Precious Moments

How Much Is Each Day Worth?

By Ed Rabinowitz

If you could take a moment of your life—not just any moment, but something special like a birth, wedding, or a graduation—and preserve it, what would that be worth? One-hundred dollars? One-million dollars? A billion? Preserving a moment in time is impossible, of course, but for the more than 1.5 million Americans who receive some form of cancer diagnosis each year, the attempt to preserve future moments comes with a price tag.

Every day, cancer patients and their families grapple with the question of how much it is worth for an opportunity to spend another 2 months, 6 months, or even 1 year with their loved ones. "You can't put a price on it," said Bob Gibbs, a 40-year-old husband and father of 4 who is a 6-year brain tumor survivor. "If you were able to put a price on it, you wouldn't be able to afford it."

The annual cost of treating cancer in the United States is rising, almost doubling from nearly $25 billion in 1987 to $48 billion in 2005, according to the Centers for Disease Control and Prevention. A significant portion of that $48 billion went for cancer drugs. If dollars spent are any indication, perhaps the answer to the question posed above is "whatever it takes."

Who Is Responsible?

Some would argue this attitude is what sent costs for cancer treatment spiraling skyward. Others cite a litigious society and a cumbersome regulatory process as contributing factors. Richard Rosenbluth, MD, director, Oncology and Supportive Care and Pain Management and In-Patient Hospice at the John Theurer Cancer Center at Hackensack University Medical Center (HUMC) in New Jersey, describes himself as passionate over the cost-versus-benefit debate in cancer care. He suggested physicians look in the mirror. "To an extent, we're responsible for having brought a lot of this on ourselves—using whatever chemotherapy was available, one cycle of drugs after another, as though money were not an issue," Rosenbluth said. He noted this was done with the best intentions. "Health was the principal concern, and trying to do the best for our patients was the principal concern."

Many physicians are hesitant to raise the issue of cost versus benefit with their patients, said Mikkael Sekeres, MD, director of the Leukemia Program at Cleveland Clinic's Taussig Cancer Institute in Ohio. He explained that when oncologists raise concerns about value when patients ask for advice regarding the best therapy to treat their cancer, patients are liable to suspect they are being offered the best treatment for the money but not the best treatment available. Sekeres predicates these discussions by telling the patient that he is not only going to talk about all the therapies available, but also about their associated costs.

"I explain that I wouldn't be a very good doctor if I sent them out of my office with a prescription for a drug that's going to cost them $70,000 a year without them being aware of that," Sekeres said.

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As most oncologists know, $70,000 a year rests at the low end of the cost spectrum for newer biologics. According to a Grail Research report, the cost per life year gained (LYG) for using bevacizumab (Avastin) to treat breast cancer is $150,000; to treat colorectal cancer with cetuximab (Erbitux), the LYG cost is $182,950; for erlotinib (Tarceva) in pancreatic cancer, the estimated LYG cost ranges from $364,680 to $498,390. The sticker shock over those prices has opened a lot of eyes, said Robert Dickinson, life sciences service officer for Grail Research. He said the high prices largely stayed "under the radar" when there were only a handful of biologics available, but the increasing number of drugs and indications for these drugs in recent years has attracted greater scrutiny. "They're on the radar screen of payers and policymakers," Dickinson said. A 2007 article published in the *Journal of Oncology* by researchers at Tufts Center for the Study of Drug Development said biopharmaceuticals accounted for 8% of oncology drugs used in 1990, a proportion that climbed to 29% in 2002 and has continued its upward trend.

The Stakes in Drug Development

According to a 2008 report in *BusinessWeek*, the Tufts researchers found that only 8% of experimental oncology drugs complete the journey from the test tube to the pharmacy. In addition, barely half the oncology drugs studied in phase III clinical trials are subsequently approved. Not including the amount spent on the hundreds of investigational drugs that never make it through the pipeline, the expense of bringing a single drug from inception to approval exceeds $1 billion.

"It's risky business," said Krysta Pellegrino, a company spokesperson for Genentech, a member of the Roche Pharmaceutical Group, referring to the monies doled out by pharmaceutical companies to bring a drug to market. "But in cancer, you're talking about helping people live longer and healthier lives, so it's worth the risk."

Pellegrino said many elements factor into pricing a cancer drug, including the need to recoup some of the development costs. Companies also consider a drug's efficacy as established in clinical trials, and they look at what other medications might be on the market for the drug's sought-after indication. Genentech also sets prices for drugs with an eye toward the future, to fund the company's continued quest "to discover new medicines for cancer and other diseases," said Pellegrino. "It's more about keeping that research and development pipeline strong."

