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LONG-TERM FOLLOW-UP IN POPULATION WITH AL RENAL AMYLOIDOSIS

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Introduction. AL amyloidosis, sistemic disorder, is due to deposition of protein derived from immunoglobulin light chain fragments. Renal involvement most often presents as asyntomatic proteinuria or clinically apparent nephrotic syndrome or renal failure with little or no proteinuria. New therapeutic strategies with bortezomib and lenalidomide have improved the prognosis. The aim of our study was to evaluate the long term efficacy of new therapeutic protocols in renal AL amyloidosis.

Methods. This is a prospective analysis of 20 patients with histological diagnosis of renal amyloidosis. Amyloid deposits are identified histologically by their diagnostic apple-green birefringence when stained with Congo red and viewed under polarized light. In order to detect serum protein network to the Amyloidosis, a proteomic approach was applied on serum based on two-dimensional electrophoresis, Western-blotting and mass spectrometry. Bortezomib-based (BD) regimen is used (Bortezomib 1.3 mg/m^2 subcutaneously on days 1-4-8-11 in the first three cycles and after on days 1-8-15-22; Cyclophosphamide 200 mg/m^2 p.o. + Dexamethasone 40 mg p.o. on days 1-8-15-22 of the 21-day cycle for 9 cycles). Hematological and organ response were evaluated according to the novel criteria of the International Society of Amyloidosis. 19 patients completed BD regimen and the patients with partial renal response (PRR: decreased of 24 hour urine protein and MDRD > 50% over baseline) were treated with 4-week cycles of Lenalidomide (dose adjustments for renal function, orally days 1-21) and dexamethasone (20 mg on days 1-4, 9-12, 17-20 in teh first 4 cycles and after 10 on days 1-4). Follow-up of 5 years from diagnosis of amyloidosys.

Results. The mean age was 63±4 aa, and 5 (25%) were males. By immunohistochemistry the protein composition of the amyloid deposit was FLC k in 7/20 and and FLC lambda in 13/20. At onset the mean proteinuria was 15.1 ± 4.21 gr/24h with average MDRD of 34.6 ml/min (III stage CKD), pro-BNP 361.1, SIV 12.5 mm. Three patients (15%) had confirmed multiple myeloma (Clone of plasma cells proliferation > 30% in the bone marrow). One patient died for cardiac arrhythmia (he received only 3 cycles). After 9 BD regimen 14 patients (70%) showed a complete renal response (CRR: MDRD > 90 ml/min, proteinuria/24h< 300 mg) and hemathological response (CHR, normal serumFLC ratio); 3 patients (15%) showed PRR and partial HR (PHR>50% reduction in dFLCs); 2 patients were started hemodialysis and showed partial HR. All 19 patients showed a complete cardiological response (normal BNP and SIV). 5 (25%) patients with PRR and PHR underwent another chemiotherapic regimen with lenalidomide and dexamethasone. We revealed severe anemia and thrombocytopenia in 1 patient and therefore we decided to discontinue the therapy, stability of ESRD and CHR in 1 patient, CRR and CHR in 3 pts. Adverse events: breast cancer in one, HZV nevralgy in 3, leiomyosarcoma cutaneous in one.

Conclusion. The new therapeutic strategies have allowed not only the short-term remission of the AL amyloidosis in 17 patients (85%), but also improved the outcome in the long-term (in 14 of them remission in over 3 years). Further studies with larger sample sizes and longer follow-up are needed to validate our results.

DOI: 10.3252/pso.eu.54ERA.2017