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Radioimmunotherapy Agent Approved for Non-Hodgkin's Lymphoma

The U.S. Food and Drug Administration has granted approval for the first radioimmunotherapy agent, Zevalin™ (ibritumomab tiuxetan, IDEC Pharmaceuticals, San Diego, CA). Zevalin, as part of the Zevalin therapeutic regimen, is indicated for patients with relapsed or refractory low-grade, follicular, or transformed B cell non-Hodgkin's lymphoma (NHL), including patients with Rituxan® (rituximab, IDEC Pharmaceuticals) refractory follicular NHL.

Radioimmunotherapy is a promising new area of cancer treatment that combines the targeting power of monoclonal antibodies with the cell-damaging ability of localized radiation. Radioimmunotherapy agents are made by linking monoclonal antibodies, which are engineered to recognize and attach to substances on the surface of certain cells, to radioactive isotopes. These radiation-carrying antibodies circulate until they locate and bind to the surface of specific cells to deliver their cytotoxic radiation directly to malignant cells. Zevalin binds to both malignant and normal B cells. Normal B cells generally are replenished within six to nine months following therapy. Lymphoma tumors are very sensitive to radiation, but targeting external beam radiation to cancerous immune system cells throughout the body is difficult. Zevalin combines a monoclonal antibody with the cancer-killing ability of radiation. Zevalin is linked to the radioisotope yttrium-90 that targets the CD20 antigen.

The Zevalin therapeutic regimen consists of Rituxan, followed by indium-111 Zevalin. Seven to nine days later, a second infusion of Rituxan is administered, followed by yttrium-90 Zevalin. The Zevalin therapeutic regimen consists of two low doses of Rituxan (250 mg/m^2), an imaging dose of Zevalin, two or three whole body scans to assess the efficacy of biodistribution, and a therapeutic dose of Zevalin, all delivered on an outpatient basis over eight days. The recommended dose is 0.4 mCi/kg for patients with platelet counts greater than 150,000 and 0.3 mCi/kg for patients with platelet counts between 100,000–149,000. For all patients, the maximum dose is 32 mCi. Zevalin is not recommended for patients with platelet counts below 100,000.

The effectiveness of the Zevalin therapeutic regimen in a relapsed or refractory patient population was based on overall response rates in two studies. The first study was conducted in 54 patients with relapsed follicular lymphoma who no longer responded adequately to Rituxan; 74% showed an overall response rate to treatment with Zevalin with 15% of patients achieving a complete remission to therapy according to the International Workshop Response Criteria (IWRC).

The second study, a phase III, randomized, controlled trial, which supported accelerated approval, was conducted in 143 patients with relapsed or refractory, low-grade or follicular NHL or transformed B cell NHL. The 73 patients who received the Zevalin therapeutic regimen showed an overall response rate of 80%, compared to 56% in 70 patients who received Rituxan alone, according to IWRC. Thirty percent of patients receiving Zevalin achieved a complete remission and 4% achieved an unconfirmed complete remission to therapy, compared to 16% of patients receiving Rituxan who achieved a complete remission and 4% who achieved an unconfirmed complete remission, according to IWRC.

In safety data based on 349 patients, the most serious adverse reactions of the Zevalin therapeutic regimen included severe infusion reactions (e.g., hypotension, angioedema, hypoxia, bronchospasm) and severe and prolonged cytopenias, including thrombocytopenia (61% of patients with platelet counts less than 50,000 cells/mm$_3$) and neutropenia (57% of patients with absolute neutrophil counts less than 1,000 cells/mm$_3$) in patients with a platelet cell count greater than 150,000/mm$_3$ prior to treatment. Severe infections (predominately bacterial in origin) and hemorrhage, including fatal cerebral hemorrhage, have occurred in a minority of patients in clinical studies. Also seen were myeloid malignancies and dyscrasias (e.g., myelodysplastic syndrome). The most common toxicities reported were neutropenia, thrombocytopenia, anemia, gastrointestinal symptoms (e.g., nausea, vomiting, abdominal pain, diarrhea), increased cough, dyspnea, dizziness, arthralgia, anorexia, and ecchymosis. Hematologic toxicity often was severe and prolonged, whereas most nonhematologic toxicity was mild in severity. The effects of the Zevalin therapeutic regimen on survival are not known.

