Radioisotopes in Lymphoma

Two California biotechnology companies recently announced advances in their respective work on radiolabeled antibodies for treatment of lymphoma.

In March 2000 Coulter Pharmaceuticals of South San Francisco received a patent for Bexxar (^{131}I-tositumomab) for the treatment of non-Hodgkin's lymphoma (NHL). Developed in partnership with SmithKline Beecham, Bexxar is a monoclonal antibody attached to ^{131}I. The antibody recruits the immune system to attack NHL cells through targeted therapeutic radiation, a process that minimizes exposure to normal tissues. Bexxar dosage depends on how rapidly an individual clears the antibody, said Dr. David Magnuson, Director of Medical Information and Safety at Coulter. Dosage is calculated on the basis of 3 infusions.

Coulter presented the combined data of several phase III clinical trials at the American Society of Hematology (ASH) meeting in December 1999. High response rates and long periods of remission were achieved with Bexxar when used in patients with low-grade or transformed low-grade NHL. Dr. Julie Vose, vice chair at the University of Nebraska Medical Center (Omaha, NE) reported combined data on 179 patients with low-grade NHL, 81% of whom responded to Bexxar. Dr. Andrew Zelenetz, chief of Lymphoma Service at Memorial Sloan- Kettering Cancer Center (New York, NY) reported that 53% of the 58 transformed low-grade NHL patients treated with Bexxar responded and another 29% experienced complete remission. Dr. Mark Kaminski, director of the Leukemia/Lymphoma Program at the University of Michigan (Ann Arbor, MI) presented data on 14 patients with small lymphocytic lymphoma treated with Bexxar. Eleven patients responded to the therapy and 3 experienced remission of disease. Coulter is in the process of filing an application with the U.S. Food and Drug Administration for clearance for Bexxar.

IDEC Pharmaceuticals of San Diego is testing its own radiolabeled monoclonal antibody for NHL. Zevalin will act as a complement to Rituxan, another monoclonal antibody. Zevalin (ibritumomab tiuxetan) targets the CD20 antigen and is linked with ^{90}Y for use in patients who are resistant to chemotherapy or to Rituxan alone.

At the same ASH meeting in December, the preliminary results of 4 clinical trials of Zevalin were offered. Dr. Thomas Witzig of the Mayo Clinic (Rochester, MN) presented data that compared Zevalin plus Rituxan to Rituxan alone in 90 patients with relapsed or refractory low-grade follicular or transformed CD20-positive, B-cell NHL. The Zevalin group had an overall response rate of 80%, whereas 44% of the Rituxan group responded. Witzig also offered results from a phase II trial that evaluated the efficacy of Zevalin at a reduced radiation dose. In 22 patients, 23% achieved a complete response, with 45% achieving a partial response.

In a third trial, Dr. Leo Gordon of Northwestern University (Chicago, IL) evaluated the efficacy and safety of Zevalin in patients with follicular NHL who did not respond to Rituxan alone. When Zevalin was part of the treatment protocol, 46% achieved a response. In a related presentation, Dr. Gregory Wiseman of the Mayo Clinic summarized the dosimetry in the Northwestern study and found that the Zevalin/Rituxan combination did not provide a higher radiation dose to normal body organs. Zevalin's makers point out that dosage will be based on patient weight and baseline platelet count without complex dosimetry.

Although the applications of radiolabeled antibodies in the treatment of NHL continue to grow, the direction of these developments is difficult to predict. Magnuson notes, "It's too early to tell what the sequential use of these different therapies will be. These are very new tools. How they are going to be used, where they are going to fall best in the therapeutic sequence, we don't know. Right now, there is no magical sequence for lymphoma therapy."

—www.auntminnie.com

Goldsmith to Receive Mellins Award

On May 6, 2000, Stanley J. Goldsmith, MD, (New York Hospital–Cornell Medical Center, New York, NY), past president of the Society of Nuclear Medicine and past editor of the *Journal of Nuclear Medicine*, will be presented the Harry Z. Mellins, MD, Award in Radiology for Career Excellence in Teaching. The award will be given by the Alumni Association of the State University of New York Hospital Downstate Medical Center at a ceremony and luncheon in Brooklyn, New York.

