Introduction

The Sixth Lugano Conference clinical papers: Many remaining questions

R. Stupp,1 S. T. Ong2 & J. E. Ultmann2
1Center for Oncology, University Hospital, Lausanne, Switzerland; 2Section of Hematology/Oncology, Department of Medicine, University of Chicago, Chicago, IL USA

We present here some of the exciting papers from the Sixth International Conference on Malignant Lymphoma, held recently in Lugano. We have divided the proceedings into two parts. This volume is the first and deals mainly with clinical aspects; part 2 covers basic sciences and pathology and will follow in another issue.

What can we learn from pediatric lymphoma?

One session at the recent conference was exclusively devoted to pediatric lymphoma. The successes in treating pediatric non-Hodgkin's lymphoma and Hodgkin's disease are striking. Intensive combination regimens with optimal supportive care have been shown to be feasible and curative for most patients. In his excellent overview, Magrath compares pediatric treatment programs with some of the more intensive combination chemotherapy regimens for adults. The success of pediatric lymphoma protocols may be based on the consistently higher dose intensity reached in the pediatric patient groups, with inclusion of high doses of methotrexate, etoposide, and cytarabine from the beginning. The applicability of pediatric protocols to adults, with the same favorable outcome, was demonstrated in Lugano by Todeschini and colleagues.

When and how to reduce toxicity?

In children, survival and cure rates of more than 90% witness the great progress in treating non-Hodgkin's lymphoma and Hodgkin's disease. The reduction of long-term toxicity has become a major focus in designing new and better treatment regimens. Radiotherapy can be eliminated for most patients with Hodgkin's disease without compromising the overall treatment outcome. In adults, the role of chemotherapy even for treatment of early-stage Hodgkin's disease is increasing, and some investigators advocate that every patient with Hodgkin's disease gets chemotherapy. At a follow-up of 15–20 years, late toxicity of treatment is the major cause of failure in patients cured of their lymphoma.

What is the best treatment for aggressive non-Hodgkin's lymphoma?

Despite intensive second- and third-generation combination treatment regimens and high response rates, overall survival has not been significantly improved by the more intensive regimens. Updated results of yet another randomized trial comparing CHOP and MACOP-B were presented in Lugano, showing five-year survival rates of 54% and 41%, respectively. Although this difference reached statistical significance, these results remain disappointing and insufficient. CHOP remains the standard treatment for most aggressive NHLs, not by virtue of its efficacy, but rather in the absence of a proven more successful treatment. The approach of Gianni, treating patients with sequential, single-agent chemotherapy at each drug's maximum tolerated dose, appears promising, and international randomized trials are in preparation.

The role of intensification with stem-cell support

High-dose chemotherapy with autologous peripheral stem-cell or bone marrow reinfusion has been a widely accepted treatment for poor-prognosis NHL. But many questions remain: When should dosages be intensified, up front or at recurrence? Which is the best conditioning regimen? How many cycles of intensification? How useful are purging and CD34 selection? To date, one randomized trial has shown an improved survival for patients with recurrent but chemoresponsive lymphoma treated with high-dose chemotherapy compared to a standard salvage regimen (DHAP). However, the impact of this strategy on the overall outcome of our lymphoma patients remains marginal. Linch and colleagues showed in a hypothetical calculation that, even if all nonresponding or recurrent patients were to be treated by high-dose chemotherapy, only a few patients would be cured. Clearly, new and better up-front treatment strategies are needed. The International Prognostic Index may be a helpful tool in identifying patients for whom a less intensive, and thus less toxic and less expensive, treatment may be sufficient.
New drugs and treatment strategies

A number of new and investigational agents are reviewed in a paper by Arbuck and colleagues. It seems unlikely that any of these substances will have a significant impact on the outcome of aggressive lymphoma. In low-grade lymphoma and CLL, the purine analogs now have an established and probably expanding role. Immunotherapy with toxin-conjugated or radioactively marked monoclonal antibodies may have a role in eliminating residual disease or as an adjunct to conventional chemotherapy regimens. Two papers in this issue review the current experience. Incorporation of immunotherapy into the overall treatment strategy and the rational use of interferons and other cytokines as maintenance after remission induction remain to be established.

In conclusion, many questions remain and major progress is still needed. We should be encouraged to enroll our patients into well-designated clinical trials, so that we will be able to define more precise treatment recommendations by the next Lugano meeting.