

COUNTERPOINTS

Current Controversies in Hematology and Oncology

Why Are Cancer Drugs So Costly?

The cost of cancer drugs is at an all-time high, with several lifesaving agents costing more than \$100,000 a year. Much of the discussion related to healthcare costs has revolved around who will pay. The aspect that often gets pushed aside is why certain treatments are so expensive.

This month, 8 panelists answer the question, “Why are cancer drugs so costly?” Our panelists comprise 2 oncologists; a fund manager; a healthcare economist; a fellow at a conservative think tank; and vice presidents from a pharmaceutical company, a pharmacy benefit management organization, and the primary trade group representing pharmaceutical research and biopharmaceutical companies.

Many of the panelists cited the high cost of research and development (R&D) as a major reason why drug costs are high. Newton F. Crenshaw, a vice president at Lilly Oncology, explained that his company spends about \$5 billion each year on R&D. Bill Chin, MD, executive vice president of Scientific and Regulatory Affairs for the Pharmaceutical Research and Manufacturers of America (PhRMA), cited the \$1.2 billion price tag to develop a single medicine.

Paul Howard, a senior fellow and director of the Center for Medical Progress at the Manhattan Institute, a think tank that receives funding from the pharmaceutical industry, also pointed to the relatively small size of the populations that use cancer drugs as a major factor in drug prices.

Hagop M. Kantarjian, MD, who with more than 100 other oncologists wrote a widely-read 2013 editorial in *Blood* on the high costs of cancer drugs, said that costs are high because pharmaceutical companies are charging what the market will bear, a practice that he said is inappropriate for lifesaving agents. Dr Kantarjian is chair of the Leukemia Department at the University of Texas MD Anderson Cancer Center in Houston, Texas, and has received funding from pharmaceutical companies.

Several panelists highlighted the skewed incentives that work against healthcare becoming more cost-effective.

Peter Kolchinsky, PhD, a managing partner of RA Capital Management, a healthcare fund in Boston, Massachusetts, wrote that many patients would never pay the high drug prices they expect insurance to cover.

Rena M. Conti, PhD, an assistant professor of health policy and economics at the University of Chicago in Chicago, Illinois, cited her own finding that the most powerful predictor of cancer drug launch prices was the prices of other recently launched drugs.

Leonard Saltz, MD, a professor of medicine at the Memorial Sloan-Kettering Cancer Center in New York, New York, was one of the panelists who criticized the law that bars Medicare and Medicaid from negotiating drug prices, even though it is required to purchase the drugs for whatever indications the US Food and Drug Administration (FDA) approves them for. Dr Saltz has received funding from pharmaceutical companies.

Warren Davis, a vice president of product management for Accredo, pointed to waste as a major factor in increasing medication costs. Accredo is a subsidiary of Express Scripts, the largest pharmacy benefit management organization in the United States.

Many of the panelists offered suggestions for how to bring drug costs down. Mr Davis said that his company supports legislation to bring biosimilars to market, and has taken steps to help physicians better manage how they prescribe cancer medications. Dr Conti recommended that outpatient oncologists not be paid based on a cost-plus basis.

Dr Saltz proposed a “pay for performance” scheme for new drugs that would focus research efforts on more substantial innovations and achievements. Dr Kolchinsky and Mr Howard suggested that pharmaceutical companies improve cost-effectiveness by developing highly effective combination therapy, potentially leading to cures.

Now, on to our panelists' own words . . .

“Counterpoints” is a new section in *Clinical Advances in Hematology & Oncology* in which we address clinical controversies and other questions of importance to oncologists and hematologists. We feature anywhere from 2 to 8 panelists for each question.

What topics would you like to see addressed in future issues? Please send your ideas to editor@clinicaladvances.com.

Without Rewards, the Cycle of Innovation Would Stop



Newton F. Crenshaw is a vice president at Lilly Oncology.

Many people feel a sense of outrage when it comes to the cost of cancer medicines. No one wants to be sick, let alone to receive a diagnosis of cancer. Coming on top of such a diagnosis, the news that a potentially effective treatment costs thousands of dollars can lead to more distress—especially when health insurance does not fill the financial gap. However, there are some important reasons why new cancer medicines are expensive, and those of us in biopharmaceutical companies need to be clear about the challenges we face in setting prices.

First, biopharmaceutical R&D is complex and costly. The company I work for spends about \$5 billion each year on R&D—that is like paying for 4 skyscrapers a year—to sustain our own large teams of scientists, partnerships with academic researchers, and clinical trials involving tens of thousands of patients.

Second, developing new medicines is one of the riskiest ways to try to earn a financial return. On average, not even 1 out of 10 potential cancer drugs that enters human testing ever receives approval from the FDA and other regulators. On the rare occasions when success occurs, so much time has elapsed during testing that an approved cancer drug usually has less than 10 years of patent protection remaining in which to reward investors. And without that reward, the cycle of continuous innovation simply would stop.

