NYT Covers Challenges to RIT Use

In an article published in the July 31 issue of the *New York Times*, reporter Alex Berenson described the remarkable responses of several patients with non-Hodgkin's lymphoma (NHL) to radioimmunotherapy (RIT) regimens with Bexxar (tositumomab and ^{131}I-tositumomab; GlaxoSmithKline, Brentford, UK) or Zevalin (^{111}In-ibritumomab tiuxetan and ^{90}Y-ibritumomab tiuxetan; Biogen Idec, Inc., Cambridge, MA). The story highlighted the small numbers of eligible patients who receive these 2 federally approved treatments and outlined challenges that have discouraged some providers from prescribing RIT or even informing their patients of this alternative to more conventional therapies. More than 60,000 new cases of NHL are diagnosed each year in the United States, with almost 20,000 deaths. Yet, according to the *Times* report, only about 10% (less than 2,000) of suitable patients received Bexxar or Zevalin in 2006.

The article cited both habit and "market-driven forces" that may influence physicians' decisions about prescribing these treatments. Other drugs are preferred and more familiar as first-line treatments in NHL, and some doctors continue to prescribe these even after they have lost their effectiveness. The result is that Bexxar or Zevalin may be prescribed as a "last resort," long after the point at which their therapeutic effects might have been most beneficial.

The financial impediments to wider use of these therapies are more troubling to both cancer patients and nuclear medicine physicians. Many oncologists have "financial incentives to use drugs other than Bexxar and Zevalin, which they are not paid to administer," noted the *Times*. The radionuclide component of the regimen requires administration in and coordination with a hospital setting. Not only is this a logistic complication for many referring oncologists, but it means that Medicare and third-party reimbursement for the treatment goes to the hospital provider.

Several patients interviewed for the study reported that they had received RIT only after asking specifically and adamantly for Bexxar or Zevalin. Although the cost of each of these regimens is high (up to $25,000 per treatment), 1 treatment usually suffices, so that the cost is comparable to that for a full 4-month cycle of chemotherapy and Rituxan. Proponents of RIT told the *Times* reporter that they feared the companies might stop manufacturing the RIT drugs. Although at Newsline press time Biogen Idec continues to manufacture Zevalin, it no longer actively promotes it. A spokesperson for Biogen Idec told the *Times* that the company planned to keep making Zevalin and continue to offer technical support to doctors using it (www.zevalin.com/SupportServices/supportService.htm). GlaxoSmithKline also said it expected to keep making Bexxar and offers resources and reimbursement strategies on its Web site (http://rrc.gsk.com/oncologyacutecare/bexxar.htm).

The New York Times

Rapid Growth in Small Animal Imaging

A markets analysis report released on August 13 by the global consulting firm Frost & Sullivan (Palo Alto, CA) indicates that a combination of federal initiatives and the established reliability of studies published through the peer-review process have led to greater adoption rates for preclinical imaging modalities in the United States. The result, the study's authors concluded, is a "profound impact on the way science is conducted and reviewed in both academic and industry settings" so that "preclinical imaging stands to shape the scientific discovery process as findings get translated to higher vertebrate systems." Revenues from the preclinical small animal imaging market in the United States were estimated at $172.5 million in 2005 and could reach $556 million in 2012.

"Being in the nascent stage only a few years ago, the U.S. preclinical small animal imaging markets have evolved into a competitive landscape with the same range of vendors and imaging capabilities as those found in clinical environments," noted Frost & Sullivan Research Analyst Subha B. Basu. "Optimizing technologies from clinical medicine, preclinical imaging modalities now extend the spectrum of equipment, from CT to MR imaging to ultrasound, as well as several new innovations in molecular imaging." The study cited key initiatives from the National Institutes of Health (NIH) and the U.S. Food and Drug Administration (FDA) as important elements in this evolution. In 2002, the NIH roadmap prioritized the need to identify in vivo biological processes through the expanding field of molecular imaging. The FDA enhanced interest in molecular and preclinical imaging with its 2003 Critical Path to New Medical Products initiative. In the ensuing 4 years, all clinical imaging modalities, from PET to MR and a range of hybrid systems, have been replicated for research in small animal models.

The report cited the dwindling availability of federal and private research grants as well as a lack of general awareness about the benefits of preclinical imaging as the most significant challenges to growth. In addition, high purchase and operational costs are significant factors, especially in academia. Almost 80% of end users in the preclinical market are in the university research setting and dependent on federal and private grant support for the purchase of new equipment.

For more information on the report, see www.frost.com or contact Melina Trevino at melina.trevino@frost.com.