Zevalin should be used only by healthcare professionals qualified by training and experience in the safe use of radionuclides and monoclonal antibodies. Deaths have occurred within 24 hours of rituximab infusions. These fatalities were associated with an infusion reaction symptom complex that included hypoxia, pulmonary infiltrates, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation, or cardiogenic shock. Yttrium-90 Zevalin administration results in severe and prolonged cytopenias in most patients.

For more information, contact IDEC Pharmaceuticals at 877-878-4332 or visit the Zevalin Web site at www.zevalin.com.

New Therapy Approved for Hormone Receptor Positive Breast Cancer

The U.S Food and Drug Administration has announced the approval of Faslodex® Injection (fulvestrant, AstraZeneca Pharmaceuticals, Wilmington, DE), indicated for the treatment of hormone receptor positive metastatic breast cancer in postmenopausal women with disease progression following antiestrogen therapy. Faslodex is administered to patients in a monthly, 250 mg intramuscular injection.

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Digital Object Identifier: 10.1188/02.ONF.999-1001

Many breast cancers contain estrogen receptors within their cells. To survive and reproduce, these cancers depend on the hormone estrogen. Researchers have found that using hormonal agents that prevent estrogen from binding to these receptors in cancer cells helps slow the growth of cancer. Faslodex's approval was based on phase III trials that compared Faslodex with Arimidex® (anastrozole, AstraZeneca Pharmaceuticals) in postmenopausal women who previously had been treated with hormone therapy. In one of the trials, the median time to progression was 5.4 months among patients treated with Faslodex versus 3.4 months for patients treated with Arimidex. The median duration of response was roughly nine months longer with Faslodex than with Arimidex. Faslodex interferes with the binding of estrogen by destroying estrogen receptors in breast cancer cells. Arimidex prevents the production of estrogen in adrenal glands.

The most commonly reported adverse events seen with Faslodex versus Arimidex treatment, regardless of investigators' assessments of causality, were gastrointestinal symptoms (i.e., nausea, 26% versus 25.3%; vomiting, 13% versus 11.8%; constipation, 12.5% versus 10.6%; diarrhea, 12.3% versus 12.8%; abdominal pain, 11.8% versus 11.6%), headache (15.4% versus 16.8%), back pain (14.4% versus 13.2%), hot flushes (17.7% versus 17.3%), and pharyngitis (16.1% versus 11.6%). Injection site reactions with mild, transient pain and inflammation were reported in 7% of patients (1% of treatments) given one 5-mL dose and 27% of patients (4.6% of treatments) given two 2.5-mL injections of Faslodex. Faslodex can cause fetal harm when administered to pregnant women. Women of childbearing potential should be advised not to become pregnant while receiving Faslodex. Faslodex is metabolized primarily in the liver; however, no dosage adjustment is needed in patients with mild hepatic insufficiency. Safety and efficacy have not been evaluated in patients with moderate to severe hepatic impairment. No dosage adjustment is needed in patients with mild to moderate renal insufficiency.

For more information, contact AstraZeneca Pharmaceuticals at 866-992-9276 or visit the Faslodex Web site at www.faslodex.com.

New Sustained-Release Opioid Analgesic Available

Ligand Pharmaceuticals (San Diego, CA) has begun marketing Avinza™ (morphine sulfate) extended-release capsules. Avinza is indicated for the once-daily treatment of chronic, moderate to severe pain in patients who require continuous, around-the-clock pain management therapy for an extended period of time.

Using proprietary controlled release technology (Spheroidal Oral Drug Absorption System or SODAS®), Avinza gives patients protection from moderate to severe pain over a 24-hour period. Avinza's novel dual release formulation contains immediate- and sustained-release morphine beads. Once steady-state plasma levels of morphine are achieved, immediate-release beads enable Avinza to provide rapid exposure to morphine. The sustained-release beads enable morphine to be absorbed by the body gradually, thus maintaining plasma morphine levels over a 24-hour dosing period.