Dickinson, who previously worked in drug development at Genentech and played an integral role in late-stage trials for the company's blockbuster breast cancer drug trastuzumab (Herceptin), echoed Pellegrino's assertions. He said that, ultimately, the price for a cancer drug is informed by "what the provider and payer communities feel is appropriate given the benefits of the product. That's what really drives the cost; that, and competition in the market."

The Price of a Year

It was October 12, 2006, when 57-year-old Michigan resident Mike Schott learned he had glioblastoma, the most aggressive form of brain cancer. "I felt as though we were hit by a truck," said Evonne Schott, Mike's wife, recalling the day they received the diagnosis.

Surgery ensued almost immediately, followed by 6 weeks of temozolomide (Temodar) and radiation. This was followed with Mike's enrollment in a clinical trial for a dose-intense version of temozolomide. Mike was unable to tolerate the stronger medication, and his tumor continued to grow. In March 2007, Mike was told he had about a month to live. That is when the couple learned about bevacizumab, which was approved for colorectal, lung, and breast cancer, but not for glioblastoma.

"There were no clinical trials at the time, so we had two options," recalled Evonne Schott. "Pay for it, or don't do it. Fortunately, my husband was successful and could afford it, so we paid for it. It

was costly, but it was worth every penny. This was our rainy day. What else is the money for if we can't save his life?"

The medication bought Mike an additional year of life—a year that Evonne described as amazing. "I watched him literally go from dying to living. From not even being able to walk, he was able to swim again the summer before he passed. Watching him swim the first time was one of the most amazing things that I've ever witnessed. You can't put a price on that," she said.

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Time eventually ran out, and Mike Schott died on March 24, 2008. The following year, Evonne traveled to Washington, DC, to speak before the FDA's Oncologic Drug Advisory Committee (ODAC), which was considering Genentech's filing for approval of bevacizumab in glioblastoma that has relapsed after initial treatment. Although the data were not from randomized studies that used overall survival as a primary endpoint, ODAC unanimously recommended the drug's approval based primarily on the tumor shrinkage observed in approximately one-fourth of patients from two phase II trials.

Today, Evonne Schott talks with families who are experiencing what hers went through with Mike's diagnosis. "Anything I can do to help support them," she said. "When you're diagnosed with something as terminal as a brain tumor, any extra time you can get with your loved one is priceless."

Survivors Weigh In

How do cancer patients decide how much the fight for that additional time is worth? Everyone's case is different, said Bob Gibbs, who received a brain cancer diagnosis 6 years ago at age 34. The father of four said his children were the driving force behind the efforts he and his wife took to research every possible option. The couple's research led Gibbs to a clinical trial for DCVax, a customized cancer vaccine under development by Northwest Biotherapeutics.

Concerned about the lack of knowledge about available treatment options at the community level, Gibbs established Miles for Hope, a nonprofit organization that seeks to increase awareness of tissue banking for brain and other solid tumors and the development of customized cancer vaccine treatments. Miles for Hope also raises funds to support these causes.

Gibbs said, "[Information on] a lot of the clinical trials that we found does not filter down to the community, regional, and neighborhood hospitals. My personal opinion is that, as part of the continuing education that nurses, oncologists, and other doctors have to go through, part of that should be what clinical trials are showing promise."

HUMC's Rosenbluth does not dispute Gibbs' assertion. Asked if the onus is on physicians to be aware of clinical trials and new drugs in the pipeline, he responded, rhetorically, "Well, who else? Is it the responsibility of a professional to know what's happening in his profession? The answer is, without question."

David Treadway knows the importance of trust in the physician-patient relationship, particularly where cancer diagnoses are concerned. Five years ago, the psychologist, writer, husband, and father of 2 adult sons found out he had stage IV non-Hodgkin lymphoma, with only a 25% chance of survival. The disease progressed rapidly and had a serious psychological impact on Treadway. "I was beginning to shut down, the way people do when they're dying," he said. Just prior to Treadway's first chemotherapy session, he received a heartfelt letter from one of his sons explaining that he was not ready to lose his father. "It was like a bucket of cold water on my head," Treadway said. "My son made me realize that it wasn't just about me, it was about the fact that the whole family had the disease, and we were all standing to lose."

Treadway said the connection he made with his physician—a young oncologist—at their first meeting was critical to his treatment success. Treadway looked directly at the doctor and said he wanted to know the best scenario and the worst scenario for someone in his situation. The doctor met Treadway's gaze head-on and said, "I don't usually have that kind of conversation with a patient who I'm meeting for the first time."

"That was great," said Treadway. "He wasn't giving me doctor-speak. He was sharing with me his personal response to what I was sharing with him. And from then on, I had a feeling of trust in this guy. I felt he was very much in the trenches with me."