Frost & Sullivan

New Initiative to Study Glycobiology of Cancer

The National Cancer Institute (NCI) announced on August 21 the funding of a new $15.5 million, 5-year initiative to discover, develop, and clinically validate cancer biomarkers by targeting the carbohydrate (glycan) part of molecules. Seven NCI-funded Tumor Glycome Laboratories are now searching for glycan-based biomarkers for melanoma and breast, ovarian, lung, prostate, colon, and pancreatic cancers. "Scientists have long recognized that certain sugar structures, which are attached to protein and lipid molecules, may be important as markers for cancer development," said NCI Director John E. Niederhuber, MD. "While this area has compelling scientific interest, its biological and chemical complexities have often discouraged investigation. Today, with the advent of advanced technologies to conduct protein and carbohydrate chemistry, research into this intriguing area has experienced renewed interest."

Numerous studies comparing normal and tumor cells have shown that changes in the glycan structures of cells correlate with cancer development. Many protein biomarkers also have glycan components, and analysis of these 2 molecular structures together may improve the value of tests such as those for prostate-specific antigen, CA-125, and carcinoembryonic antigen. It is also anticipated that the elucidation of glycan interactions with protein biomarkers within cells may provide powerful new applictions for both PET and fluorescent molecular imaging in a range of cancers.

The NCI's Tumor Glycome Laboratories are the principle component of the new trans-NIH Alliance of Glycobiologists for Detection of Cancer and Cancer Risk. The other components of the alliance are the Consortium for Functional Glycomics funded by the National Institute of General Medical Sciences (NIGMS) and several Glycomics and Glycotechnology Resource Centers supported by the National Center for Research Resources (NCRR). The NCI's Early Detection Research Network (EDRN) is also an alliance member, providing support for design and statistical analysis, patient accrual, and collection of clinical specimens to facilitate validation studies using EDRN's existing components.

"Looking at different types of biomarkers and new ways to identify them is critically important to both the basic understanding of cancer and the ability to identify early cancer and risk for cancer," said Sudhir Srivastava, PhD, chief of the Biomarkers Research Group in NCI's Division of Cancer Prevention. "We believe this new Alliance of Glycobiologists will accelerate the pace of biomarker development and discovery."

The 7 Tumor Glycome Laboratories projects funded by NCI are at Cellexicon, Inc. (La Jolla, CA); Stanford University (Palo Alto, CA); Indiana University (Bloomington, IN); Northeastern University (Boston, MA); University of Georgia (Athens), University of Nebraska (Lincoln), and the University of California at San Diego.

For more information on the Tumor Glycome Laboratories and the NIH Alliance of Glycobiologists for Detection of Cancer and Cancer risk, see the NIGMS Consortium for Functional Glycomics at http://functionalglycomics.org and the NCRR Glycomics and Glycotechnology Research Centers at www.ncrr.nih.gov/Glycomics.

National Cancer Institute

Biomarkers Consortium Grows

Contributing membership in The Biomarkers Consortium now totals 30 companies, nonprofit trade associations, and advocacy groups, including SNM. This large-scale initiative was formally launched in late 2006 to identify and qualify new, quantitative biomarkers for use by biomedical researchers, regulators, and health care providers. According to a July update from the Foundation for the National Institutes of Health (FNIH), the Biomarkers Consortium "will harmonize approaches to identifying viable biomarkers, verify their individual value, and formalize their use in research and regulatory approval." The overall aim of the consortium is to accelerate delivery of technologies, medicines, and therapies for successful prevention, early detection, diagnosis, and treatment of disease. To date, the participating organizations have committed an aggregate of nearly $2 million to fund the first year of the central activities of the consortium, which is managed by FNIH. In addition to FNIH, founding members include NIH, the Food and Drug Administration, and the Pharmaceutical Research and Manufacturers of America.

The 30 contributing members are the Academy of Molecular Imaging; the Advanced Medical Technology Association; the Alzheimer's Association; the American Association for Cancer Research; the American Cancer Society; the American College of Neuropsychopharmacology; the American Society of Clinical Oncology; the Association of Clinical Research Organizations; AstraZeneca; BG Medicine; the Biotechnology Industry Organization; Boehringer–Ingelheim Pharmaceuticals, Inc.; Bristol-Myers Squibb; EMD Serono; the Michael J. Fox Foundation for Parkinson's Research; GlaxoSmithKline; GVK BIOSciences; Johnson & Johnson; the Kidney Cancer Association; the Leukemia & Lymphoma Society; Eli Lilly & Company; Luminex Corporation; Merck & Co., Inc.; Novartis; Novo Nordisk; Pfizer Inc; the Pharmaceutical Research and Manufacturers of America; the Radiological Society of North America; F. Hoffmann–La Roche; and SNM.

