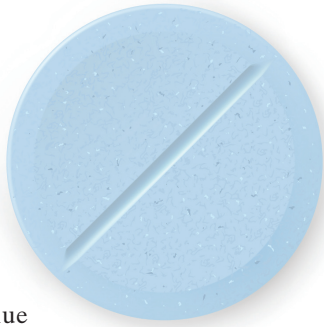

0.5
1
2
2.5

PREFERENTIAL TREATMENT

Pharma firms have begun partnering with managed care companies to find real-world drug evidence and improve outcomes. But can this strategy provide the proof payers demand before giving products preferential treatment? **Elizabeth Jeffords** on the perils and the potential



In the past 20 years, pharmaceutical R&D costs have increased exponentially, with worldwide pharma development nearly doubling from $69 billion in 2002 to $132 billion in 2011, according to statistics from Parexel Biopharmaceutical. And the average amount spent on discovery per NDA approval has grown from $963 million in 2000 to $3.29 billion in 2010.

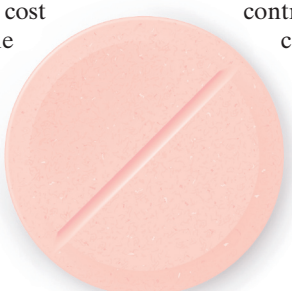
Meanwhile, the number of NME approvals and mean time to approval has remained relatively flat in the last 15 years. As such, the number of Phase I trial starts increased precipitously, from 498 in 2006 to 1,479 in 2010. This volume is a factor of larger and longer trials, tighter regulatory scrutiny and shrinking pipelines.

And if a company is lucky enough to reach an approval, the payoff is shrinking, too. In the 1960s the average time on market until a second competitor would enter was 13.5 years, in the early 2000s just 1.1 years, says the Tufts Center for the Study of Drug Development. With healthcare reform putting pressure on benefit design, the advent of a pathway for biosimilars, and increased competition for a limited pipeline, the downward trend can only continue.

Traditionally, the answer to this dilemma has been to raise prices on drugs (at least where this is possible, i.e., the US). When price multiplied by quantity equals revenue, and the quantity is diminished or constrained, price is your remaining variable. That's why we've seen an industry average annual drug price increase of 8.3%, AARP figures show, while inflation is barely there.

However, increasing price is not sustainable in the long term, nor is it a source of competitive advantage. But what is a strong sustainable competitive advantage? Traditionally, strategic marketing, thought leader advocacy or strong field execution were adequate, but today these seem more like commodities as the regulations get tighter and tighter. Now, and increasingly tomorrow in a system ruled by cost controls, the only true source of sustainable competitive advantage is value. By definition, the purpose of ethical pharmaceutical companies is to provide value to patients, so value brings us back to basics.

IMAGES: ISTOCK



Here's the one concern with value propositions: In the current environment, regulatory hurdles don't always match patient or medical needs. Some studies are nearly impossible to practically conduct in double-blind controlled settings due to regulatory constraints (pediatric studies), cost (head-to-head) or time (preventative medicine).

In many cases, standard of care is changing faster than you can run a trial, so the trial you started five years ago may be largely irrelevant by the time of launch. And the real incentives come well after launch, with some drugs taking years to recoup costs.

So a typical trial-based "value" strategy is to take the fastest and safest route to market, and expand from there. Sometimes the FDA requires post-approval commitments, but companies also use investigator sponsored trials and, hopefully, line extensions, which let a company capture more value by reaching a larger segment of the market. But trials can't solve every data need, and sometimes clinical data isn't enough to build the most relevant value proposition.

Enter comparative effectiveness research (CER), to fill the gap left by traditional regulatory research. Comparative effectiveness as a concept isn't new—you take two or more treatments, you compare them, and research tells you which is better or more appropriate.

So why is it different than any other clinical data? Well, for one, it isn't always controlled. And sometimes, it isn't even about effectiveness in the true sense of measuring efficacy. Different versions of CER look for different endpoints—surrogate markers, cost, safety signals or other determinants of value without obtaining complete benefit/risk. This type of research can be performed by the government, academic institutions, managed care intermediaries, payers, or local physician groups—anyone who has the time, the inclination and a way to gather the data. Sometimes even patients get frustrated enough to take matters into their own hands, with sites like patientslikeme.com branching out into community observational trials.

Europe, one could argue, is more advanced. But much of the CER seen there is cost-effectiveness research. In Health Technology Agency (HTA) countries (the commonwealth countries UK, Canada and Australia but spreading across Europe), a drug's cost is compared in a complicated formula to years of life saved. Then a value cut-off is applied, above which a drug is judged to be not cost effective.

Such countries as France, Italy and Japan are going the less onerous route of assigning a "value" score to an incoming drug and assigning price (in)flexibility based on that rating. And some countries like Germany and Spain have reacted to economic hardship by mandating a flat drug discount. But is that where the US is heading?

