



Designated by the
National Cancer Institute

Roswellness *for Doctors*

Updates on Cancer Advances and Patient Care

*In the Business to Save Lives...
through Research, Prevention and Innovative Treatment*



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The PITFALLS of Off-Label Drugs



by **Maureen Kelly, RN**
Assistant Vice President for Clinical Affairs

A Knight Ridder study estimates that 115 million prescriptions for off-label uses of drugs were written in 2002 – double the total for 1997. In response to this significant rise in off-label prescriptions, some medical institutions are beginning to impose restrictions on the off-label use of drugs, due to concerns about patient safety, the need to systematically collect information about a drug's effectiveness for new applications, and cost. Both hospitals and payers are taking a harder look at the pitfalls associated with off-label prescribing, especially in the field of oncology.

Why? Patient safety is of paramount concern. Cancer drugs in particular are highly toxic and can produce debilitating side effects – even when used in accordance with FDA-approved prescribing information. Prescribing such drugs for untested and unapproved uses may place the patient at greater risk.

Second, when such drugs are utilized outside the parameters of a labelling indicator or clinical study, no mechanism is in place to systematically collect data on

patient outcomes. Information which could be critical to the development of effective new therapies is therefore lost to the medical community. Documented results are essential to the development of new cancer treatments and therapies.

Third, many new cancer drugs are extremely expensive, some costing upward of \$4,000-\$6,000 per dose. Many insurance companies will not cover the cost of medications for off-label use – and Medicare is now considering a proposal to limit coverage for all off-label prescriptions. Because the cost is financially out of reach for most patients, hospitals and institutions may not receive any reimbursement for these services.

Although these concerns are prompting some cancer hospitals to set conditions for off-label prescriptions, at present there is no sign of an across-the-board prohibition. That's because off-label use has led to effective new applications. The American Cancer Society acknowledges that off-label drugs "provide millions of cancer patients with some of the most

cutting-edge treatments available." The U.S. General Accounting Office reports that a third of drugs prescribed by cancer doctors in 1991 were off-label, and that more than half of all cancer patients received drugs that were prescribed off-label.

In most instances, only the newest drugs will be affected by restrictions on off-label use. For example, both Medicare and local payers will likely require strict on-label use for recently approved cancer drugs, including:

- Avastin® (bevacizumab), used in combination with 5-fluorouracil for first-line treatment of metastatic carcinoma of the colon or rectum;
- Erbitux® (cetuximab), used in combination with irinotecan for treatment of EGFR-expressing, metastatic colorectal carcinoma in patients who are refractory to irinotecan-based chemotherapy, and as a single agent for the treatment of EGFR-expressing metastatic colorectal carcinoma in

patients intolerant to irinotecan-based chemotherapy;

