quantitative RT-PCR. Leukemia 1999;13:1825–32.
14. Beillard E, Pallisgaard N, van der Velden VHJ, Bi W, Dee R, van der Scoot E, et al. Evaluation of candidate control genes for diagnosis and residual disease detection in leukemic patients using "real-time" quantitative reverse-transcriptase polymerase chain reaction (RQ-PCR) – an Europe Against Cancer Program. Leukemia 2003;17:2474-86.
15. Gabert J, Beillard E, van der Velden VHJ, Bi W, Grimwade D, Pallisgaard N, et al. Standardization and quality control studies of "real time" quantitative reverse transcriptase polymerase chain reaction (RQ-PCR) of fusion gene transcripts for residual disease detection in leukemia – An Europe Against Cancer Program. Leukemia 2003;17:2318-57.
16. O'Brien SG, Guilhot F, Larson RA, Gathmann I, Baccarani M, Cervantes F, et al. Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia. N Engl J Med 2003;348:994-1004.
17. Kantarjian H, Sawyers C, Hochhaus A, Guilhot F, Schiffer C, Gambacorti-Passerini C, et al. Hematologic and cytogenetic responses to imatinib mesylate in chronic myelogenous leukemia. N Engl J Med 2002;346:645-52.
18. Hughes TP, Kaeda J, Branford S, Rudzki Z, Hochhaus A, Hensley ML, et al. for the International Randomised Study of Interferon versus STI571 (IRIS) Study Group. Frequency of major molecular responses to imatinib or interferon α plus cytarabine in newly diagnosed chronic myeloid leukemia. N Engl J Med 2003;349: 1423-32.
19. Rosti G, Martinelli G, Bassi S, Amabile M, Trabacchi E, Giannini B, et al. Molecular response to imatinib in late chronic phase chronic myeloid leukemia. Blood 2003 (in press).
20. Merx K, Muller MC, Kreil S, LahayeT, Paschka P, Schoch C, et al. Early reduction of BCR-ABL mRNA transcript levels predicts cytogenetic response in chronic phase CML patients treated with imatinib after failure of interferon-α. Leukemia 2002;16:1579-83.
21. Branford S, Rudzki Z, Harper A, Grigg A, Taylor K, Durrant S, et al. Imatinib produces significantly superior molecular responses compared to interferon alfa plus cytarabine in patients with newly diagnosed chronic myeloid leukemia in chronic phase. Leukemia 2003;17:2401-9.
22. Lange T, Bumm T, Otto S, Al-Ali HK, Kovacs I, Krug D, et al. Quantitative RT-PCR should not replace conventional cytogenetics for monitoring CML patients during the early phase of imatinib therapy. Haematologica 2004;12:49-57.
23. Bumm T, Muller C, Al Ali HK, Krohn K, Shepherd P, Schmidt E et al. Emergence of clonal cytogenetic abnormalities in Ph- cells in some CML patients in cytogenetic remission to imatinib but restoration of polyclonal hematopoiesis in the majority. Blood 2003;101: 1941-9.
24. Goldberg SL, Madan RA, Rowley SD, Pecora AL, Hsu JH, Tantravahi R. Myelodysplastic subclones in chronic myeloid leukemia: implications for imatinib mesylate therapy. Blood 2003;102:1143.

Chronic lymphocytic leukemia in 2003

During the last decade, there has been a resurgence of interest in research about chronic lymphocytic leukemia (CLL). An understanding of the molecular basis of this hematologic malignancy has led to the appreciation that several different B-cell diseases are represented under this name.

Several lines of data now suggest that B-cell chronic lymphocytic leukemia may actually be two diseases, reflecting the mutated and unmutated state of the immunoglobulin heavy-chain gene. The current use of fluorescent *in situ* hybridization permits a more accurate evaluation of the cytogenetics of the malignant cells, identifying distinct subsets of patients with strong correlations between the chromosome abnor-

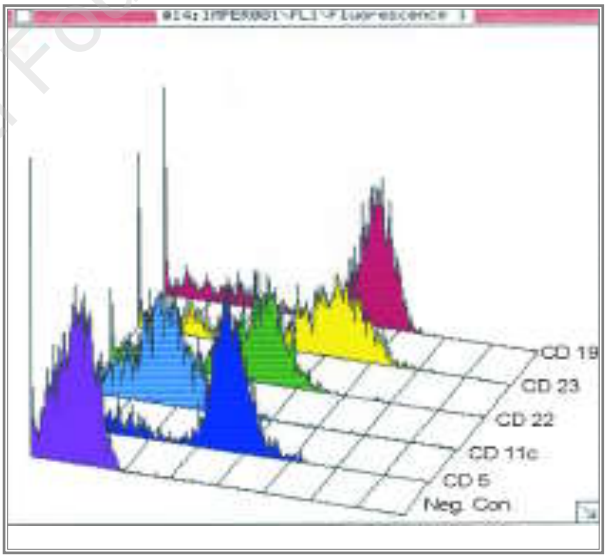

Figure 1 (above). FACS profile in a B-CLL case with a typical immunophenotype ($CD5^+/CD19^+/CD23^+/CD22^{\pm}/CD11c^-$). *Reprinted from: Liso V. et al. Haematologica 2003; 88(Suppl 17):2-5.*

