## W8: SERUM TRANSFORMING GROWTH FACTOR-BETA1 (TGF-BETA1) LEVELS PREDICT SURVIVAL AND TIME TO TREATMENT IN WALDENSTROM'S MACROGLOBULINEMIA (WM).

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Serum transforming growth factor-beta1 (TGF-beta1) is a pleiotropic cytokine involved in normal hematopoiesis as negative regulator of B-cell proliferation and immunoglobulin production. It was found to play a role in the pathogenesis of many hematologic malignancies, including multiple myeloma. Its' role has not been extensively investigated in WM.

The purpose of this study was to update and expand former results from our group on correlations between serum TGF-beta1 levels and disease charateristics, time to first treatment (TFT) and overall survival (OS) in a series of WM patients with a long follow-up

We studied 77 WM patients from diagnosis to last follow-up or death; their files were reviewed after patients' informed consent was obtained, and clinical and laboratory characteristics and treatment details were collected. Patients' sera, drawn at diagnosis and kept frozen, were retrospectively analyzed. Serum TGF-beta1 measurements were done by ELISA according to the manufacturer's instructions. Statistical analysis was performed by SPSS software, v 22.0.

Patients' median age was 70 years, 67% were males and 95% were symptomatic or became symptomatic during follow-up time. At the time of diagnosis 27% of patients presented severe anemia (Hb < 10g/L), 12% blood lymphocytosis, 17% thrombocytopenia, 41% increased beta2-microglobulin (b2M> 3,5mg/L), 18% elevated LDH, while median IgM levels were 2000mg/dl and median bone marrow lymphoplasmacytic infiltration 45%. Seventeen percent of patients presented lymphadenopathy and 12% splenomegaly. Median survival of the whole series was 106 months and median follow-up time was 143 months. It should be noted that all over their disease course patients received new agents (80% rituximab, 30% DRC, 30% BDR, 18% ibrutinib). Median serum TGF-beta1 levels were 34420 pg/ml (range 1665-615000) in WM patients and 32902 pg/ml in 20 healthy individuals (range 1941 – 58123). Patients with TGF-beta1 levels above median had a longer TFT than the others (p= 0,017) and an significantly improved OS (p=0,002). Among clinical and laboratory findings at diagnosis, serum TGF-beta1 correlated only inversely with platelet counts (p=0,01).

In conclusion, although serum TGF-beta1 levels did not correlated with clinical and laboratory findings at diagnosis, they were highly prognostic of outcome and patients with increased serum TGF-beta1 had a longer TFT and OS than the others. New agent treatment did not obcured serum TGF-beta1 prognostication in WM.