Finally, new cancer medicines are expensive because they can provide the most valuable benefit imaginable: a longer life. As a survivor of diffuse large B-cell lymphoma—who would have left behind a wife and 4 children and missed 4 wonderful and productive years (and counting)—I am not able to quote a number that captures the value of my cancer remission. Not every cancer treatment produces a lasting remission, but surely it is appropriate to set prices reflecting the value that innovative medicines can contribute to such a result.

Understanding these factors is only the beginning of the dialogue that is needed about how to manage the cost of treatment and the value of innovation to society. My colleagues and I are ready to be a part of that dialogue.

Charging What the Market Will Bear Is Inappropriate



Hagop M. Kantarjian, MD, is chair of the Leukemia Department at the University of Texas MD Anderson Cancer Center in Houston, Texas.

Nearly all the drugs approved for cancer indications in 2012—12 out of 13—cost more than \$100,000 per year, according to an analysis I did for *Cancer* in 2013. Why are they so expensive? The reason is simple: pharmaceutical companies are charging what the market will bear.

Charging what the market will bear is appropriate for many commodities. If you can charge \$142 million for a triptych by Francis Bacon, knock yourself out. But for commodities that involve human suffering, I believe that pricing should follow the doctrine of “just price.” That is, the supplier should be able to earn a reasonable profit, while people in need should be able to obtain the item at an affordable price. This logic applies to cancer drugs as much as it does to food during a crisis.

Pharmaceutical companies point to the cost of drug development as one factor that justifies their prices, and it is expensive—although not as expensive as they claim. Furthermore, the majority of basic research in cancer is funded with taxpayers’ money. What do US patients and the American healthcare system get in return? According to a 2005 article in *BMJ*, prices that are 50% to 100% higher than those for the same patented drug in other parts of the world, meaning that our population is hit hard not once, but twice. Countries such as Canada negotiate with drug companies for bulk deals on drugs. Medicare, however, is specifically barred from negotiating prices, thanks to 2003 legislation sponsored by the pharmaceutical lobby.

I believe that pharmaceutical companies should adopt a fair price strategy for cancer drugs that covers the true cost of developing the drug, allows for a healthy profit margin, and reflects the benefit to the patient—so that a drug that extends life for just a few months costs less than one that adds years to a patient’s life.

As doctors, we are obligated to “first do no harm” to our patients. If the high prices of cancer drugs harm our patients by plunging them into debt or making treatment inaccessible, we should take steps to advocate for lower prices.

Greater Effectiveness for the Same Cost



Peter Kolchinsky, PhD, is a managing partner of RA Capital Management, a healthcare fund in Boston, Massachusetts.

The next time you prescribe a \$100,000 drug that offers a few months of death delay, imagine if insurers started writing checks directly to patients (to use at their discretion). Some would use the money to pay for the drug, of course, but others might pay for a child's college education or leave their spouse more financially secure.

Patients who have already paid into the system gain little from healthcare becoming more cost-effective, however. Shielded by co-pay assistance, they understandably demand everything they can tolerate. Payers, acting as administrators instead of customers, pass costs along to members or taxpayers rather than face “death panel” headlines.

We cannot expect anyone to act against self-interest. Companies charge what the market will bear, and payers avoid negative publicity. The main threat to the biopharmaceutical industry is that moral outrage from prominent oncologists may embolden Congress to change the rules—maybe even allow Medicare to negotiate prices.

Fortunately, there is a way out for the biopharmaceutical industry that plays to its strengths: offer cost-effectiveness by boosting effectiveness. Incremental drugs can be combined and sequenced into high-impact “solutions” sold as a fixed-price package that would be worth it to patients. The days of single-drug development must end; we need more companies to follow the example of Roche and Novartis, which test combinations of novel oncology candidates before approval to allow the ultimate commercialization of more effective solutions. Solution development has been the norm in HIV and hepatitis C; the prices are high but the effects are profound.

Meanwhile, the rest of us should take solace in knowing that small-molecule drugs eventually go generic; imatinib (Gleevec, Novartis) will someday cost pennies per pill. But with red tape threatening the advent of cheaper biosimilars to relatively simple biologics such as antibodies, what hope is there for us ever getting generic versions of complex biologics like cancer vaccines and oncolytic viruses? The development of novel small-molecule-based solutions should be encouraged and rewarded—maybe with an extra 3 years of patent/market exclusivity—because compared with non-genericizable biologics, the long-term costs of small-molecule agents should be the least of our worries.

The System Over-Rewards Incremental Gains



Leonard Saltz, MD, is a professor of medicine and chair of the Pharmacy and Therapeutics Committee at the Memorial Sloan-Kettering Cancer Center in New York, New York.