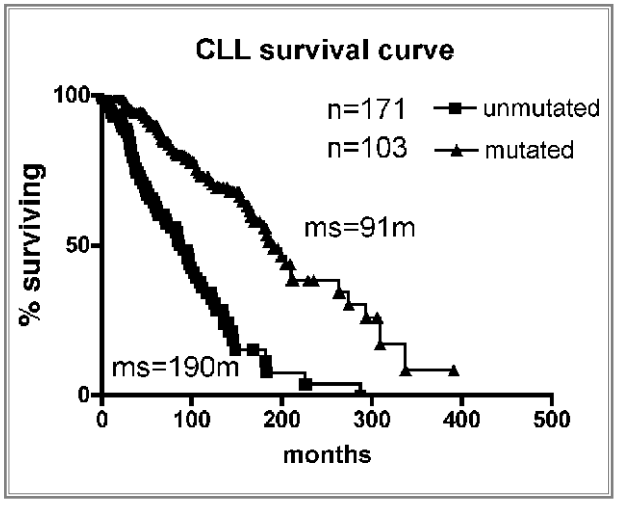

Figure 2 (left). Survival curve of mutated vs. unmutated cases of CLL (n = 274). *Reprinted from: Hamblin T. Haematologica 2003; 88(Suppl 17):14-7.*

Table 1. Infection prophylaxis in CLL patients treated with innovative therapies.

RISK FACTORS

Binet stage B and C
Previous chemotherapy
Neutropenia
Renal dysfunction
Minor or no response to fludarabine
CD4 count <200 cells/mL
Age> 65
Ig titer < 400 mg /dL

PROPHYLAXIS

Pneumocystis carinii: Trimethoprim- sulfamethoxazole (particularly in steroid therapy) One tablet 3 times a week

Fungi: Fluconazole or itraconazole 400 mg daily (if colonized)
Herpes: acyclovir 400 mg twice daily (800 mg twice daily if previous severe infection)

Ig replacement: only patients with recurrent and severe bacterial infections caused by *Staphylococcus*, *Streptococcus pneumoniae* and *Haemophilus influenzae* 250 mg/kg every four weeks

Reprinted from: Nosari et al. Haematologica 2003; 88(suppl.17):43-9.

mality, clinical course, response to therapy and outcome. There have also been important therapeutic advances in the last years. Several recently reported trials have helped to transform our paradigms for the treatment of CLL. A clear example of this is that fludarabine is now used as the preferred initial treatment for the disease. Nevertheless, the failure to cure patients has led to new strategies being explored and to the development of new drugs.

An increasing number of new biological agents are being evaluated, including Campath-1H, recently approved for the treatment of fludarabine-resistant CLL. There has been a marked increase in the use of submyeloablative transplants, offering a more immunology-based therapy than does standard bone marrow transplantation, potentially with less toxicity.

A meeting on recent advances in chronic lymphocytic anemia took place in Milan, Italy, on November 14, 2003. The papers presented have been published in a supplement of this journal;[1-11] the supplement is downloadable free of charge from *http://www.haematologica.org/free/cll2003.pdf.*

Enrica Morra, Marco Montillo
Division of Hematology
Niguarda Cà Granda Hospital
Milan, Italy

References

1. Liso V, Delia M, Capalbo S. Morphologic and immunophenotypic characterization of chronic lymphocytic leukemia. Haematologica 2003; 88 Suppl 17:2-5.
2. Pizzolo G. Soluble molecules as prognostic factors in B-cell chronic lymphocytic leukemia. Haematologica 2003; 88 Suppl 17:6-8.
3. Castoldi G, Cuneo A. Cytogenetic and molecular cytogenetic features in chronic lymphocytic leukemia. Haematologica 2003; 88 Suppl 17:9-13.
4. Hamblin T. Immunoglobulin genes: characteristics and prognostic prediction in early stage chronic lymphocytic leukemia. Haematologica 2003; 88 Suppl 17:14-7.
5. Brugiatelli M, Mamone D, Mannina D, Neri S, Jaksic B. Therapy of B-cell chronic lymphocytic leukemia: traditional approach or new strategies? Haematologica 2003; 88 Suppl 17:18-21.
6. Morrra E. Evolving strategies in the treatment of chronic lymphocytic leukemia with purine analogs. Haematologica 2003; 88 Suppl 17:22-5.
7. Hallek M. Risk adapted management of chronic lymphocytic leukemia: update on the cooperative trials of the German Chronic Lymphocytic Leukemia study group. Haematologica 2003; 88 Suppl 17:26-30.
8. Montillo M, Rossi V, Tedeschi A, Cafro A, Luchesini C, Ricci F, et al. Combination of chemotherapy and immunotherapy in chronic lymphocytic leukemia. Haematologica 2003; 88 Suppl 17:31-8.
9. Regazzi M, Iacona I, Montagna M. Clinical pharmacology of monoclonal antibodies rituximab and CAMPATH-1H. Haematologica 2003; 88 Suppl 17:39-42.
10. Nosari A, Molteni A. Risk of infections of new therapeutic approaches for chronic lymphocytic leukemia. Haematologica 2003; 88 Suppl 17:43-9.
11. Farina L, Zallio F, Mariotti J, Carrabba M, Corradini P. Graft-versus-leukemia effect after reduced-intensity conditioning and allogeneic stem cell transplantation in patients with chronic lymphocytic leukemia. Haematologica 2003; 88 Suppl 17:50-2.