Avinza capsules are available in 30 mg, 60 mg, 90 mg, and 120 mg strengths and contain immediate-release and extended-release beads of morphine sulfate for once-daily oral administration. Avinza capsules should be swallowed whole, or the contents of the capsules may be sprinkled on applesauce immediately prior to ingestion. The capsule beads are not to be chewed, crushed, or dissolved because of the risk of rapid release and absorption of a potentially fatal dose of morphine. The 60 mg, 90 mg, and 120 mg capsules are for use only in opioid-tolerant patients.

As with any opioid, adjusting the dose of Avinza for an individual patient and taking into account the patient's prior experience with opioid analgesics are critical. Avinza is not intended for use on an as-needed basis. The safety and efficacy of using Avinza in the postoperative setting have not been evaluated,

and Avinza is not indicated for postoperative use. Avinza is contraindicated in patients with known hypersensitivity to morphine, morphine salts, or any components of the product. Avinza should be administered cautiously and in reduced dosages in patients who are elderly or debilitated or have severe renal or hepatic insufficiency, Addison's disease, hypothyroidism, prostatic hypertrophy, or urethral stricture. When patients who have been receiving treatment with Avinza for more than a few weeks must end therapy, healthcare providers should counsel them on the importance of safely tapering the dose and inform patients that abruptly discontinuing the medication could precipitate withdrawal symptoms. The daily dose of Avinza must be limited to a maximum of 1,600 mg per day. Avinza doses over 1,600 mg per day contain a quantity of fumaric acid (a component of Avinza capsules that promotes absorption of the drug within the gastrointestinal tract by acting as an osmotic agent and a local pH modifier) that has not been demonstrated to be safe and may result in serious renal toxicity.

In addition to analgesia, the widely diverse effects of morphine include drowsiness, changes in mood, respiratory depression, decreased gastrointestinal motility, nausea, vomiting, and alterations of the endocrine and autonomic nervous systems. As with other opioids, patients taking Avinza should be advised of the potential for severe constipation and given appropriate laxatives or stool softeners as well as other treatments that should be initiated from the onset of opioid therapy. Avinza is a mu-agonist opioid and is a schedule II controlled substance.

For more information, contact Ligand Pharmaceuticals at 800-964-5836 or visit its Web site at www.ligand.com.

NEW PROGRAMS

National Institutes of Health Launches New Information Center

The National Human Genome Research Institute and the National Institutes of Health's Office of Rare Diseases, both in Bethesda, MD, have launched a new information center that delivers free and immediate access to information specialists who can provide accurate, reliable information about genetic and rare diseases to patients and their families.

More than 6,000 genetic and rare diseases afflict more than 25 million Americans, but many of these illnesses affect relatively few individuals. As a result, information about rare disorders may be limited or difficult to find. The new service, called the Genetic and Rare Diseases Information Center, will help relieve this problem by providing reliable information about individual disorders. The center provides experienced information specialists who personally answer questions from patients and family members on the phone, by e-mail, or via fax. The center provides authoritative information about specific illnesses from existing public domain sources, including reliable Web sites, brochures, articles, and book chapters. Experts at the information center ensure that the information sent out is current and accurate. The center, however, does not provide genetic counseling and does not offer diagnostic testing, referrals, medical treatment, or advice.

Calls are answered Monday–Friday from 12–6 pm EST by phone and TTY. For more information, contact the Genetic and Rare Diseases Information Center at 888-205-2311 (888-205-3223, TTY; 202-966-5689, fax; gardinfo@nih.gov, e-mail).

Volunteer Your Computer to Cure Cancer

The National Foundation for Cancer Research (NFCR) (Bethesda, MD), Oxford University's NFCR Center (Oxford, UK), and United Devices, Inc™ (Austin, TX) have joined forces to launch a virtual computer project that screens new drugs to combat cancer. The Intel-United Devices Cancer Research Project is asking for volunteers to lend their personal computers to help process molecular research being conducted by the NFCR and the department of chemistry at the University of Oxford in England. To participate, volunteers simply download a very small, free, and noninvasive software program

that works like a screensaver. The program runs when volunteers' computers are not being used and does not interrupt regular computer use. A similar initiative, designed to screen molecules that may be potential inhibitors of the anthrax protein, completed work in just 24 days that traditionally would have taken years.