There are many reasons why cancer drugs are so expensive, but 2 in particular stand out: (1) we have created payment and drug approval systems that uncouple cost from value, and (2) we reward incremental advances as if they were major ones.

Insurance pays for cancer drugs. If individuals were paying directly for drugs that cost \$5000 to \$10,000 per month—often for modest gains and with side effects—few people could afford them and fewer would elect to purchase them. Market forces would then put downward pressure on prices until they reached affordable levels. Potential purchasers would carefully consider value: cost vs benefit.

Our drug approval system contributes to the problem. The FDA reviews drugs for safety and efficacy, but has no set minimum amount of benefit to define efficacy. At the same time, the FDA is forbidden by law from considering price.

Another government agency, the Centers for Medicare and Medicaid Services (CMS), is the primary purchaser of these drugs. CMS is required to purchase the drugs for whatever indications the FDA approves them for, *and is forbidden by law from negotiating price*. Essentially, one government agency approves the drug without consideration of price or incremental value, and another government agency must then buy the drug for that approved indication at whatever price the pharmaceutical company sets.

Given this system, a drug does not need to produce a large effect to have a high price tag. The small, incremental benefit is easier to achieve, and so is a safer business strategy for drug companies to pursue. The result is small incremental benefits that are billed as if they were major advances, and aiming for these incremental gains has become a routine business strategy.

Arguments that this sort of compensation is necessary to maintain R&D investment are specious. The current system over-rewards incremental gains and offers minimal incentive for major innovation and advancement. Compensation tied to achievement (a “pay for performance” scheme for new drugs) would incentivize R&D to kill marginal products sooner, thereby reducing development costs, and would focus research efforts and investments on more substantial innovations and achievements.

Impressive Gains With Innovative Medicines



Bill Chin, MD, is an executive vice president of Scientific and Regulatory Affairs for PhRMA.

The cost of cancer medicines reflects complex factors, and patients and their loved ones struggle with the question of whether or not the cost is worth it. The reality is that these medicines offer significant returns for patients, the healthcare system, and society while accounting for only a small share of overall health spending.

Despite their small part of health costs relative to other health services, cancer medicines have an important impact on the lives of patients afflicted with cancer. Since 1980, the survival of cancer patients has increased by 3 years, according to an analysis by Sun and colleagues that was presented at the 2008 annual meeting of the American Society of Clinical Oncology (abstract 6616). A full 83% of these gains are attributable to new treatments, including medicines with impressive gains in breast cancer, colon cancer, and non-Hodgkin lymphoma.

Discovering and developing new cancer medicines is a long, difficult, and expensive process. It takes about 10 to 15 years to move from the drug discovery and clinical development stage to having a new medicine available for patients. On average, it takes \$1.2 billion to develop and register just 1 medicine, if one accounts for the large failure rate wherein only 1 in 5000 to 10,000 early drug candidates make it from the laboratory to patients. Despite these obstacles, the biopharmaceutical industry's commitment to patients is evident in the nearly 1000 therapeutics currently in development to fight many types of cancer.

These medicines are shifting the paradigm of how we approach cancer, with more targeted therapies to combat disease. Some cancers are on the verge of a cure, and others have turned into chronic diseases. Beyond treatment, biopharmaceutical companies are also working to prevent cancer from ever occurring, such as with the human papillomavirus virus (HPV) vaccine. The continued research and discovery of new cancer medicines is saving lives, and there is no stronger evidence than the 13.7 million cancer patients in the United States who can call themselves cancer survivors.

For our patients and loved ones, the road to effective therapy and improved survival is long and hard, but the promise of progress makes the trip a worthy one.

Waste and Missed Opportunities Drive Costs Upward



Warren Davis is a vice president of product management for Accredo, which is a subsidiary of Express Scripts.

As the price of cancer treatment rises and payers shoulder more of the cost of care, it is vitally important to reduce waste. Without waste reduction, pharmacy benefits are unsustainable.

According to the results of a collaborative, multi-year study from Eviti, Inc., 28.7% of cancer treatments prescribed to patients did not meet evidence-based standards or could not be medically justified, needlessly increasing costs by an average of \$25,579 per case and putting patients at risk without delivering additional clinical benefit.

Furthermore, according to the Express Scripts *Drug Trend Report*, 37% of oncology patients do not properly take the regimen they are prescribed. Nonadherence becomes an enormous driver of waste for drugs that can cost tens of thousands of dollars a month; cancer is the third-largest specialty therapy class for claims under our company's pharmacy benefit.

Another reason costs continue to rise is that US regulators have not approved generic versions of biologic medications, which comprise the bulk of recently launched and soon-to-be launched cancer therapeutics. Even if fewer than a dozen biosimilars reached the market, the savings could be tremendous: in the United States alone, the country would realize \$250 billion in cost savings between 2014 and 2024. As with small-molecule, oral medications, biosimilars would be permitted only after a period of patent protection that would allow drug makers to recoup the cost of innovation.

