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MORE THAN A SURFACE MARKER: THE RELEVANCE OF CD200 SERUM LEVELS IN PREDICTING PROGNOSIS OF CHRONIC LYMPHOCYTIC LEUKEMIA.

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The evaluation of CD200 expression has shown to be a useful tool to better classify chronic lymphoproliferative diseases. Chronic lymphocytic leukemia (CLL) overexpresses surface CD200 with respect to other lymphoid leukemias, in particular mantle cell lymphoma. Moreover, there is some evidence that serum levels of soluble CD200 (sCD200) could be related to disease progression in pts with CLL. However, very little is known about sCD200 prognostic significance.
In light of this, serum samples were collected at diagnosis from 272 pts with CLL (median age 66 yrs, range 33-90; 58% males) and from 78 age and sex-matched healthy subjects (median age 63 yrs, range 42-100; 58% males), used as normal controls. Human CD200 (OX-2 membrane glycoprotein) ELISA kit (Wuhan Fine Biotech Co., Ltd., Wuhan, Hubei, China) was used to quantify sCD200 in serum samples. A significantly higher concentration of sCD200 in CLL pts than in controls (median, 1281 pg/ml vs 799 pg/ml; p=0.0002) was found. In pts with CLL, sCD200 was significantly higher in those ≥66 vs <66 yrs old (median, 1560 pg/ml vs 1193 pg/ml; p=0.0001), in those with Binet stage C vs A/B (2055 pg/ml vs 1274 pg/ml; p=0.0045), in those with unmutated vs mutated IgVH (1601 pg/ml vs 1131 pg/ml; p<0.0001), and in those with unfavorable (del11q or del17p) vs favorable (normal or del13q or tris12) FISH (1897 pg/ml vs 1239 pg/ml; p=0.0077). On the contrary, gender, bulky disease, whole blood cell or lymphocyte count, β_2-microglobulin serum levels and presence of autoimmune complications did not significantly correlate with sCD200. Time-to-first-treatment (TTFT) was shorter in pts with higher sCD200 levels (sCD200 >1281 pg/ml vs <1281 pg/ml, median TTFT, 61 vs 109 months; p<0.001). Furthermore, baseline sCD200 values appear to have an impact on response to therapy (median in CR vs PR/NR pts, 1308 pg/ml vs 1590 pg/ml; p 0.0468), and this difference seems to increase if only pts who received chemotherapy or chemo-immunotherapy are considered (1244 pg/ml vs 1602 pg/ml; p=0.0193). However, we did not find an association between baseline sCD200 values and response to targeted agents. Finally, sCD200 also had an impact on overall survival (OS) (sCD200 >1281 pg/ml vs <1281 pg/ml; median OS, 222 vs 299 months; p=0.005).
A correlation between sCD200 serum levels at diagnosis and the prognosis of pts with CLL was found: higher sCD200 correlated with more aggressive clinical and biological features and was able to predict a worse prognosis. It has been previously shown that CD200 can be released from CD200+ neoplastic cells by ectodomain shedding. Both the membrane and soluble forms of CD200 are also able to engage CD200 receptor, which in turn can result in increased tumor growth, by means of a negative impact on tumour immunosurveillance. Our data further support the relevant role of CD200 not only as a diagnostic tool but also as a prognostic indicator and a potential therapuetic target in CLL.