The Biomarkers Consortium is now actively soliciting biomarker project concepts from the biomedical research community. If adopted by the consortium, concepts are developed into formal project proposals. Upon approval of project plans by the consortium's executive committee, FNIH then undertakes fundraising for project implementation. For example, to date more than $6 million has been raised from the

private sector to support the consortium's lung cancer and lymphoma cancer biomarker projects, the first projects approved by the consortium.

Concept submissions must succinctly and clearly define the background and rationale for the proposed project and describe findings that demonstrate the feasibility of the proposed study and the likelihood of the expected outcome. Complete information on the Biomarkers Consortium, including its online project concept submission process and how organizations can become involved in the consortium, is available at www.biomarkersconsortium.org.

Foundation for the National Institutes of Health

3D Images of Cells

Employing a reconstruction method similar to that used in 3D CT, researchers at the Massachusetts Institute of Technology (MIT; Cambridge, MA) reported in the September issue of *Nature Methods* (2007;4:717–719) on the development of a new imaging technique that can create 3D images of a living cell. Choi et al. from the G.R. Harrison Spectroscopy Laboratory at MIT described quantitative 3D mapping of refractive indices in live cells and tissues using a phase-shifting laser interferometric microscope with variable illumination angle. The researchers demonstrated tomographic imaging of cells and multicellular organisms and time-dependent changes in cell structure. They noted that this technique will permit "quantitative characterization of specimen-induced aberrations in high-resolution microscopy and have multiple applications in tissue light scattering." In an accompanying press release, Michael Feld, PhD, senior author and director of the Harrison Lab, said "Accomplishing this has been my dream, and a goal of our laboratory, for several years. For the first time the functional activities of living cells can be studied in their native state."

To create a 3D image, the researchers combined 100 2D images acquired from different angles. The resulting images are essentially 3D maps of the refractive index of the cell's organelles. At the time of preparation of the original article, the entire process took about 10 seconds, but the researchers recently reduced this time to 0.1 seconds.

Using the new technique, the researchers obtained 3D images of cervical cancer cells, showing internal cell structures, and several other cell types. They also imaged C. elegans specimens. The image of a cervical cancer cell reveals the cell nucleus, the nucleolus, and a number of smaller organelles in the cytoplasm. The researchers are currently attempting to better characterize these organelles by combining these techniques with fluorescence microscopy.

"One key advantage of the new technique is that it can be used to study live cells without any preparation," said Kamran Badizadegan, MD, principal research scientist in the laboratory and an author of the article. No freezing, staining, or other preparative processing is required. "When you fix the cells, you can't look at their movements, and when you add external contrast agents you can never be sure that you haven't somehow interfered with normal cellular function," said Badizadegan.

The current resolution of the new technique is about 500 nanometers, but the team is working on improving the resolution. "We are confident that we can attain 150 nanometers, and perhaps higher resolution is possible," said Feld. "We expect this new technique to serve as a complement to electron microscopy, which has a resolution of approximately 10 nanometers."

Massachusetts Institute of Technology

SINAPSE Network Launched in Scotland

The Scottish Funding Council and 6 Scottish universities announced in early August the launch of a new £40 million initiative to improve the infrastructure for neuroimaging research in Scotland. Called SINAPSE (Scottish Imaging Network: A Platform for Scientific Excellence), the project includes chairs, faculty, and graduate students from the University of Edinburgh, the University of Aberdeen, the University of St. Andrews, the University of Dundee, the University of Stirling, and the University of Glasgow.

The objectives for this network are to: (1) develop the Scottish academic imaging expertise to address a broad range of clinical questions by making key appointments to chairs in image analysis, neuroimaging physics, and functional imaging, supported by intermediate-level researchers in image acquisition/paradigm design, image analysis, and tracer development; (2) re-establish world-leading, cutting-edge imaging equipment for the Scottish brain research community, compatible between imaging centers; (3) increase patient access to clinical research by supporting government initiatives to develop clinical research collaborations in key disease areas and the Scottish Executive's PET imaging initiative; (4) encourage the further career development of intermediate-grade researchers to full independence and provide cohesive doctoral training programs between universities to develop future generations of imaging researchers in Scotland; (5) increase the ability of brain researchers to conduct clinical trials; (6) attract funding from national and international government organizations, the European Union, nongovernment sources, and industry; and (7) have a direct impact on patient health.

SINAPSE

Americans and Cancer Information

According to *Cancer Communication: Health Information National Trends Survey 2003 and 2005*, released by the National Cancer Institute (NCI) on August 29, the Internet remains a frequent first source for Americans about general health and cancer information. Confidence in the quality of such online information has declined, however, and most individuals surveyed expressed greater confidence in direct communication with health care professionals. The publication includes the results of the Health Information National Trends Survey (HINTS), a study conducted by NCI in alternate years since 2003. The randomly dialed

(Continued on page 31N)

previous animal research and clinical psychopharmacological studies."