Our company supports legislation to bring biosimilars to market, and we also offer solutions to help manage today's costs and challenges. For example, our Oncology Therapeutic Resource Center offers end-to-end patient care, including counseling and adherence support from specially trained, highly experienced oncology nurses and pharmacists.

We also help physicians better manage how they prescribe cancer medications. Our oncology decision support tools give physicians immediate access to evidence-based suggestions to enable optimal treatment decisions.

Waste today, coupled with the missed opportunities of biosimilars tomorrow, are 2 reasons cancer costs are on an unsustainable trajectory. Our company is focused on doing our part to bend the cost curve down while ensuring quality cancer care.

Short-term Costs Can Lead to Long-term Gain



Paul Howard is a senior fellow and director of the Manhattan Institute's Center for Medical Progress.

Drug development is incredibly expensive, and the period during which companies can recoup their up-front costs and earn profits is limited by the patent time that remains after a product launches. Pricing pressures for cancer drugs are compounded by the relatively small size of the populations that use them. Cancer drugs, especially targeted medicines, may treat only a few thousand patients—unlike cholesterol-lowering drugs that will treat millions. This means that costs and profits must be recouped over a much smaller population.

When looking at the high cost of cancer medicines, stakeholders need to remember that an innovator company captures just a fraction of the “social surplus” generated by new oncology medicines. For example, the success of imatinib in treating chronic myelogenous lymphoma (CML) led to the development of second-generation medicines with better efficacy and comparable safety. After imatinib goes generic in 2015, providers and insurers will undoubtedly use generic versions to push competitors for pricing concessions. Finally, newer approaches to treatment that use combination therapy may eventually make it possible to cure CML and discontinue drug therapy, with potentially significant healthcare savings. Imatinib, in other words, will have an incredibly “long tail,” benefiting patients, researchers, and companies for years to come.

The oncology armamentarium has never been more promising. Novel immunotherapies, drug conjugates, and diagnostic tools promise better outcomes and less toxicity for cancer patients. To make these innovations financially sustainable, and unleash the potential of the market to deliver both breakthrough treatments and important incremental innovations, we should develop better economic models that capture the full value of new treatments. Those metrics can inform an intelligent pricing discussion among stakeholders, and help guide long-term R&D investments.

Data sharing networks like Project Data Sphere, launched by the CEO Roundtable on Cancer, are already offering promising platforms for sharing precompetitive data. The goal is to streamline drug development by promoting new approaches that can better inform basic research, lower costs, and increase R&D productivity.

Short-term pricing concerns should be seen as an opportunity for stakeholders to move toward a new paradigm for oncology innovation, maximizing patient access today and innovation tomorrow.

Eliminate Cost-Plus Reimbursement for Drugs



Rena M. Conti, PhD, is an assistant professor of health policy and economics at the University of Chicago in Chicago, Illinois.

Initial prices for novel cancer drugs launched between 1996 and 2012 grew at a rate of 6% to 8% annually after controlling for potential improvements in clinical benefits, according to a recent estimate by my collaborator David Howard and myself. This rate outpaced the rate of inflation for other consumer goods. We found that the most powerful predictor of cancer drug launch prices was the prices of other recently launched drugs. Prices for generic cancer drugs also appear to be increasing, according to the National Community Pharmacists Association.

Why do novel cancer drug prices increase so much? One reason is that patients and their insurers have been willing to pay extraordinarily high prices for novel cancer drugs with little regard to their expected incremental efficacy. This is in part because many patients' expected survival upon diagnosis is low, and few alternative treatment options may be available. Additionally, patients are largely shielded from difficult decision-making by their physicians and generous insurance coverage. Hence, it is the job of the oncologist to weigh expected incremental survival gain against the side effects of novel drugs. These same oncologists commonly face financial incentives to use expensive branded physician-administered drugs over less costly alternatives, as Medicare and private insurers reimburse them on a cost-plus basis.

The incidence and unusually long persistence of drug shortages—especially for generics—also contributes to rising prices among branded and generic cancer drugs. Conventional economic wisdom suggests that during a shortage, existing manufacturers will raise prices, quantity demanded will fall, and new suppliers will enter or existing suppliers will increase quantity. One reason current shortages are unusually persistent is related to constrained capacity among committed suppliers. Without increase capacity commitments from existing suppliers or entry into the market by other suppliers, we should expect these high prices to persist. The two-quarter lag in Medicare reimbursement for physician-administered cancer drugs makes acquisition cost increases acutely felt by oncologists and other purchasers.

A variety of approaches have been proposed to rein in high and rising prices. Many of these either eliminate incentives for innovation, or are too Draconian in their rationing. One solution that sidesteps these concerns is to stop paying oncologists and hospitals on a cost-plus basis.