

Worth the Cost?

Pharmacotherapy Outcomes Research Evaluates New Drugs

Prescription drug prices have nearly doubled in the last 10 years. The rising costs are due in large part to the continual influx of new drugs into the marketplace. They may promise better treatment, but they also can require more expensive technologies, which contribute to skyrocketing health insurance premiums. It's enough to give everyone—patient, provider, and insurer—a headache, especially in these tough economic times when an essential question remains unanswered: Is the cost of the new drug justified, if it offers only a slim improvement over existing ones?

Diana I. Brixner, Ph.D., R.Ph., set out to address this predicament. Not long after she was hired as chair of the Department of Pharmacotherapy at the University of Utah College of Pharmacy in 2002, she established the college's Pharmacotherapy Outcomes Research Center (PORC), which she directs.

"There are limited financial resources to spend on pharmaceutical therapy. This puts pressure on pharmacy directors and insurance companies in the United States—and health policy and government regulators around the world—to decide whether they should pay for that new drug technology," said Brixner, who just completed a term as president of the International Society for Pharmacoeconomics and Outcomes Research.

"Managed health care and insurance companies especially are interested in the work we do," added Brixner. "The results of our studies help them make decisions on whether they'll provide coverage for a drug."

PORC's research combines two relatively new scientific disciplines: pharmacoeconomics, which compares the value of one

Stimulus Boost

The pharmaceutical industry sponsors most research in pharmacoeconomics and outcomes. A favorable evaluation may convince insurance companies to pay for their products.

"The problem comes when a pharmaceutical company chooses not to fund a study, because they view it as too high risk," explained Diana I. Brixner, Ph.D., R.Ph., executive director of the University's Pharmacotherapy Outcomes Research Center (PORC). "For example, our studies on real-world databases could prove that your product, which costs 10 times more than a similar product, is actually not more valuable. The whole topic is very controversial."

But perhaps not for long. Dependence on industry funding will almost certainly change after distribution of funds from President Barack Obama's 2009 economic stimulus package, which sets aside \$1.1 billion for Comparative Effectiveness Research (CER) as a means to ultimately cut health-care costs. The National Institutes of Health already has designated \$200 million in grants to be awarded in the 2009 and 2010 fiscal years to high-priority research areas, including CER.

"Our center is well positioned and very much looking forward to the opportunity to be able to expand our funding to government-supported grants," said Brixner. "This new funding stream allows us to develop proposals looking at comparative treatments from the perspective of the health-care provider and patient." —Julie Kiefer

pharmaceutical drug to another, and outcomes research, which evaluates the efficacy of drug interventions on patient health. Even after clinical trials have proven that new drugs are safe and effective, pharmaceutical companies run up against “new hurdles to address,” explained Brixner. Clinical trial populations in which the drugs are tested are small and relatively homogeneous, and patients’ intake of the drug in question is highly controlled. So not only must the cost of the new technology be addressed, but also the question as to whether the drug will live up to its therapeutic promise in the real world.

These questions concerned the developers of exenatide, a new class of medications that are a synthetic version of a hormone found in the saliva of Gila monsters. Eli Lilly and Company, and Amylin Pharmaceuticals, which manufactures the drug as Byetta, contracted with PORC to evaluate it. For patients with hard-to-control type 2 diabetes mellitus, exenatide was just what they needed. Where other treatments had failed, exenatide successfully stabilized blood sugar levels when used in combination with other diabetic drugs. It also induced significant weight loss with some overweight patients losing up to 30 pounds. This finding alone sets exenatide apart from other diabetic medications, because weight loss in itself dramatically improves the outcome of the disease.

PORC statistically analyzed a national database of 8 million patient electronic medical records (EMR) to assess exenatide’s efficacy. The U of U study proved that the drug is just as effective in controlling diabetes and inducing weight loss in a real-world

setting as it did in clinical trials. The study also showed that exenatide was not being abused as a weight loss drug: another major concern of the drug’s developers.

“We’re about to publish the final results of the study in *Diabetes, Obesity and Metabolism*. Publication in this well-known, clinically oriented journal is telling for two reasons,” explained Brixner. “On the one hand, it acknowledges the benefit of the study to clinicians and physicians. On the other hand, it shows that this type of work—understanding how drugs work in large populations—is now more accepted.”

