NHL: Diverse Diseases Requiring Diverse Treatments

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One of this year's spotlight sessions will shine on follicular lymphomas (today at 4:30 p.m.). Follicular lymphomas (FL) are second in prevalence only to diffuse large B-cell lymphomas (DLBCL). FL is generally thought to be indolent with a median survival of eight to 10 years. But high-grade FL can behave like DLBCL, and there is always the risk of transformation into aggressive lymphomas. The underlying molecular defect in most cases of FL is the translocation of BCL-2 oncogene next to the immunoglobulin heavy chain (t(14,18)), leading to overexpression of BCL-2 and thereby preventing apoptosis.

Although there is no consensus on whether, or with what, to treat low-grade FL, emerging evidence supports a key role for anti-CD20 monoclonal antibody therapy in event-free and possibly overall survival. Dr. Jane Winter from Northwestern University will detail the use of rituximab (Rituxan®) in advanced stage FL, either as a single agent or in combination with an anthracycline-containing regimen. Immunoradiotherapy using anti-CD20 antibodies tositumomab and ibritumomab with isotopes was described in detail by Dr. Oliver Press from the Fred Hutchinson Cancer Research Center.

Follicular lymphomas were also the focus of an Education Session. Dr. Laurie Sehn from the University of British Columbia and Dr. Myron Czuczman from Roswell Park Cancer Institute both emphasized the importance of having accurate prognostic factors for both the clinician and patient. The mainstay for clinical prognosis remains the Follicular Lymphoma International Prognostic Index (FLIPI); however, it does not adequately discern poor-outcome patients. New results from pharmacogenomic array experiments have revealed that gene expression profiles are correlated with outcome. Surprisingly, the expression profiles are of the surrounding nonmalignant cells and not the lymphoma cells themselves. For instance, the T cell and macrophage signature profile portends a more favorable prognosis than a dendritic cell signature, with median survivals of 13.6 years versus 3.9 years, respectively. There was also discussion of whether PCR-based monitoring of BCL-2/IgH-positive cells would be clinically useful for determining complete molecular response or screening for relapse.

Dr. Sehn also detailed the status of molecular profiling in DLBCL. It has been shown previously that gene signatures of germinal center B cells are more favorable than activated peripheral blood B cells, with a near-doubling of five-year overall survival rates from 35 percent to 60 percent. However, it is unknown whether this advantage will be as significant with the addition of rituximab to the chemotherapy regimens.

Finally, Dr. Lisa DeAngelis from Memorial Sloan-Kettering described the frustrations in primary central nervous system lymphoma (PCNSL) therapies. PCNSL is an extranodal lymphoma that arises anywhere in the CNS, such as the brain, eyes, or spinal cord. Primary treatment for PCNSL is radiotherapy. New data suggest that the use of high-dose systemic methotrexate in combination with radiotherapy can lead to significantly improved three-year relapse risk, from 25 percent to 83 percent. However, chemoradiotherapy led to progressive subcortical dementia in 24 percent of patients by five years, and was even higher in elderly patients, up to 83 percent in one study. Preliminary studies suggest that elderly patients should be treated with chemotherapy containing high-dose methotrexate alone. A recent EORTC phase II study demonstrated an overall median survival of 14 months, obviously better than seven months median survival for patients treated with whole-brain radiotherapy.

The impact of anti-CD20 immunotherapy continues to resonate in the lymphoma field, driving us to reevaluate many aspects of the current standard of care. New pharmacogenomic data provide hope for other prognostic factors or targets for therapy, especially in difficult lymphomas such as primary CNS lymphomas.