Advances in Lymphoma Research
Cancer Treatment and Research
Emil J Freireich, M.D., D.Sc.(Hon.), Series Editor

Advances in Lymphoma Research

edited by

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Introduction

In 1993, Fisher et al. published the results of a randomized trial comparing three third-generation regimens against the classic CHOP combination. For several years, the oncology community had been convinced that the third-generation regimens were clearly superior to CHOP. It came as a shock to many that there was no difference in outcome between the four arms of this clinical trial. The logical conclusion is that CHOP is as good as any of the other regimens tested in that study. Unfortunately, this excellent study has been misinterpreted by many as proving that there has not been any progress in the field of lymphoma during the last 20 years. Furthermore, it has led to a fatalistic attitude in the reasoning of many clinicians who feel that 'nothing works better than CHOP' and therefore that it is not worth testing new drugs or developing novel regimens.

However, the process by which we move forward in the oncology field is seldom by dramatic breakthroughs. Frequently, what appears at first glance to be a breakthrough turns out later to be just a modest step forward. Several steps forward eventually add up to a major advance, but this advance goes unnoticed because of the slow nature of the process. In this volume, we have chosen to discuss several of these steps, which we feel are clearly making a positive impact on the field of lymphomas and which soon should make a major difference in therapeutic results.

The purine nucleoside analogs are a new family of drugs that are powerful inducers of apoptosis. Since one of the underlying biological features of low-grade lymphomas is the inhibition of apoptosis, these agents might prove to be an important therapeutic advance. Interestingly, these drugs have proven to be active in low-grade disorders and are currently being tested in combination regimens by some investigators; Dr. McLaughlin and his colleagues and Drs. Saven and Piro discuss fludarabine and 2-CDA in chapters 1 and 2, respectively.

In order to continue to advance in the management of lymphomas, it is essential to understand better this group of diseases. For a long time, there were no substantial new findings in the field of Hodgkin's disease, but lately a tremendous amount of information has been generated concerning the histologic diagnosis of this disorder and its differentiation from other cell types such
as Ki-1 anaplastic large cell lymphoma as well as from diffuse large cell lymphoma. A few years ago, we never faced this problem, but as we learn more about these disorders — particularly with the advent of more sophisticated immunophenotyping and genotyping — some old concepts are being replaced by new knowledge. Likewise, it has recently been recognized that the nodular sclerosis subtype can be divided into two histologic grades with apparently different prognostic implications and with inherent problems in differential diagnosis from other lymphomas. Drs. Osborne and Bueso-Ramos discuss this grading in detail in chapter 3. In regards to other cell types, it is increasingly being recognized that mantle cell lymphoma represents a new entity with characteristic clinical and biological features as well as a particular natural history. In chapter 4, Drs. Rodriguez and Pugh discuss the experience at M.D. Anderson Cancer Center with this histological type.

No serious discussion of lymphomas would be complete without considering the prognostic features associated with outcome. In fact, any future advances in the management of these disorders will rely heavily on a good understanding of the factors associated with an unfavorable outcome when standard therapy is used. This knowledge will allow us to select specifically patients for experimental treatment modalities such as high-dose chemotherapy and bone marrow transplantation. The results of salvage chemotherapy with either standard-dose or high-dose regimens should also take these factors into consideration. Drs. Coiffier, Rodriguez, and Blay and Philip discuss these aspects in chapters 5, 6, and 7, respectively.

We are in the middle of an explosion of knowledge about the biology of cancer. Lymphomas are no exception. Several recent advances in the understanding of the biological features of lymphomas are beginning to bear fruit in regard to potential clinical applications. In chapter 8, Dr. Miller and his colleagues discusses the potential clinical applications of interfering with the multiple drug resistance phenotype. In chapter 9, Drs. Neff and McIntyre discuss the adhesion molecules on the surface of lymphocytes and lymphoma cells and explain how clinicians can benefit from this new knowledge. The bcl-2 gene rearrangement can be detected by PCR, and in chapter 10, Dr. Gribben discusses the application of this technique to monitoring minimal residual disease.

We hope that readers will be convinced after reading this volume that even though the pace has been slow, clear advances in this field have taken place, some of which are already benefiting our patients and other that soon will.