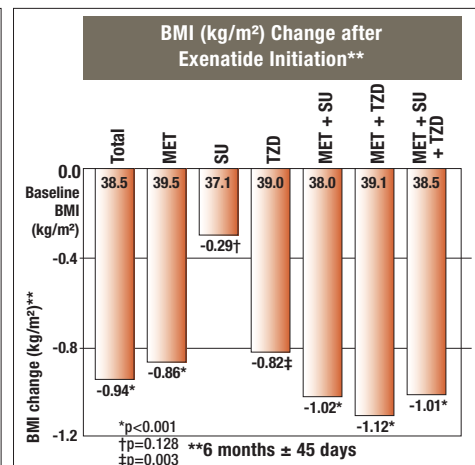
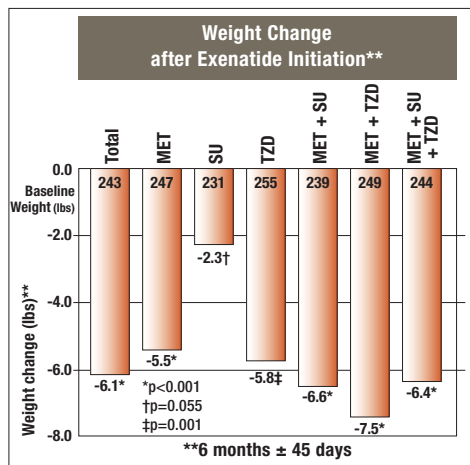
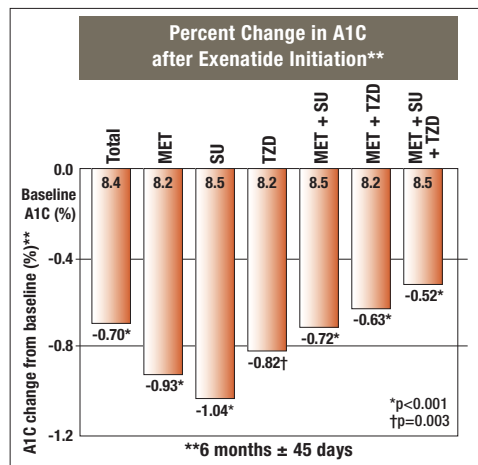
It may seem counterintuitive that pharmaceutical companies would turn to academic centers like PORC, rather than private entities, to evaluate their products. After all, the prerogative of academic researchers is to publish their findings—whether or not the drug performs well. Yet, in an age where claims made by pharmaceutical companies are held under intense scrutiny, teaming with academic researchers offers an essential attribute: credibility.

Pharmaceutical companies seek out PORC over nearly one dozen other centers of its kind nationwide, because U researchers understand their perspective—a rare finding among academic institutions, according to Brixner. Nearly one-third of the PORC faculty, including herself, has industry



Diana I. Brixner, Ph.D., R.Ph., PORC director, is shown with associate director Joseph E. Biskupiak, Ph.D., M.B.A., left, and Carl V. Asche, Ph.D., M.B.A.

PORC’s research combines two relatively new scientific disciplines: pharmacoeconomics, which compares the value of one pharmaceutical drug to another, and outcomes research, which evaluates the efficacy of drug interventions on patient health.



Exenatide, a new class of medications for patients with hard-to-control type 2 diabetes mellitus, has proven to be effective not only in controlling diabetes but in inducing weight loss, according to a recent PORC study. These graphs are from the presentation “Real-World Six-Month Outcomes of Patients Initiating Exenatide in a Primary Care Electronic Medical Record Database.”



COURTESY: nanomedich

Think small, Really small

To gain the biggest benefits, Hamid Ghandehari, Ph.D., thinks small. The University of Utah professor of pharmaceuticals and pharmaceutical chemistry is using nanoscale polymers to aid in selective targeting of tumor angiogenesis.

Nanotechnology refers to the science of materials at a very small scale—10 to 100 billionths of a meter. This emerging field, scarcely known a decade ago, has grown significantly to include nanomedicine: the medical application of nanotechnology that covers a wide range of diagnostic and therapeutic uses. At the U, these include drug delivery, diagnostic agent delivery, biocompatibility and toxicology of nanomaterials, tissue engineering, diagnostic imaging, and environmental testing.

In October 2008, Ghandehari and Marc Porter, Ph.D., professor of chemical engineering and bioengineering, co-founded the Nano Institute of Utah. Ghandehari serves as co-director; he also directs the recently established Utah Center for Nanomedicine. The institute promotes interdisciplinary collaboration, drawing together researchers from chemistry, materials science, engineering, drug delivery, and clinical translational research, among other disciplines. “The Nano Institute helps organize investigators to go after research subjects that are beyond the capacity of one lab,” noted Ghandehari, who holds a joint appointment as U professor of bioengineering.