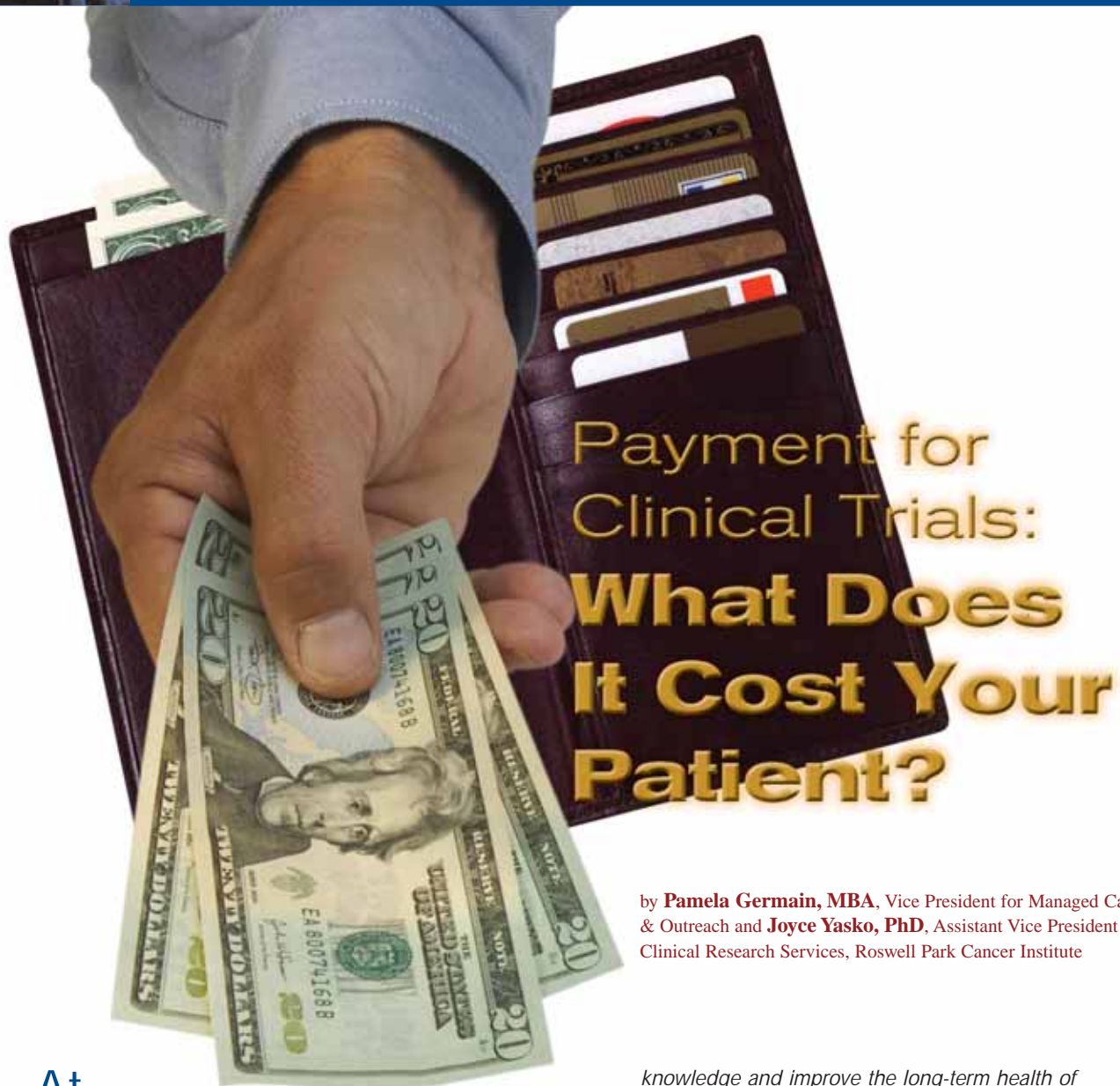
- Ontak® (denileukin diftitox), for treatment of patients with persistent or recurrent cutaneous T-cell lymphoma whose malignant cells express the CD25 component of the IL-2 receptor.

The best interest of patients and the advancement of science will require oncologists, pharmaceutical companies, the government, insurance companies and hospitals to work together to develop a tenable policy, somewhere between permitting unrestricted off-label use of drugs and forbidding off-label use under any circumstances. Medicare's existing guidelines provide a starting point. There are clear-cut rules for approving new indications for drugs: either off-label indications must be listed in pharmacological compendia, or, at the local level, institutions may request approval from a local Medicare intermediary by submitting peer-reviewed articles that build the case for a new application.

Clearly, more clinical trials and studies are needed. To make the studies financially feasible, costs should be borne jointly by drug companies, hospitals, the government and insurance companies. By providing free drugs for both first trials and new-application trials, drug companies will stand to benefit when study results support the use of new applications. By covering standard-of-care costs for patients involved in those studies, government and the insurance companies will lay the groundwork for significant improvements and cost reductions in our nation's health system.

Most important, the off-label policy that evolves from such studies and trials will provide patients with faster access to promising new drugs without putting them at undue risk, thus ushering in a higher standard of medical care.

For those struggling with this issue, please feel free to contact Maureen Kelly at 716-845-1410 or at maureen.kelly@roswellpark.org.



