Treatment and outcome of 267 patients with IgM-related AL amyloidosis

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AL amyloidosis is caused deposition of monoclonal immunoglobulin light chain and is associated with IgM-paraproteinemia in 5% of cases – mostly due to underlying Waldenstrom's macroglobulinaemia. The standard treatments for AL amyloidosis are typically regimes derived from multiple myeloma and are inappropriate in this group of patients. Response to alkylating agents is poor and there is no agreed standard treatment. We describe here the treatment and outcome of 297 patients with IgM-related AL amyloidosis, with particular focus on the impact of outcomes when treated with regimes developed specifically for Waldenstrom's macroglobulinaemia.

267 consecutive IgM patients with AL amyloidosis were identified form the databases of amyloidosis groups based in London, UK, Pavia, Italy and Limonges/Tolouse/Paris, France - evaluated between 1988 and 2011. The analysis of initial 150 of these patients is presented here with final analysis of all 267 cases presented at the meeting. 74% of patients had underlying lymphoma, mainly of lymphoplasmocytic subtype; lymph node amyloid was present in 27%. Commonest organ involved was the kidney (59%) followed by heart (31%). Serum free light chain ratio was abnormal in 83/119 evaluable patients with baseline difference between uninvolved and uninvolved FLC (dFLC) >50 mg/L in 66 cases. 135 patients required therapy, of whom 124 were evaluable for frontline regimen: chlorambucil/melphalan in 57, rituximab-based in 28 (R-CVP 9, FCR 7, RCD 5, R-CHOP 3, others 4), purine analogs in 9 (FC 5), oral cyclophosphamide-thalidomide-Dex(CTD) in 8, vincristine-adriamycin-dex (VAD) in 8, CHOP/CVP in 5, CVD in 1, and high dose melphalan followed by autograft (HDM) in 2. Median time to next treatment was 10 months with a better outcome for frontline HDM, CHOP/CVP and FCR (median 49, 16 and 13mo, respectively) with 50% responders.

Considering all lines of therapy (>2 regimens in 60 patients), 47 patients received Rituximab, 36 purine analogs, 5 bortezomib and 5 HDMel. Median OS was 37 months with a survival advantage for patients receiving HDMel, bortezomib combination (median OS not reached) and FCR (78mo) compared to (R)CHOP/CVP or FC regimens (median OS 42 and 31mo). Approximately 45 % of patients achieved hematologic and dFLC >PR (6 dFLC-VGPR) with a median OS of 69 vs 16 months for non responders .

Patients with IgM related AL amyloidosis should be treated with appropriately tailored regimens for Waldenstrom's macroglobulinaemia to achieve at least PR. Exposure at some stage to CVD, FCR or HDM appears to be associated with better survival.