MOLECULAR REMISSION IS AN INDEPENDENT PREDICTOR OF PFS IN WM

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Introduction. MYD88 (L265P) somatic mutation is the molecular hallmark of Waldenström Macroglobulinemia (WM) and has relevant implications for diagnosis, prognostication and prediction of response to BTK inhibitors. In the multicenter, observational BIOWM trial (NCT03521596) of Fondazione Italiana Linfomi (FIL) minimal residual disease (MRD) after treatment was assessed with droplet digital PCR (ddPCR) in bone marrow (BM), peripheral blood (PB) or plasmatic cell-free (cf) DNA.

Main points. Paired BM, PB and plasma samples of 100 WM patients enrolled in the study and treated with chemo-immunotherapy frontline were collected at baseline (T0) and after therapy (T2)**.** Undetectable MRD (uMRD) by dd-PCR was achieved in 52/92 patients (57%) after therapy. The rate of uMRD was respectively 94%, 76% and 67% in PB, cf-DNA and BM, ($P<0.001$). The median follow-up of patients was 49 months, with a 4-year PFS of 70% and 4-year OS of 84%, respectively. Patients achieving uMRD had a better PFS from the end of treatment as compared with patients with detectable MRD after therapy (4-year PFS 91% vs 62%, $P=0.010$).

Conclusions. Our findings suggest that MYD88 (L265P) is a suitable target for MRD analysis. Moreover, uMRD is a predictive factor for PFS and may thus represent a surrogate endpoint for outcome in future clinical trials.