RETROSPECTIVE ANALYSIS OF 56 CASES OF TRANSFORMED WALDENSTROM MACROGLOBULINEMIA. A STUDY ON BEHALF OF THE FRENCH INNOVATIVE LEUKEMIA ORGANIZATION (FILO).

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Histologic transformation (HT) to an aggressive non-Hodgkin lymphoma is a well-described event in the natural history of patients with indolent lymphomas, mainly follicular lymphomas and chronic lymphocytic leukemia/small lymphocytic lymphoma. HT has been reported also in lymphoplasmacytic lymphoma (LPL)/Waldenström macroglobulinemia (WM) but only case reports or small patients series are available.

We retrospectively searched the databases of 14 French and Belgian centers for patients with sequential or simultaneous diagnosis of LPL/WM and diffuse large B-cell lymphoma (DLBCL). Fifty-six patients (39 men and 17 women) were analyzed of whom 8 had simultaneous diagnosis of LPL/WM and DLBCL. At the time of diagnosis of LPL/WM, the median age was 65 years (range, 33-85 years). Thirty-one percent of patients presented lymphadenopathy and 27% splenomegaly. The median level of serum monoclonal IgM was 17.7 g/L (range, 2.3-66.7 g/L). According to the IPSSWM, 12 patients (38%) were low, 13 (40%) were intermediate and 7 (22%) were high-risk. The median number of therapies for WM was 2 (range, 0-5), including chlorambucil (60%) and fludarabine-based regimens (48%). Only half of the patients were exposed to rituximab. The median time from LPL/WM diagnosis to HT was 59 months (range, 4 to 300 months).At the time of onset of DLBCL, 32

patients (57%) presented altered ECOG performance status (≥ 2) and B symptoms were found in about half of the patients.Tumor mass higher than 5 cm and extranodal involvement were found in 54% and 95% of patients respectively. The median serum IgM level was 6.7 g/L (range, 0-40 g/L). Serum lactate deshydrogenase levels were elevated in 72% of cases. Histology was mainly represented by DLBCL, only 2 cases were described as B-cell lymphoma, intermediate between DLBCL and Burkitt lymphoma. In situ hybridization for EBER was negative in 17 of 18 informative cases. The median number of lines of therapy given for HT was 1 (range, 0-5). First-line treatment for HT consisted of CHOP-like regimen +/- rituximab in 47 patients (85%). Five patients (9%) received DHAP association and 3 (5%) GEMOX due to cerebral involvement and/or previous CHOP-exposure. Rituximab was part of the first-line treatment for HT in 49 patients (89%). Six patients underwent autologous stem cell transplantation (SCT) and 3 allogeneic SCT. The overall response rate after first-line treatment for HT was 55% (complete response, 45%) and the median progression-free survival and overall survival after HT were 18 and 25 months respectively (figure). The majority of deaths were attributed to disease progression (75%) or infections (18%).

HT appears to be a critical event in the clinical course of patients with LPL/WM, associated with poor outcome. Risk factors for developing DLBCL and molecular pathogenesis of transformation in patients with LPL/WM remains to be studied.

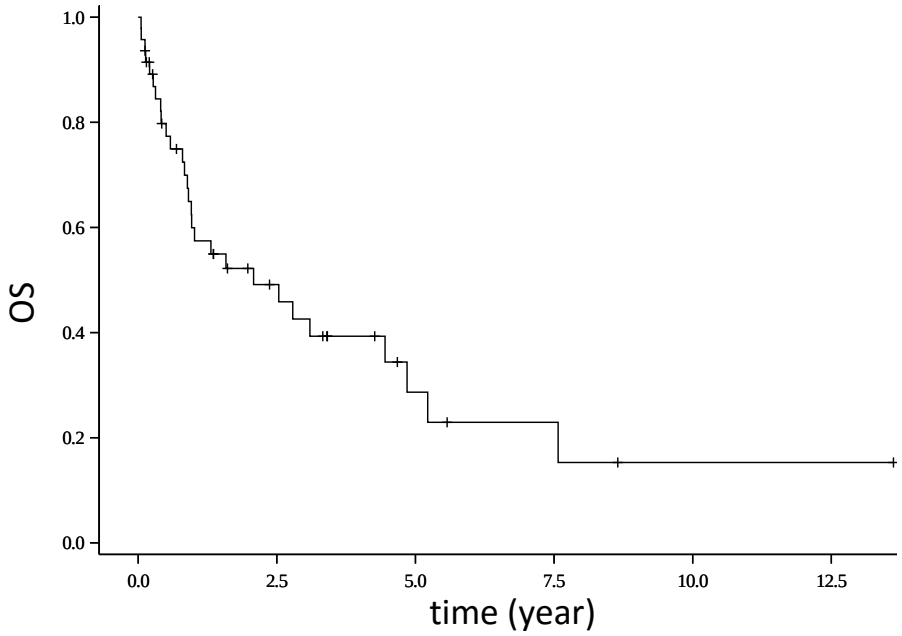

Figure :overall survival of patients since HT