Payment for Clinical Trials: What Does It Cost Your Patient?

by **Pamela Germain, MBA**, Vice President for Managed Care & Outreach and **Joyce Yasko, PhD**, Assistant Vice President for Clinical Research Services, Roswell Park Cancer Institute

knowledge and improve the long-term health of future generations of cancer patients?

It is important for patients to understand from the very beginning that these studies provide access to the latest drugs and therapies, many of which provide benefits not available with standard therapies. However, while the manufacturers of drugs being evaluated usually provide them free of charge, other aspects of treatment will be billed as they would be if the patient was not participating in a clinical research study.

Costs are shared by the study sponsor, the patient's insurance company, the institute, and the patient.

Before a clinical trial begins at Roswell Park Cancer Institute (RPCI), a budget is established that shows clearly the breakdown of costs and the portion for which each party is responsible. These include:

- **Investigational costs**, which are assumed by the study sponsor – usually a pharmaceutical company or an NIH grant. These include anything not associated with standard of care – for example, in Phase I or Phase II trials, pharmacokinetic (PK) procedures that monitor how a drug is metabolized at specific intervals after administration. Because PK monitoring usually provides no direct medical benefit to the patient, the procedure cannot be classified as standard of care.
- **Standard-of-care procedures** are billed to the insurance company or paid by the patient. These include care that would be necessary for cancer treatment. Medicare and some payers will cover standard-of-care costs for Phase I through Phase III trials that are determined to have therapeutic intent.
- **Costs not covered by the payer or the study sponsor.** The patient must pay these costs.



In an effort to seek broader coverage for care associated with clinical research studies, RPCI works proactively with our region's three principal payers to underscore the importance of clinical research in the improvement of cancer care. This is especially critical in the case of employers' self-funded insurance plans, which tend to be more rigid about cost containment, often rejecting claims for any items or services that are deemed to be investigational or experimental. RPCI negotiates coverage with insurers, emphasizing the fact that it has a Scientific Review Committee and an Institutional Review Board (IRB) that subjects every study to a critical review and advances those that meet stringent criteria and offer therapeutic and promising effects. Our extraordinarily high standards enable us to build accountability over the long term so that payers can better understand the value of

clinical research and the careful planning and control that accompanies the research process.

We've recently initiated a data system that identifies the patients at RPCI who are participating in clinical research studies and the insurance companies that provide their health coverage. Ultimately this information will enable payers to compare the outcomes and associated costs of their members who have participated in clinical research and those with the same diagnoses who are treated with conventional therapies. A comparative cost analysis will help determine which method of care is less expensive, as there is little evidence in the literature of studies providing comparative cost information. It is hoped that this type of collaboration will make payers more receptive to reimbursing providers for care associated with clinical research studies.

In addition, Roswell Park Cancer Institute is refining the financial-clearance process that precedes a patient's consent to participate in a clinical research study. The informed consent form outlines the study protocol- associated cost and the portion of the cost each party is expected to pay. This process also will provide specific information about the components of a research study and what components the patient's insurance company will and will not pay for and those research study costs that he/she must assume.

As a comprehensive cancer center, Roswell Park Cancer Institute is actively engaged in seeking a cure for cancer. That goal is predicated partly on the recruitment of patients who might realize significant benefits from enrolling in a clinical research study. Removing barriers, such as misperceptions about costs, that may impede a patient's access to all therapeutic options, is an important component of our work.

To learn more about clinical trials at RPCI, contact Joyce Yasko at 716-845-8660 or at joyce.yasko@roswellpark.org. or call the Referral Office at 1-800-ROSWELL.

At comprehensive cancer centers, many patients are eligible to participate in clinical trials.

In our experience, we have found that many potential participants assume – albeit erroneously – that they will receive drugs and services at no charge simply because they have volunteered to take part in a clinical research study. Surprised to learn that there will be costs incurred for participating in clinical trials, patients ask: *Why should we have to pay for the privilege of testing a new cancer treatment that may not offer any benefit to us? Aren't we essentially giving enough by volunteering to advance medical*

your partners for a Cancer Cure are @ www.roswellpark.org



Roswell Park Cancer Institute was the first facility in the nation dedicated to the understanding and treatment of cancer. It remains one of the world's foremost cancer research centers, developing new therapies, technologies, diagnostics, and pharmaceuticals that are changing the lives of cancer patients globally.

