W30: THREE CASES OF IgM-RELATED AL AMYLOIDOSIS ASSOCIATED TO WALDENSTROM MACROGLOBULINEMIA WITH MYD88^{L265P} MUTATION, TREATED WITH BORTEZOMIB BASED REGIMENS: A SINGLE-CENTER EXPERIENCE.

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Background: AL amyloidosis associated with IgM monoclonal gammopathy, lymphoplasmocytic lymphoma (LPL) and Waldenström macroglobulinemia (WM) is an infrequent pathological entity representing just 5-8% of all the AL amyloidosis. The biological features of AL amyloidosis are less understood and the optimal therapeutic management is not known. Indeed, while MYD88^{L265P} is a common mutation in WM, its role in WM-related AL Amyloidosis is still under investigation.

Aims: We report on three patients with WM and AL Amyloidosis positive for MYD88^{L265P} mutation, treated with Bortezomib-based regimens.

Results:

A 72 years-old man presented with renal insufficiency (creatinine of 236 umol/L) and weakness at diagnosis. Serum and urine tests detected Bence Jones (BJ) proteinuria (□) of 1.26 g/24h, IgM/□ MC of 47.17 g/L, □ sFLCs of 1,080.0 mg/L (dFLC 1,066.8 mg/L), altered NT-proBNP. The bone marrow biopsy (BMB) was positive for LPL with trisomy of chromosome 3q and 18 and MYD88^{L265P} mutation, the abdominal fat biopsy showed AL amyloidosis. A WM (IPSSWM high-risk) and AL amyloidosis (□) (Standard Mayo- and Renal-stage II) was diagnosed: he was treated with bortezomib, rituximab, dexamethasone (BRD) for 8 cycles, achieving a VGPR for WM and a PR for AL amyloidosis, according to IWWM and ISA response criteria, with a substantial clinical improvement.

A 72 years-old woman presented with an IgM/□□MGUS. Blood and urine tests revealed mild anemia, creatinine of 155 umol/L, BJ proteinuria (□) of 0.57 g/24h,□MC of 14 g/L, □ sFLC of 335 mg/L (dFLC 212 mg/L), altered NT-proBNP and TnI. BMB showed massive LPL infiltration, trisomy of chromosome 18 and MYD88^{L265P} mutation. An endomyocardial biopsy confirmed AL-amyloidosis (□). A WM (IPSSWM high-risk), with AL amyloidosis (□) (Standard Mayo-stage IIIa and Renal-stage II) was diagnosed: she was treated with Bortezomib- dexamethasone, because of clinical worsening. After 2 cycles no bioumoral or clinical response was observed. She died because of a cardiac arrest.

A 62 years-old man presented with a new asymptomatic IgM/□ MC of 5g/L. Serum and urine tests showed creatinine of 144 umol/L, BJ proteinuria (□) of 1.58 g/24h, □ sFLC of 76.3 mg/L (dFLC 57.7 mg/L), altered NT-proBNP and TnI. BMB revealed massive LPL infiltration, normal

karyotype and MYD88^{L265P} mutation. Abdominal fat biopsy showed AL amyloidosis (□). A WM (IPSSWM high-risk), with AL amyloidosis (□) (Standard Mayo-stage IIIa and Renal-stage was diagnosed: he underwent BRD therapy. After five months he achieved a PR for WM and no response for AL amyloidosis.

Conclusions

Our report suggests that clinical features of MYD88^{L265P}-mutated IgM-related AL amyloidosis may not be different from other types of AL amyloidosis. Indeed, none of the three patients displayed a neuropathic involvement, and all

had cardiac or renal disease. There is no standard of care yet and the goal should be to eradicate the lymphoproliferative clone that could sustain the amyloidogenic damage. MYD88^{L265P} mutation, amyloidosis' stage and high dFLC burden could play a role in the responsiveness to therapy and in defining the outcome.