Molecular Psychiatry

Thalidomide and Thyroid Cancer

Ain et al. from the Veterans Affairs Medical Center (Lexington, KY) and the University of Kentucky (Lexington) reported in the August issue of *Thyroid* (2007;17:663–670) on the results of a phase II trial of thalidomide for therapy of radioiodine-unresponsive and rapidly progressive thyroid carcinomas. The study included 36 patients with follicular, papillary, insular, or medullary thyroid carcinomas and distant, radioiodine-unresponsive metastases (defined as volumes increasing at a rate ≥30% per year before entry into the study). Daily thalidomide was initiated at 200 mg, increasing over 6 weeks to 800 mg or maximum tolerated dose. Toxicities and responses, including tumor volumes, were assessed at 8-week intervals throughout the study. Of the 28 patients who were evaluable for inclusion in results analysis, 5 (18%) had partial responses (median duration, 4 months) and 9 (32%) had stable disease (median duration, 6 months). Median survival for responders was 23.5 months and for nonresponders was 11 months. The most frequent toxicity-associated complication was fatigue (77%). Four patients had grade 3–4 infections (without neutropenia), 1 had pericardial effusion, and 1 had pulmonary embolus. The authors concluded that "thalidomide confers therapeutic benefit in subsets of thyroid cancer patients with rapidly progressive, distantly metastatic disease."

Thyroid

Viral-Derived Peptide for Cancer Imaging

Hausner et al. from the University of California, Davis and the Queen Mary's School of Medicine and Dentistry (London, UK) reported in the August 15 issue of *Cancer Research* (2007;67:7833–7840) on the use of a peptide derived from the foot-and-mouth disease virus for PET imaging of $\alpha_v\beta_6$ expression in human cancers. The authors previously identified this peptide as a potent and highly selective inhibitor of $\alpha_v\beta_6$ expression. In vitro and in vivo studies in cancer xenografts in mice reported in this article provide supportive data. In the mouse studies, viral-derived peptide was found to have rapid uptake and selective retention (>5 hours) in $\alpha_v\beta_6$-positive but not in $\alpha_v\beta_6$-negative tumors, as well as fast renal elimination. Specific imaging of $\alpha_v\beta_6$-positive tumors was achieved, and the peptide was described as "an important new tool for early detection and improved management of many types of cancers."

Cancer Research

(Continued from page 26N)

telephone survey recorded the responses of more than 6,300 people in 2003 and more than 5,500 people in 2005.

Use of the Internet as a source for cancer-specific information remained relatively unchanged during the study period. However, the number of people using the Internet to communicate with their health care providers or providers' offices through a Web site (including e-mailing questions and scheduling appointments) increased from 7% in 2003 to 10% in 2005. Use of the Internet to gather health information about topics other than cancer increased from 2003 to 2005. In 2003, 51% of respondents reported looking for health information for themselves and 46% for someone else. In 2005, these respective percentages were 58% and 60%. Women were more likely to search for cancer information from all sources than men, and people aged 50–64 years were most likely to search for cancer-specific information.

"The survey is not only a surveillance tool but can be used to study relationships of how knowledge about health care is dependent on channels of communication," said Bradford Hesse, PhD, chief of NCI's Health Communication and Informatics Research Branch.

The researchers also looked at changes in cancer knowledge and beliefs and worked with statisticians and geographic information systems specialists to create maps to visualize regional geographic variation, much like a weather map. These maps are created by using information from neighboring states to provide information for areas with relatively small sample sizes. The maps in the report will allow researchers and health care providers to visually identify areas of the country in need of improved or targeted health communication. The maps also illustrate knowledge about breast and colorectal cancer screening recommendations, as well as general knowledge about the human papillomavirus, cervical cancer, and lung cancer. The maps, as well as data from both the 2003 and 2005 HINTS surveys, are available to researchers and health care providers throughout the country for their own programs and planning.

"Population-based surveys such as HINTS give us a rich source of knowledge about the awareness of the American public," said NCI Director John E. Niederhuber, MD. "Our next step must be to research how best to translate newfound understandings of patterns and preferences into better ways of educating and serving all of our patients through cancer prevention, screening, treatment, and survivorship."

For more information about HINTS, see http://cancercontrol.cancer.gov/hints.

National Cancer Institute

FDA Approves NDA for ^{13}N-Ammonia Injection

On August 23, the U.S. Food and Drug Administration (FDA) approved a new drug application (NDA) for a ^{13}N-ammonia injection product, under the title "Ammonia N 13 Injection." The approved NDA reference number