To the editor:

CD38 expression does not change in B-cell chronic lymphocytic leukemia

Since the first description by Damle et al,[1] several investigators demonstrated the independent prognostic significance of CD38 expression in predicting survival of patients suffering from B-cell chronic lymphocytic leukemia (B-CLL).[2-9] But despite confirming its prognostic value, Hamblin et al recently reported that CD38 expression may vary during the course of the disease, enriching the scientific debate about the biological significance of the expression of this molecule on neoplastic B lymphocytes.[8] In addition, Chevallier et al have shown that CD38 expression may change during the evolution of the disease, suggesting that such an expression may be a secondary event in B-CLL.[9] In particular, they recorded an increased expression during the disease progression in some cases. Other investigators, however, reported that CD38 expression is a constant overtime in some of their patients serially tested.[1,7]

In light of this, we reviewed 162 B-CLL patients diagnosed and followed up at our institutions in the last 3 years. We analyzed 29 patients in which CD38 expression on peripheral B cells was evaluated more than one time, to verify whether a change in the immunophenotypic profile occurred.

To detect the percentage of neoplastic B cells displaying the CD38 molecule on their surface, we used a 3-color fluorescence staining: peridinin chlorophyll A protein (PerCP) for CD45s, fluorescein isothiocyanate (FITC) for CD19s, and phycoerythrin (PE) for CD38s. All monoclonal antibodies were purchased from Becton Dickinson Immunocytometry System (BDIS, San Jose, CA). CellQuest software and FACSCalibur flow cytometer (BDIS) were used. All cases were immunologically typical ($CD5^+CD23^+$) B-CLL. Positivity was defined as expression of CD38 on $CD19^+$ cells of at least 30%. Globally, CD38 expression was recorded on 34% of B-CLL patients. In the patient group in which the determination of CD38 expression was done more than one time, the mean number of determinations was 2.4 (range, 2-5), and the mean time between the first and the last determinations was 17 months (range, 2-41 months). As shown in Table 1, we did not find a variation in CD38 expression of more than 10% between the first determination and the second determination. Interestingly, variations were not recorded in patients with progressive disease (stage shift and/or increase in peripheral blood lymphocytes or in node size) and in patients with stable disease as well. Moreover, no

Table 1. CD38 expression in 29 B-CLL patients sequentially evaluated

Case no.	First determination, %	Time between the 2 determinations, mo	Last determination, %	Disease status at last determination
1	8	41	10	PBLC increased, Rai stage shift from 0 to I
2	1	16	2	PBLC increased, *Herpes zoster*
3	0.8	18	0.6	Spontaneous spleen rupture, then stable disease with lymphocytosis only
4	3	40	7	PBLC increased, Rai stage shift from I to IV
5	1	36	0.2	PBLC increased, Rai stage 0
6	1	23	2	Rai stage II, broncopneumonia
7	14	10	15	Relapse after fludarabine-based regimen therapy, Rai stage IV
8	13	6	16	Rai stage I, stable
9	4	18	1	Rai stage 0, PBLC increased
10	2.6	10	0.5	Rai stage 0, stable
11	1	12	0.7	Rai stage I, stable
12	4.1	2	4.1	Rai stage IV, acute renal failure*
13	30	9	37	Rai stage I, stable
14	90	13	88	Rai stage I, stable
15	19	14	12	Rai stage II, PBLC increased
16	7	8	6	Rai stage I, PBLC increased
17	4	12	6	Rai stage I, stable
18	0.7	4	0.7	Rai stage 0, stable
19	57	6	58	Rai stage I, stable
20	69	12	72	Rai stage I, stable
21	54	18	49	Rai stage IV, progression after several lines of therapy
22	7	12	6	Rai stage 0, gastric cancer
23	10	20	14	Rai stage 0, stable
24	1	8	2	Rai stage I, stable
25	0.1	40	0.1	Rai stage 0, stable
26	0.5	6	0.5	Rai stage IV, stable
27	45	18	43	Rai stage II, stable
28	0.9	39	1.2	Rai stage 0, stable
29	1.3	22	0.8	Rai stage 0, stable

PBLC indicates peripheral blood lymphocyte count.