The project uses a drug discovery software application, known by the acronym THINK (To Have INformation and Knowledge). The THINK application continuously runs on volunteers' computers like a screensaver, using very little resources. When computers are idle, the THINK screensaver leaps to the foreground, enabling users to watch as the software analyzes a packet of molecules that eventually might prove promising for cancer drug development. The project software cannot detect or transfer anything but project-specific information on volunteers' machines as it screens molecules that may be developed into drugs to fight cancer. Each computer analyzes a few molecules and then sends the results back over the Internet for further research. The goal is to enlist enough volunteers to provide very rich and thorough results to the University of Oxford for further research. This project is anticipated to be the largest computational chemistry project ever undertaken and represents a genuine hope to find a better way to fight cancer. The results of this study are the intellectual property of the University of Oxford and NFCR, who will make the scientific findings of this project available to the greater scientific community. This project is an historic first use of the Internet as a computing platform to solve a critical, real-world problem with a scope and speed that simply could not be achieved using traditional computing models. A number of security features have been built into the project to ensure the privacy of individual computer users and minimize security risks to participants.

Background information on the project, the results it has achieved thus far, instructions for downloading the software, frequently asked questions, details about the security features, and an active forum with other project participants are available at the United Devices Web site. New volunteers can learn more about the project or download THINK and an initial packet of molecules from the Web site at www.ud.com.

Pharmaceutical Companies Form Alliance to Offer Savings on Medications

Millions of American seniors are caught in a gap between not qualifying for prescription drug coverage under Medicaid yet not having the financial resources to pay for the medicines they need. As a result, these seniors often choose to go without necessary medications, potentially jeopardizing their health. Several pharmaceutical corporations recently have launched programs to make prescriptions more affordable for low-income, older individuals who lack drug coverage.

A new pharmaceutical company alliance has been formed to offer savings on more than 150 medications to limited-income seniors through one free card. The Together Rx™ Card offers access to savings on more medicines than any existing pharmaceutical company savings program, making it easier for 8–11 million Medicare enrollees who have no prescription drug coverage to get the medicines they need to help them maintain active and independent lifestyles.

Through the Together Rx Card program, Medicare enrollees without public or private prescription drug coverage and with incomes of up to $28,000 ($38,000 for couples) can obtain savings of about 20%–40% or more off the price they usually pay for prescription medicines by purchasing them directly from the manufacturers through a variety of savings options.

In addition, individuals of more limited income who meet eligibility requirements for patient assistance programs (PAPs) may qualify for further savings and, in some cases, free medicines. The members of Together Rx are committed to maximizing enrollment in the Together Rx Card and identifying patients who may qualify for independent PAPs.

The founding members of Together Rx, L.L.C. are Abbott Laboratories, AstraZeneca Pharmaceuticals, Aventis Pharmaceuticals, Bristol-Myers Squibb Company, GlaxoSmith Kline, Johnson and Johnson, and Novartis Pharmaceuticals Corporation. Together, they offer savings on more than 150 prescription medicines, including 26 different medicines used to treat the conditions most commonly affecting older Americans (e.g., diabetes, hypertension, high cholesterol, cancer, infections, epilepsy, allergy, asthma, arthritis, depression). For more information and an application form, call Together Rx at 800-865-7211 or visit its Web site at www.togetherrx.com.

Eli Lilly and Company Creates Discount Program for Medicare Recipients

Eli Lilly and Company (Indianapolis, IN) is launching LillyAnswers℠, a companion to the LillyCares patient assistance program. The LillyAnswers card allows seniors and people with disabilities who receive Medicare coverage to pay a flat $12 fee for a 30-day supply of any retail-distributed Lilly drug. The LillyAnswers program also will supply educational materials and information to help people deal with the complex challenges illnesses present. Under the LillyAnswers card program, all Lilly retail products will be offered, except controlled substances, as well as products not distributed by retail pharmacies. The program offers many medications commonly prescribed to seniors, such as Evista® for osteoporosis, Humulin® and Humalog® for diabetes, Prozac® for depression, and Zyprexa® for schizophrenia.

For more information on the LillyAnswers program, call 877-RX-LILLY or visit its Web site at www.lillyanswers.com. The LillyCares patient assistance program provides products to uninsured patients who need Lilly medicines but cannot afford them. For more information about this program, contact LillyCares at 800-545-6962.