PRESENTING FEATURES AND PROGNOSIS OF B-CELL CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS LESS THAN 50 YEARS OLD

To the Editor:

The recent report by Montserrat et al[1] provides a comprehensive evaluation of widely accepted prognostic factors in younger patients with B-cell chronic lymphocytic leukemia (B-CLL). This is of particular interest because studies addressing this topic and dealing with immunologically proven B-CLL are virtually absent thus far. The above-mentioned report[1] stressed that the clinical approach of younger B-CLL patients does not need new prognostic models[2] because staging systems and prognostic factors that are used currently can be successfully applied to this subset of patients.

We would like to confirm these conclusions by using our experience of 45 B-CLL patients younger than 50 years referred to two hematologic institutions in southern Italy during the last 20 years. They accounted for 7.1% of the whole population of B-CLL patients observed. B-CLL diagnosis has been confirmed by cell surface markers in the great majority of cases (84.4%). Median age was 45 years (range, 33 to 49), with six patients (13%) between 30 and 40 years and 39 patients (87%) between 41 and 49 years. Male/female ratio was 1.6. Similarly to Montserrat et al's[1] experience, we did not find any significant difference in comparing younger patients with older patients for Rai and Binet stage distribution, peripheral blood lymphocytosis, pattern of bone marrow histology, and lymphocyte doubling time. Only hemoglobin level was significantly higher in younger than in older cases (13.6 ± 2.1 *v* 12.2 ± 2.6 g/dL; $P < .001$). In detail, stage distribu-

tion at diagnosis was as follows: 12 cases were in Rai 0 (26.6%), 26 in Rai I + II (57.7%), 7 in Rai III + IV (15.5%); 23 in Binet A (51.1%), 15 in Binet B (33.3%), and 7 in Binet C stage (15.5%). Moreover, patients have been scored according to the total tumor mass (TTM) system,[3] a quantitative CLL staging based on the sum of: (1) the square root of peripheral blood lymphocytosis in nl (TM1); (2) the diameter of the largest palpable lymph node (TM2); and (3) the enlargement of spleen below the costal margin in cm (TM3). Twenty-four (53.4%) cases presented a low (<9) TTM score, and the remaining cases (46.6%) had a high (>9) TTM score. The distribution between low and high TTM score was comparable in younger and older patients. Eleven (24.4%) cases with TM 1 < TM2 + TM3 were clinically defined as tumoral forms of B-CLL (lymphoma-like).

Bone marrow biopsy was available in 24 cases with 2 nodular pattern (8.3%), 17 interstitial (70.8%), 2 mixed (8.3%), and 3 diffuse (12.5%). Doubling time (DT) of lymphocytes could be evaluated in 20 patients only; it was greater than 12 months in 18 (90%) cases and ≤12 months in two (10%) cases. Unfortunately, the small number of patients with available data on bone marrow biopsy and DT prevented the prognostic evaluation of both of these parameters in the present series.

At the time of this analysis 20 of 45 patients (44.4%) have died. Overall median survival was 7 years and overall probability (±SD) was 66% ± 1.0% at 5 years and 30% ± 2.0% at 10 years. Both Rai and Binet classifications had prognostic impact on survival ($P < .001$). TTM score system also discriminated different prognostic groups. In fact, cases with low and high TTM had a 7-year survival probability of 81% ± 1.3% and 32% ± 3.2%, respectively ($P < .001$). Furthermore, lymphoma-like B-CLL patients had a life expectancy significantly shorter than cases with a leukemic pattern (7-year survival rate, 36% ± 2.4% *v* 63% ± 1.4%).

The recent concepts of "smoldering" CLL[4] can be successfully applied to the present series of younger B-CLL patients. Fifteen of 23 stage A patients (65.2%) fulfilled the criteria of "smoldering" CLL.[4] Only one patient died 111 months after diagnosis; the remaining patients are alive 3 to 190 months after diagnosis with a 15-year survival probability of 83%.

Although obtained in a smaller number of patients, our results are similar to those reported by Monserrat et al[1] and by the International Workshop on CLL/Working Group,[5] thus confirming that younger B-CLL patients have similar presenting features and prognostic factors as older ones. On the other hand, as suggested by Montserrat et al,[1] the optimal approach of younger patients with advanced or progressive disease is far from being reached, and more intensive treatment procedures might affect their overall survival.[6]

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