*Patient underwent hemodialysis when PBLC was 90 000/μL. During the procedure the PBLC decreased to 10 000/μL and after renal function recovery increased to 17 000/μL. All 5 determinations of $CD19^+CD38^+$ B cells ranged from 3.8% to 4.1%.

differences were found among circulating and bone marrow B cells in terms of CD38 expression in those cases in which the determination was performed on both samples (data not shown). In addition, other conditions, such as spontaneous spleen rupture, viral infection (ie, *Herpes zoster*), broncopneumonia, or hemodialysis for acute renal failure were not able to induce an expression of CD38 in 4 cases with $CD38^-$ B-CLL tested before these events occurred.

In our opinion, methodological reasons could explain the discordant data reported so far, including the use of cryopreserved samples,[10] different cytometers and operators during the time of the study, and different clones of CD38 monoclonal antibodies and gating strategies to detect it.

In conclusion, though our results need to be further corroborated on a greater number of patients followed up for longer time, our feeling is that CD38 expression does not change during the disease course of B-CLL.

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To the editor:

The nosology of myelodysplastic syndromes

A recent letter by Lichtman[1] discusses very eloquently the pitfalls, inconsistencies, and illogicalities of the current nosology of clonal myeloid diseases. Dr Lichtman argues that the terms refractory anemia and myelodysplasia should be made obsolete because they are misnomers and exhorts the hematology community to take up the challenge of rectifying this flawed, albeit World Health Organization–approved, nomenclature. He has also made suggestions for a revised classification of myelodysplastic syndromes in one of his recent articles.[2]

Although Dr Lichtman's arguments are very sound and valid, his suggestions[2] for a revised terminology of "refractory anemias" and "myelodysplastic syndromes" are, unfortunately, far from satisfactory. His proposal for a revised classification of myeloid neoplasms is based on the following categorizations: minimal- to moderate-deviation clonal myeloid disorders, ineffective erythropoiesis (precursor apoptosis) is prominent, overproduction of cells is prominent, moderately severe–deviation clonal myeloid disorders, severe-deviation clonal myeloid disorders, and very severe–deviation clonal myeloid disorders.

Table 1. A proposal for a revised nosology of myeloid neoplasms

Category	Characteristics
Clonal myelopathy, stage I	Monocytopenia (anemia, neutropenia, or thrombocytopenia) with no increase in bone marrow blasts
Clonal myelopathy, stage II	Bi- or tricytopenia with no increase in bone marrow blasts
Clonal myelopathy, stage III	Cytopenia with excess blasts (marrow blast population below 30% of the nucleated cells)
Clonal myelopathy, stage IV	Acute myeloid leukemia (marrow blast population above 30% of the nucleated cells)

In my opinion, the above approach is, although based on a rational pathophysiologic basis, not particularly suited for day-to-day clinical use. I would like to put forward another suggestion for a revised nosology of myeloid neoplasms (Table 1). This proposed nomenclature would have a number of advantages, compared with the current classification of myelodysplastic syndromes or the one suggested by Dr Lichtman. First, it would accurately identify the conditions included as "clonal diseases," thus rectifying the single most important drawback of the currently used classification. Second, it would provide information about the pathologic/clinical progression of the underlying disease, analogous to those classifications successfully used for several nonhematologic neoplastic diseases. Third, unlike the current system of terminology of myelodysplastic disorders that appears to give an impression that the primary pathology lies in the erythroid lineage due to the usage of terms "refractory anemia," "refractory anemia with excess blasts," and so forth, the proposed classification would not give that erroneous impression. Finally and perhaps most importantly, this system would be very simple, uncomplicated, and comprehensible to nonhematologists and patients. For these reasons, I believe that this proposal deserves consideration.

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