Perhaps not yet. What is used as a substitute for this level of access or price control in the US is a mix of formulary status and contracting at the payer level. If you cannot control a drug's "gross" price, the next best thing is to control its "net" or average price, or whether your patient population can afford to access the drug. Given the fragmented nature of the US commercial payer system, and the prevalence of public payers (Medicaid, Medicare) in some of the more expensive disease states like oncology, cost is often controlled this way.

In competitive classes, payers frequently ask for discounts to control formulary access. But this is typically pay-for-access contracting, without adding specifics to the value proposition. Ideally, negotiations would also include the ability to provide outcomes-based or value-based contracting to the price equation.

For example, in the UK there have been pilots where only those patients responding to a drug within a given timeframe are paid for; or where any use beyond a certain cap of time would be paid by the manufacturer (Celgene's cancer drug Revlimid, for example).

In the US, this type of value-based contracting is very difficult due to EMR (electronic medical record) data constraints, a fragmented payer system, government-price reporting impacts of contractual payments, time pressures and competing priorities.

Despite the difficulties, there is a growing interest in getting to value-based pricing, but that confers the knowledge of a defined and proven value. To help get the US further along in the pursuit, the healthcare reform law of 2010 laid down provisions to create the PCORI (Patient Centered Outcomes-Research Institute). PCORI has a mission to develop guidelines and to generate powerful information to help serve patient interests. This non-governmental non-profit has a strong chance of providing a rigorously scientific bent to CER, but to date, is still in the formative stages.

In the absence of national comparative effectiveness, payer-based studies are a differentiated response. In either a high-share regional with a high degree of formulary control, a national payer with a good integrated data platform, or an integrated delivery network, it is possible to run comparative effectiveness studies with post-hoc analyses of a patient population set using data originally collected for other reasons (e.g., paying claims).

This is useful data to understand "real-world" results of various treatments, but by its nature is retrospective, with wide inclusion criteria (if any) and can be agenda-based. Because of the nature of the original data collection and analyses, the data would not be considered adequate for standard regulatory considerations. But if you're a payer, and you have tight controls over the drugs used in your population, it can be very powerful. And that power can be concerning to pharma. Concerning enough that some pharma firms have chosen to join payers in the pursuit rather than be left out.

In the next few years, we will see manufacturer/payer pilots doing just that—two companies partnering to try to answer important medical questions that could be unanswerable by other means. (See sidebar for three examples.) These pilots typically serve the needs of both entities. For the payer, it can mean support for burgeoning CER departments, or support of the final outcome as translated to protocols and guideline, as well as insights into new treatments. For the manufacturer, it can mean deeper insights into patient subsets and real-world data to support launches and beyond.

For the payer, the watch-outs are to maintain some level of objectivity (that the outcomes aren't considered compromised by having a manufacturer involved). And for the manufacturer, the impetus is to ensure that the studies remain transparent, unbiased and include open review of design, methodology and results.

In the end, we are truly driven by what is best for patients, and the real test of the value of CER will be whether the patient wins. If CER is used to perform substandard clinical trials, or to create cost-based excuses to prevent needed treatments, there could be abuse of the system. We know there are some unintended consequences of healthcare reform which may seem counterintuitive.

However, the hope is that comparative effectiveness avoids those traps and keeps a tight focus on patients getting the most effective treatment. That is certainly the PCORI mission and, ideally, the mission of those manufacturers and payers working together today on pilots. In the long term, to assure this happens, we'll need to have quality standards in place and a focus on the studies that matter. What happens in the future of CER is about as easy to predict as the shape healthcare reform will take in the mid 2010s. It isn't easy to predict, but it will be a fascinating study in scientific resilience. ■

Elizabeth Jeffords is senior director, strategic pricing & contracting, Genentech.

Pact with the payer

Manufacturers are starting to pair up with payers/PBMs in the US in an attempt to answer important medical questions. Here are three recent tie-ups, all focused on finding real-world data outside of controlled clinical trials.

AstraZeneca and Wellpoint: "We are seeking to answer a fundamental question with this research: How can we improve overall patient health while lowering the total cost of care—especially in the treatment of chronic diseases?" said James Blasetto, MD, AZ vice president of US strategic development.

Pfizer and Humana: "Through this innovative partnership we hope to improve outcomes and health for patients," especially involving chronic conditions such as pain, cardiovascular disease and Alzheimer's, said Steven Romano, MD, SVP of Pfizer's primary care medicines development group.

Sanofi and Medco: "This work will bring transformative change to the drug development process required to improve the quality of patient care, while effectively meeting payer and other stakeholder evidence requirements," said Jean-Pierre Lehner, MD, chief medical officer, Sanofi.