Ghandehari himself collaborates with researchers from the U College of Pharmacy who are experts in drug delivery to employ nano-scale polymers to aid in selective targeting of tumor angiogenesis. In another project, Ghandehari takes the novel approach of using recombinant DNA technology to clone and express nano-scale biopolymers. While polymers are traditionally manufactured chemically, he uses structures from nature and the machinery of the cell to manufacture polymers. The engineered polymers can then be used for localized delivery of viral gene carriers for the treatment of head and neck tumors.

Ghandehari and Porter are part of Utah Science and Technology Research (USTAR): a statewide initiative to help align top researchers with product commercialization opportunities. “With this program comes the infrastructure to bring new technologies to widespread use and a critical mass of investigators in key areas,” noted Ghandehari, a USTAR professor who plans to bring his drug-targeting innovations to industry within the next 10-15 years.

His new research also represents a completed circle for Ghandehari, who received a bachelor of science degree in pharmacy in 1989 and a Ph.D. in pharmaceuticals and pharmaceutical chemistry in 1996, both from the U. His return in 2007 was due not only to the excellent reputation of the colleges of Pharmacy and Engineering in drug delivery and biomaterials research, but also to Utah’s quality of life. “It’s a great place to live,” he added. —Cameron S. Metcalf

experience. “Because of my background, I recognize that there are shareholders, market-share goals, and sale projections that the industry needs to meet,” she explained. Her resumé lists a number of corporate leadership positions, including executive director of managed care accounts at Novartis and director of outcomes research at Ciba Pharmaceuticals. “But we need to balance that with the reality of what the society is willing to pay for.”

Most of the 36 research sponsors that PORC has worked with over the past six years have been from the pharmaceutical industry. The center conducts about 30 studies per year, each ranging from a few months to a few years, bringing in over \$11 million in total revenue to date.

Another draw for pharmaceutical companies is the collaborative culture that characterizes the U. PORC’s 16 research faculty and staff come from a variety of professional backgrounds, and include pharmacists, statisticians, medicinal chemist, health economist, and public health scientist. “Pharmacoeconomics and outcomes research is a very interdisciplinary field. You need to tap into expertise that is beyond what any one person has,” said Brixner.

When considering pharmacotherapy’s chair position six years ago, Brixner already was intimately familiar with the cooperative spirit among U researchers. She received her doctorate from the U’s top-tier medicinal chemistry program in 1987. “It was the combination of intellectual talent and the willingness to collaborate that brought me back to the University of Utah,” she noted.

Access to other researchers and resources within the University health sciences is allowing PORC to take on a new challenge: gathering information about sarcopenia, a progressive, age-related loss of muscle mass. “The condition is not well-defined by physicians. That makes doing outcomes research very difficult,” said Brixner.

In the first stage of the study that began in January, PORC is mining a large national database for medical characteristics that sarcopenia patients have in common. Next, in collaboration with Utah Health Research Network (UHRN) physicians, PORC will design a survey to test whether some of these are defining characteristics of the condition. The custom survey will be administered to patients and physicians at University of



Diana I. Brixner, Ph.D., R.Ph., meets with the staff of the Pharmacotherapy Outcomes Research Center, which contributes to improving patient care through outcomes research and assessment.

Utah Hospital and University of Utah Health Care community clinics.

“Once we create a way to define sarcopenia, then we can do the typical outcomes studies that we do for other diseases where the diagnoses and procedures to treat them are very clear,” said Brixner. “The survey approach we’re doing is very unique. It’s a model others can follow in order to do real-world studies for any disease that is vaguely defined.”

Brixner’s group may incorporate surveys of University Health Care patients into future studies: a methodology that circumvents existing databases, which often don’t contain all the necessary information for outcomes research. “With a patient population of 400,000, University Health

Care is large enough to study most common primary diseases and what potential benefits of commonly prescribed medicines might be,” she said.

PORC’s work illustrates the diversity of work available to the 21st-century pharmacist. “The four departments in the College of Pharmacy really flow from drug discovery to application in patient care,” noted Brixner. “Medicinal chemistry discovers the drug; pharmacology and toxicology makes sure the drugs don’t cause any harm; and pharmaceuticals and pharmaceutical chemistry designs the formulation.

“For me the critical component of everything is what is the impact on patient care and at what cost to society and to the health-care budget.” ▣

