Hgb level (Hgb > 105 g/L [10.5 g/dL] or ≤ 105 g/L [10.5 g/dL]) showed a similar mean increase in Hgb level from baseline for the higher and lower Hgb strata at 4 weeks and at last value; however, the transfusion rate was relatively lower in the higher Hgb stratum (7.1% compared with 28.2% for the ≤ 105 g/L [10.5 g/dL] stratum).[7] The proportion of responders (patients with Hgb level increase ≥ 20 g/L [2 g/dL]) was also greater in the higher stratum (80.5% vs 68.5% in the ≤ 105 g/L [10.5 g/dL] stratum). With respect to cost effectiveness, fewer patients in the higher (15%) versus the lower (25%) stratum required doubling of their starting dosage.

Interim results of an open-label randomized trial in patients with hematologic malignancies and Hgb levels of 100 g/L (10 g/dL) or more and 120 g/L (12 g/dL) or less show a positive effect of epoetin alfa.[9] Patients were randomized to either once-weekly epoetin alfa immediately (EPO) or to observation, during chemotherapy, with epoetin alfa offered if Hgb level decreased to less than 90 g/L (9 g/dL) (OBS). From baseline to end of treatment, the EPO group experienced significant increases in Hgb level ($P = .007$) and improvements in QOL. Furthermore, patients in the EPO group had a significantly greater decrease in clinic visits ($P = .002$) and days requiring assistance ($P < .001$), suggesting that treatment of mild anemia (Hgb 100-120 g/L [10-12 g/dL]) may reduce health care resource utilization.

Final results, not yet peer-reviewed, from a double-blind, placebo-controlled clinical trial in breast cancer patients receiving adjuvant or neoadjuvant chemotherapy, support efficacy of early intervention.[8] Breast cancer patients with mean Hgb levels of 128 g/L (12.8 g/dL) receiving once-weekly epoetin alfa experienced an improvement in Hgb levels (+8 g/L [+0.8 g/dL]) after 16 weeks, and attenuated declines in both QOL and fatigue versus patients receiving placebo. In contrast, patients receiving placebo experienced a more than 20 g/L (2 g/dL) mean decrease in Hgb level after 2 cycles of anthracycline-based chemotherapy.[8] Therefore, studies in patients with diverse malignancies suggest that epoetin alfa can maintain or improve Hgb level[7-9] and QOL,[8,9] and decrease transfusions[7] in patients with baseline Hgb level more than 100 g/L (10 g/dL). These results suggest a basis for a stronger recommendation regarding epoetin alfa use in patients with Hgb levels higher than 100 g/L (10 g/dL).

The focus of this letter is to draw attention to developments in 2 critical areas of anemia management: anemia-related QOL and optimal Hgb management. New analyses and data are relevant and may serve to augment the guidelines. As standards of care in anemia management continue to evolve, consideration of emerging data will be an essential part of the review process for clinical practice guidelines.

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To the editor:

Expression of Fcγ receptors type II (FcγRII) in chronic lymphocytic leukemia B cells

We have read with interest the paper from Damle et al[1] analyzing the surface membrane phenotype of B lymphocytes in chronic lymphocytic leukemia (B-CLL). The authors stated that the leukemic cells from all B-CLL patients evaluated (irrespective of immunoglobulin heavy chain (IgV_H) gene mutational status) bear the phenotype of antigen-experienced B cells based, among other features, on the very low expression of Fcγ receptors type IIb (FcγRIIb, CD32), which is the main isoform of FcγRII in B lymphocytes.[2] We would like to comment on this issue on the basis of our own results, which differ from those of Damle et al.

We analyzed membrane expression of FcγRII by flow cytometry in leukemic cells from 52 B-CLL patients who were classified by Rai stage system as indolent (0-I), intermediate (II), or aggressive (III-IV) disease. We have used 3 different monoclonal antibodies (mAbs): clones AT10 and 2E1, which recognize all isoforms of FcγRII; and clone IV.3, which recognizes FcγRIIa when used as Fab fragment but is capable of reacting with FcγRIIb when used as a whole molecule.[3] IV.3 Fab was tested because, to our knowledge, it is the only mAb capable of discriminating between FcγRII isoforms by fluorescence-activated cell sorter analysis; in fact, mAb II8D2 used by Damle et al has been shown to react with both isoforms.[4] By using IV.3 Fab, we found that FcγRIIa is expressed only marginally in B-CLL cells from some patients (data not shown). On the other hand, more than 95% of leukemic cells, in all samples analyzed, were stained with mAbs AT10, 2E1, or IV.3 (whole molecule), which can be attributed to the