Treadway said he was fortunate that his insurance policy covered "an enormous cost" of the treatment. Meanwhile, a friend's son was dealing with the very same illness, but with a less generous insurance policy. Treadway described hearing how the family and many of the families in his cancer support group are forced to make difficult clinical decisions based on finances as "torturous."

Finding Access

Getting the right medication to the right patient at the right time is the key to success when treating any medical condition. The pharmaceutical company is not blind to the realities of today's world, which leave many patients unable to afford lifesaving therapeutics. Pellegrino said Genentech has long operated according to the principle that it is pointless to develop medications if people cannot get access to them.

"We have a group of 400 people whose sole job is to help people work through reimbursement, access, and payment issues," Pellegrino said. "That ranges from helping patients do benefit investigations and fighting their insurers if they're denied, all the way to providing free drugs if a patient does not have insurance or is deemed under insured." The company has also placed a cap on the cost of bevacizumab at $55,000 a year for patients with an annual household income ≤$100,000, provided it is prescribed for an approved indication.

Other pharmaceutical companies have taken similar steps. In May 2006, Bristol-Myers Squibb announced it was capping the price of cetuximab at $10,000 per month. Patients spending more than this may be eligible for free or discounted drugs through a charitable program. Four months later, Amgen capped patients' copayment share for panitumumab (Vectibix) at no more than 5% of annual gross income. Under Amgen's program, patients spending more than this are eligible for free drugs through an assistance program. Almost every manufacturer of a biologic used to treat cancer has a Patient Access Program to help patients in need. (Visit www.OncLive.com, Resources, "Support and Assistance Guide," for information on these programs.)

One vehicle that cancer patients should not rely on for low-cost or free drugs is the clinical trial, said Dickinson. "I would be careful about portraying drugs in clinical trials as a way to potentially reduce costs." While clinical trials are worth considering for appropriate patients, such decisions should be based on whether the investigational drug appears to meet or exceed the standard of care available outside of a clinical trial. Steering financially compromised patients into trials for affordability reasons as opposed to serving their best interests medically invites a host of ethical questions.

Changing Landscape Pressures Oncologists

A new dynamic is on the horizon in the oncology market. In the past, payers left decisions regarding third-, fourth-, and fifth-line therapies to the physician and patient. But Ed Kissell, vice president of analysis for IntrinsiQ, a company that captures treatment decisions and details from more than 600 oncologists and nearly 20,000 unique patients, said stakeholders are beginning to put pressure on oncologists.

"We're beginning to see signs in breast cancer," Kissell said. "We're beginning to see signs in colorectal cancer, where previously there was an opportunity that a patient would receive both Erbitux and Vectibix. That likelihood is decreasing. Physicians are deciding to pick one EGFR over the other."

One way insurance companies are exerting their influence is by demanding that providers of oncology services rely on utilization tools when making treatment decisions. For example, Grail Research reports indicate that 36.4% of commercial health plans and 43.5% of Medicare Advantage plans used Quantity Limitations strategies in 2008 to guide breast cancer treatment decisions. Step Therapy, Prior Authorization by Diagnosis, Prior Authorization by Test Results, and

Michael Schott before his brain cancer diagnosis, standing with (R to L) his wife Evonne and his stepsons, Sam and Tommy.

Coinsurance Cost Share are other utilization tools currently in place.

Physicians themselves are becoming more cognizant of rising costs. Rosenbluth said in his specialty of geriatric oncology, the number one question being asked is how often patients need to be assessed for the effectiveness of treatment. "Are we overdoing it on CAT scans? Are we overdoing it on PET scans? These are very high-ticket items, so we're doing a lot less of those tests," he explained.

With medical costs showing no signs of halting their upward trajectory, comparative effectiveness research (CER)—that is, research comparing the benefits and effectiveness of similar treatment options—will likely begin to play a greater role in influencing the price of cancer drugs. The Patient Protection and Affordable Care Act, which the president signed into law in March 2010, grants $1.1 billion to fund CER. It also establishes the nonprofit Patient-Centered Outcomes Research Institute (PCORI), tasked with funding, prioritizing, and publishing CER. While the law prohibits PCORI from making any treatment recommendations, it does not prevent physicians or payers (private and public) from using the published findings to guide treatment decisions. In addition, the Department of Health and Human Services recently announced that it has commissioned creation of a "multipayer, multi-claim" database to assist those conducting CER.