STR Trials Target Ewing's Sarcoma

NeoRx (Seattle, WA) announced on March 24 that its Skeletal Targeted Radiotherapy (STR) radiopharmaceutical therapy agent has begun testing in patients with Ewing's sarcoma at Children's Hospital and Regional Medical Center in Seattle, WA. The trial is being conducted in conjunction with the University of Washington Medical Center and the Fred Hutchinson Cancer Research Center, also in Seattle.

"Ewing's sarcomas are sensitive to conventional radiation," said Douglas Hawkins, MD, the study's principal investigator. "We hope that demonstrating safety and efficacy of STR in

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patients with advanced disease might lead to using it in earlier stage patients, where potential exists for synergy with chemotherapy and possible durable complete remissions. With STR, the doses of radiation are substantially higher and the safety profiles considerably better than for the standard approaches, and these are the desired characteristics for potentially improved cancer therapies."

STR links ^{166}Ho with a drug that targets the bone, especially those areas of bone undergoing increased metabolism. These areas often take up the drug in greater quantities, providing the opportunity to deliver more radiation to areas of bone directly affected by tumor. By injecting STR into the blood, the radiation can localize in tumors in the bone.

NeoRx has recently completed accrual on a phase I/II trial using STR in patients with multiple myeloma. Evaluation of these patients is ongoing. A phase III trial for patients with multiple myeloma is slated to begin later this year.

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imaging, *SNM: Procedure Guideline Manual 1999,* and *Outcomes and Technology Assessment in Nuclear Medicine*. These may be purchased on the SNM Web site at www.snm.org. For more information on any of the programs listed in this article, please contact Sandra H. Griffith at 703-708-9000, ext. 1321, or by e-mail at sgriffith@snm.org.

HCFA Local Carrier Sends Draft Policy to Reviewers

In 1997 the Health Care Financing Administration (HCFA) defined a new entity, the independent diagnostic testing facility (IDTF), intended to replace the designation of independent physiological laboratory (IPL). An IDTF is a facility with a supervising physician that is independent of either a physician's office or a hospital. However, at that time the HCFA did not define the supervision required or the specific guidelines for an IDTF.

Recently, Xact Medicare Services, a contracted HCFA carrier for Pennsylvania, sent out a first draft of a local medical review policy on IDTFs that encompasses diagnostic tests in a variety of specialties. Reviewers were asked to comment on the level of supervision, additional physician specialties, and nonphysician personnel requirements.

Randall Winn, MD, a member of SNM and a reviewer of the draft policy, provided a copy of the policy to SNM. On initial review, SNM staff discovered that certified nuclear medicine technologists (CNMTs) were omitted from the table of nonphysician qualifications. SNM staff sent a letter to Xact pointing out this omission and provided additional information on the educational and training requirements of CNMTs.

Although this document affects only the region covered by Xact, other carriers across the nation may be preparing their own IDTF guidelines. A careful review of these documents will be necessary to ensure that similar mistakes are not made. Those wishing to review the Xact draft policy document may do so by contacting the SNM public affairs department.

Society Prepares Letter on NRC Inspection Document

In February the Nuclear Regulatory Commission (NRC) announced plans to initiate a new medical inspection pilot program that would "...streamline inspection and enforcement of materials licensees." The temporary instruction manual for this pilot program claims it is performance-based and risk-informed and that it focuses inspection efforts on licensee performance for radiation safety elements with safety-significant outcomes. However, a comment letter currently being prepared by SNM staff criticizes the inspection document for instituting a level of inspection effort and detail that to an outside observer would indicate that a highly risky procedure was being reviewed. The letter goes on to say that the SNM looks forward to the NRC publishing an inspection document that recognizes the low level of risk involved.

Upcoming Events

APC codes changes go into effect, July 1

Documents Available

SNM Comment Letter on IDTF
SNM Comment Letter on NRC Inspection Manual
APC Alert 1
APC Taskforce Memo on HOPPS

—William Uffelman and Amanda Sullivan