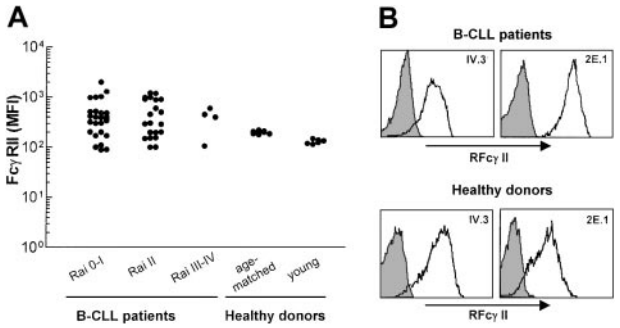

Figure 1. Expression of FcγRII in B cells from B-CLL patients and healthy donors. (A) $CD19^+$ lymphocytes from peripheral blood were stained with anti-FcγRII (clone AT.10, purified mouse IgG1; generous gift from Dr M. Daeron, Institut Curie, Paris, France) and anti–mouse IgG fluorescein isothiocyanate (FITC), $F(ab')_2$ fragments (Coulter-Immunotech, Marseille, France). Results are expressed as the mean fluorescence intensity (MFI) of FcγRII expression in $CD19^+$ cells for each sample analyzed. MFI of control isotype ranged between 8 and 10 in all cases. (B) Representative histograms of FcγRII expression (white histograms) assessed by direct immunofluorescence analysis with anti-FcγRII (clone IV.3-FITC [whole molecule], Medarex, Annandale, NJ, or clone 2E1-PE, Coulter-Immunotech). Gray histograms indicate control isotype.

presence of FcγRIIb. Moreover, we found that B-CLL cells displayed comparable or even higher levels of FcγRII expression than B lymphocytes from healthy volunteers (Figure 1). No significant differences in FcγRII expression were observed between $CD5^+$ and $CD5^-$ B lymphocytes from control donors (not shown). Discrepancy between Damle et al's findings and ours could not be attributed to antigen loss due to cryopreservation, as we obtained comparable results with fresh and thawed B-CLL cells.

In conclusion, our findings show that B-CLL cells from patients in early or advanced stage disease express comparable or even higher levels of FcγRII than normal peripheral B lymphocytes, suggesting that FcγRII expression is not a useful parameter to define antigen experience of B-CLL cells. However, given that FcγRII is far from being just a cell marker, we believe that the receptors' role in B-CLL deserves further analysis. The main isoform expressed by B cells, FcγRIIb, functions as an inhibitory receptor.[2,5] Its coaggregation with B-cell receptors (BCRs) dampens B-cell activation by recruitment of a limited number of Src homology 2 domain (SH2)–containing phosphatases, predominantly SHIP (SH2-containing inositol phosphatase), which causes a dramatic and immediate hydrolysis of PIP3 (phosphatidylinositol 3,4,5-trisphosphate).[5] FcγRIIb and SHIP are able to inhibit not only BCR-mediated signals but also signals induced by other cell surface receptors that require PIP3 generation.[6] On the other hand, FcγRIIb can also signal independently of BCR colligation to directly mediate an apoptotic response.[7] Whether or not this receptor is functional in B-CLL cells remains to be solved.

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To the editor:

Imatinib mesylate elicits positive clinical response in atypical chronic myeloid leukemia involving the platelet-derived growth factor receptor beta

Atypical chronic myeloid leukemia (aCML) is a chronic myeloproliferative disorder with a clinical and hematologic picture similar to chronic myelocytic leukemia (CML) but lacking Philadelphia chromosome and *BCR-ABL* rearrangement. Cytogenetic studies have shown either a normal karyotype or numeric chromosomal changes.[1] Recently the molecular cloning of t(5;10)(q33;q22) has been reported in 2 patients with aCML.[2,3] This translocation creates a H4(D10S170)/platelet-derived growth factor receptor beta (PDGFβR) fusion transcript and suggests an association between deregulated tyrosine kinases and aCML. We report on a patient with an aCML and a t(5;10) who achieved a clinical and cytogenetic response after imatinib mesylate therapy.

The patient, a 44-year-old man, presented with leukocytosis and splenomegaly. The white blood cell count was 158×10^9/L (3% myelocytes; 6% metamyelocytes; 4% bands; 68% neutrophils; 8% eosinophils; 10% lymphocytes; 1% monocytes), hemoglobin level was 91 g/L, and platelet count was 352×10^9/L. Analysis of peripheral blood smear revealed a remarkable dysplasia in myeloid cells. Cytogenetic analysis showed the following: 46,XY,t(5;10)(q33;q22)[24]/46,XY[1] after G-banding and fluorescence in situ hybridization (FISH) studies (Figure 1A). Both FISH and polymerase chain reaction (PCR) studies failed to demonstrate the presence of BCR-ABL fusion. Therefore, nested reverse transcriptase (RT)–PCR analysis using specific primers flanking the predicted breakpoints was performed. Using 2 different sets of primers the region implicated in the translocation was amplified (Figure 1B). These results demonstrated that t(5;10)(q33;q22) involved the genes H4 and PDGFβR. Sequencing of the amplified bands confirmed that there was a fusion H4-PDGFβR occurring at exactly the same breakpoint as found in the previous t(5;10) reports.[2-4] Based on the presence of PDGFβR rearrangement, the patient began treatment with imatinib, at a daily dose of 400 mg. The therapy was well tolerated, without obvious side effects. Clinical and cytogenetic complete response to imatinib was