Founded in 1898, RPCI is the only National Cancer Institute-designated comprehensive cancer center in Upstate New York. Its 25-acre campus, located near the shore of Lake Erie, consists of 15 buildings with a new 119-bed hospital building, a comprehensive diagnostic and treatment center and a newly built medical research complex.

TEN REASONS FOR CHOOSING A COMPREHENSIVE CANCER CENTER FOR YOUR PATIENT'S CARE

1. A multidisciplinary team of experts who devote 100% of their work lives to the study, prevention, diagnosis, treatment and management of these cancers.
2. An individualized care plan that meets the medical, psychosocial and spiritual needs of patients and their families.
3. A full range of diagnostic options.
4. A full complement of surgical options, including new treatments in medicine and radiation therapy.
5. Comprehensive treatment services in one coordinated setting.
6. Access to the latest, most promising clinical trials for cancer.
7. Rehabilitation programs, genetic counseling and cancer registries.
8. A resource center for up-to-date information and resources.
9. An effective pain management program.
10. Physicians who take a national leadership role in standardized best practice guidelines and improving the quality of care and life for all patients.

SPECIALIZED TREATMENTS

- ♦ Clinical Trials ♦ Blood & Marrow Transplantation
- ♦ Clinical Genetics Testing and Counseling ♦ High-dose Chemotherapy
- ♦ Photodynamic Therapy ♦ Gamma Knife
- ♦ Follow-up Clinic for Long-Term Survivors of Childhood Cancer
- ♦ Minimally Invasive Surgical Procedures
- ♦ Regional Center for Maxillofacial Prosthetics
- ♦ The Buffalo-Niagara Prostate Cancer Consortium
- ♦ Center for HIV-related Malignancies

MULTIDISCIPLINARY CENTERS

- ♦ Breast Center ♦ Pediatric Center ♦ Gynecology Center
- ♦ Chemotherapy and Infusion Center ♦ Gastrointestinal Center
- ♦ Dermatology Sarcoma and Melanoma Center
- ♦ Head and Neck/Dental Center ♦ Hematology Center
- ♦ Neuro-oncology Center ♦ Pain Management Center
- ♦ Thoracic Center ♦ Urology Center

At Roswell Park, a multidisciplinary team approach to care is taken, which means each and every staff member is on your team.

Below are 16 of RPCI physicians who are included in the *Best Doctors in America* listing.



Donald Trump, MD



Maria Baer, MD



Myron Czuczman, MD



Wesley Hicks, Jr., DDS, MD, FACS



Ellis Levine, MD



Philip McCarthy, Jr., MD



Allan Oseroff, MD, PhD



Martin Brecher, MD



Daniel Green, MD



Stephen Edge, MD, FACS



John Gibbs, MD, FACS



William Kraybill, MD



Boris Kuvshinov, II, MD



Thom Loree, MD, FACS



Robert Huben, MD



Shashikant Lela, MD

Saturday, June 18, 2005

American Society of Clinical Oncology (ASCO)

7:30 am – 12:30 pm
Gaylord-Cary Room
Hilleboe Auditorium
Roswell Park Cancer Institute

This program is designed to provide primary care physicians, oncologists, urologists, gastroenterologists, gynecologists, pharmacists, nurse practitioners and physician assistants with a summary of the latest data and research findings in breast, lung, GI and GU cancers presented at the 2005 Annual Meeting of the American Society of Clinical Oncology (ASCO). The program will focus on how these new data and research will impact the practice of oncology.

Following this program, participants should be able to:

- Describe recent advances in the diagnosis and management of major cancer sites
- Discuss appropriate uses for newly approved drugs and therapies
- Identify practice behaviors that could be affected by new research findings presented at the 2005 ASCO meeting

Call 716-845-5706 for more information, or visit our website at www.roswellpark.org.

A maximum of 4.5 hours of AMA Category 1 credit will be offered.

Roswell Park Cancer Institute is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

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Continuing Medical Education Calendar

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