cases, the cell cycle characteristics of PC were simultaneously evaluated: 97% of PC were in G<sub>0</sub>G<sub>1</sub> and 3% were in S+G<sub>2</sub>M. In 7 of the 9 cases, the PC population had a similar proportion of proliferating cells to that observed in the B-lymphocyte counterpart.

In summary, the cell cycle analysis shows that IgM monoclonal gammopathies are low proliferative disorders. The similar pattern of cell cycle distribution and DNA ploidy observed for B-lymphocytes and PC, indicate that both populations are part of the same clone and contribute similarly to the tumor expansion.