"There hasn't been a lot of that done in the biologic sphere," Dickinson said, "but we feel that, increasingly, insurance companies are going to want to see head-to-head studies between drugs in order to provide justification for the cost." Some of the pharmaceutical companies have initiated their own CER efforts, he said. AstraZeneca sponsored a trial between cediranib (Recentin) and bevacizumab in first-line metastatic colorectal cancer (a flop for cediranib), and GlaxoSmithKline is comparing lapatinib (Tykerb) and trastuzumab in adjuvant breast cancer.

Some oncologists and patient advocates see the move by payers to implement closer adherence to standards of care as a good thing. But when a list of treatment alternatives for any type of cancer is only a search engine away, it is likely to become increasingly difficult for oncologists to explain why a payer might not cover a drug the patient views as a potential lifeline.

Delicate Decisions

Sally Ratcliffe, LGSW, is an oncology social worker for the Institute for Cancer Care at Mercy Medical Center in Baltimore, Maryland. She often serves as a conduit between the medical profession and patients and their families. She said it is just as important to meet cancer patients' psychosocial needs as it is to meet their biomedical needs. Patients often share their concerns more readily with a social worker or another support person, such as a pastor, than with a physician.

"You have to let the patient know they have a choice and to remind them that they are the ones who still have to make the decision," Ratcliffe said. "Even if the doctor says, 'This is what I recommend,' you educate the patients to ask the right questions." Ratcliffe said you start by asking what is important to them. "And sometimes it's not just what's important to them, but what's important to their family," she added.

Sekeres also believes the patient's family plays an important part in treatment discussions. He said it is important for doctors to develop the skill of "reading the room" while talking with patients about therapy. "When you ask a patient about treatment options, and the patient looks first to their spouse or to their kids before answering, you can see the influence of the other family members," he explained. Sekeres said recognizing the patient's motivation is important, because a patient who settles on a treatment course to please a family member in the room but is not fully committed "just won't do as well." He added, "If they take on an aggressive treatment course for someone else, they will tend to have many more side effects."

Rosenbluth said physicians must remember that their responsibility is not only to prolong life when possible, but also to ameliorate suffering in patients who have poor quality of life. "That second point is often overlooked," he said, noting that palliative care and hospice should be considered viable options for some patients. "We're delighted when we see a response and when patients live longer than the median survival that was anticipated. But often we can't prolong life, and we need to focus on what we can do, which is relieve suffering."

Amber Turner experienced cancer twice with her mother, and she said she believed at the time that God taught her everything she needed to know about a cancer journey. Then, when she was diagnosed with triple-negative breast cancer at age 36, she realized just how little she knew. She had a bilateral mastectomy followed by 16 total chemotherapy treatments—all given with her 4-year-old daughter Lainey sitting with her in a recliner. Turner said the experience gave her new insight into the delicate decisions that confront patients with cancer every day.

"Some folks who are against these life-extending drugs, maybe some of them haven't been touched by cancer in their families," said Turner, who is now cancer-free. "It's like they view cancer patients as being on total life support, laying in a bed with no quality of life. But I have friends who are on nothing but a drug like Avastin and they're living with cancer in their bones, in their lungs, yet they're out and about, living and thriving. They get to go to their grandchildren's recital. You can't tell me that's not good quality of life. Every month does matter." OBTN

Other High-Ticket Healthcare Items

While the value of life-sustaining care in terminal cancer is often questioned, many noncancerous conditions are also expensive to treat. For example, a 2008 Milliman Research Report assessed the cost for an intestinal transplant and 180-day follow-up care at $1,121,800, with a 5-year survival rate in 2005 of 47%. Not including additional medical costs for drugs to prevent rejection or complications, amortizing the transplant costs over 5 years equates to $224,360 annually. In 1994, the Multi-Society Task Force on the Permanent Vegetative State placed the annual median costs per patient at $126,000 to $180,000 per year. Decisions for the care of these patients are left to the physician, the patient (via a living will, in some cases), and the patient's family.

Perhaps it is the cumulative expense for the vast number of cancer patients that has prompted calls for greater assessment of cost-effectiveness in oncology care, especially when it comes to biologic therapies. According to the Agency for Healthcare Research and Quality, the following were the top 10 most costly medical conditions to treat in the United States in 2005:

1.	Heart conditions	**$76 billion**
2.	Trauma disorders	**$72 billion**
3.	Cancer	**$70 billion**
4.	Mental disorders	**$56 billion**
5.	Asthma and pulmonary disease	**$54 billion**
6.	High blood pressure	**$42 billion**
7.	Type 1 and 2 diabetes	**$34 billion**
8.	Osteoarthritis and other joint diseases	**$34 billion**
9.	Back problems	**$32 billion**
10.	Normal childbirth	**$32 billion**