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

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BACKGROUND

The evaluation of CD200 expression has shown to be a useful tool to better classify chronic lymphoproliferative diseases. CLL overexpress CD200 with respect to other lymphoid leukemias. 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 its prognostic significance.

METHODS

Serum samples were collected at diagnosis from 272 pts with CLL (median age 66 yrs, range 33-90) and from 78 age- and sex-matched healthy subjects (median age 63 yrs, range 42-100), as normal controls. Human CD200 (OX-2 membrane glycoprotein) ELISA kit (Wuhan Fine Biotech Co., Ltd., Wuhan, China) was used to quantify sCD200 in serum samples.

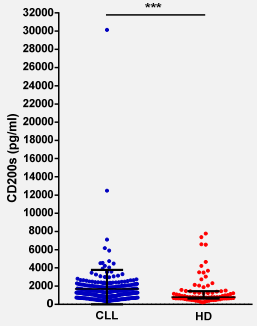

Figure 1. sCD200 in patients with CLL (blue) and in HD (red).

RESULTS

We found a significantly higher concentration of sCD200 in serum samples from CLL pts than in controls (median, 1281 pg/ml vs 799 pg/ml; p=0.0002) (Fig. 1). 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, b_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) (Fig. 2). 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). On the contrary, an association between baseline sCD200 values and response to targeted agents was not found. 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) (Fig. 2).

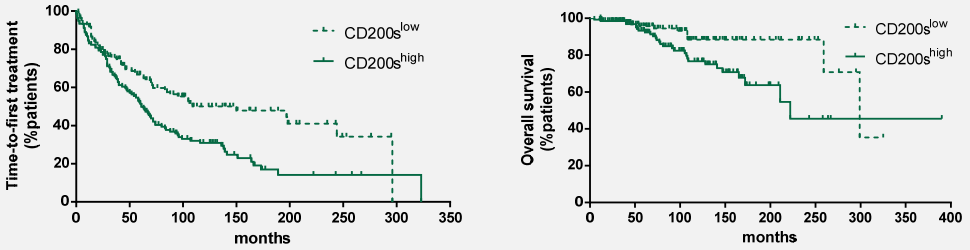

Figure 2. Time-to-first treatment (left) and overall survival (right) for patients with $sCD200^{low}$ vs $sCD200^{high}$

CONCLUSIONS

Higher sCD200 correlated with a more aggressive behavior and was able to predict a worse prognosis. CD200 can be released from CD200+ neoplastic cells by ectodomain shedding and both surface and sCD200 are able to engage CD200 receptor, which in turn can result in increased tumor growth, by means of a negative control of immunosorveillance

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