Price of Precision: Patients, Oncologists Highlight Costs of Fighting for Access to Newest Drugs

The new generation of advanced cancer therapies dangle the hope of extended survival to patients but paying for them is an increasing and often untenable burden.

By Catherine Shaffer

THE SIDE EFFECTS of cancer treatments are notoriously arduous, but the market entry of high-priced biomarker-informed drugs and immunotherapies has introduced another type of toxicity to the cancer lexicon – financial toxicity.

Cancer care is one of the most expensive types of healthcare in the US and is often the cause of financial hardship among patients and survivors. According to the National Cancer Institute (NCI), patients' economic burden associated with cancer care amounted to $21 billion in 2019 – $16 billion in out-of-pocket costs and around $5 billion in costs arising from the time patients need to travel for and to receive care.

Low income, uninsured, and minority patients are at higher risk of experiencing financial hardship due to cancer treatment. A study published in *JCO Oncology Practice* in November 2021 found a strong association between race and financial toxicity due to cancer among patients in the US. However, even middle-income patients

with good health insurance can't easily afford such treatments. Another study published in *JAMA Network Open* earlier this year in February found that, worldwide, while the rate of financial toxicity among breast cancer patients was higher in low- and middle-income countries, more than 30 percent of patients in high-income countries also experienced financial toxicity.

Although the cost of the newest, most innovative therapies are significant contributors to cancer patients' financial burden, additional expenses stemming from next-generation sequencing and imaging can add to costs as well. Patients struggling to pay often cope by making lifestyle adjustments or taking a modified treatment regimen, and more recently, oncologists are finding that more of their patients are refusing therapy due to cost.

Monica Bryant, a cancer rights attorney and chief operating officer of Triage Cancer, an organization that educates cancer patients and caregivers on practical and legal issues, sees patients grappling with three main types of financial toxicities when trying to get on biomarker-driven therapies: difficulty getting reimbursed for genomic testing necessary for informing treatment; covering out-of-pocket costs despite having insurance; and not having insurance at all.

As lung cancer patient Chloe Mitchell put it, she has been "in the cancer battle" for six years, except instead of waging war against the disease, she has been fighting to get access to a pricey but effective biomarker-informed treatment. Speaking under a pseudonym because she's worried about retaliation from her health insurance company, Mitchell recounted how most

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of her time as a metastatic non-small cell lung cancer patient has been spent mired in red tape and appealing repeated coverage denials, instead of focusing on her health.

Mitchell was diagnosed in 2016 at age 57 with stage IIIB NSCLC and was initially treated with cisplatin and etoposide. About nine months later, new scans showed the tumors were still growing, so she began a second round of platinum-based chemotherapy, which also did not stop the cancer. Mitchell's next step was to apply to join a clinical trial in which Takeda was studying its tyrosine kinase inhibitor Exkivity (mobocertinib) in patients with EGFR- or HER2-positive NSCLC. Her insurance provider at the time, Anthem Blue Cross Blue Shield, initially declined to cover the next-generation sequencing test – the test that ultimately revealed she had a HER2-positive tumor, making her eligible for the drug.

"That [NGS test] is what informed all of these decisions [for] targeted treatments that they don't want to pay for," said Mitchell. "If people take that denial [for the test] and stop there, they're going to just get the limited standard-of-care options."

Two years after Mitchell got tested, the Centers for Medicare & Medicaid Services extended national coverage for US Food and Drug Administration-approved NGS testing for advanced cancer patients. This inevitably nudged NGS testing toward standard practice in many cancer care settings and may have also spurred some commercial payors to take an easier stance on covering such testing. Yet, patients and providers say it's still all too common for them to have to tussle with payors to get tests reimbursed.

Mitchell's cancer responded to Exkivity for about two and a half years. When she stopped responding to Exkivity, she began receiving off-label treatment with AstraZeneca and Daiichi Sankyo's Enhertu (trastuzumab deruxtecan), which at that time in 2021 was approved for HER2-positive breast cancer.

In August 2022, the FDA approved Enhertu for the 2 percent to 4 percent of NSCLC patients with HER2-mutated tumors, along with two companion diagnostics, Thermo Fisher Scientific's Oncomine Dx Target Test and Guardant Health's Guardant360 CDx liquid biopsy test to identify eligible patients.

Anthem has balked at covering Enhertu for the entire time Mitchell has been taking it, she said, agreeing only to pay for it in two-to-three month increments and only after confirming she is still benefitting from the therapy. Anthem initially denied coverage for Enhertu when Mitchell switched from Cigna and back to Anthem on January 1, 2022. After going through the appeals process, Mitchell received coverage approval for six months of treatment, which she believes was possible only because the representative on the phone was unusually sympathetic to her situation. Even though the FDA has approved Enhertu for HER2-mutated NSCLC, Mitchell remains uncertain about her continued access to the drug based on her difficult experience with Anthem.

In the six and half years Mitchell has been in treatment for cancer, she has been able to live a fairly normal life, travel, see her two sons get married, and welcome grandchildren into the

family. These are "things I originally didn't think I would live to see," she said. "They tell you half the people who get my diagnosis will be dead within six months."

But the repeated coverage denials have weighed on her, and added to that, she has had to negotiate with her insurance companies and healthcare providers about how to receive her medications. For example, Anthem initially refused to cover Enhertu if she got it at her NCI-designated cancer center because it administered the drug at a markup. It directed Mitchell to use an independent infusion center instead, which offered the drug at $13,000 every three weeks. Mitchell attempted to coordinate receiving care from a specialist at the NCI-designated cancer center while getting Enhertu infusions at another clinic, but eventually, upon appeal, the insurance company agreed to cover the treatment through Mitchell's original doctor.

Anthem, at one point, offered Mitchell an opportunity to sign up for a program that the insurers' representatives promised would allow automatic approval for her cancer treatments. However, this came with a stipulation that she must receive care from a team of doctors contracted with Anthem. Looking into the future when she may no longer be responding to Enhertu, Mitchell asked if she would be able to access investigational therapies within clinical trials. "They didn't really want to talk specifics unless I enrolled in the program," which Mitchell said made her suspicious about how open these Anthem-contracted doctors would be to prescribing cutting-edge or investigational treatments. "The things that have worked for me have been these newer clinical trial drugs and targeted therapies," she noted.

In another example, during a period when Mitchell was insured through Cigna, the company suddenly refused to fill her Enhertu prescription through the pharmacy at her cancer center. The payor told her that in order to combat the high costs of certain medications, it had started its own pharmacy that she would need to use. It turned out, however, that Enhertu was one of the drugs Cigna couldn't supply to Mitchell in a timely fashion, and the insurer eventually had to "back down," she said.

Anthem Blue Cross Blue Shield and Cigna did not respond to requests to comment for this article.

Under the constant stress of out-of-pocket costs and never-ending insurance appeals, Mitchell said her family has had to sacrifice in other areas of their lives. She has curtailed vacation plans and not contributed as much as she wanted toward her children's education due to the ever-looming possibility that she will lose insurance coverage for Enhertu.

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"At some point, am I going to say I'd rather leave this money to help my kids continue their educations rather than chase some treatment? It definitely weighs on me," Mitchell said. In the meantime, she said she takes comfort in the fact that she still has the wherewithal to spend countless hours on appeals and fighting her way through the system.

Appealing, and other alternatives

Triage Cancer's Bryant said situations like Mitchell's are not uncommon among patients with commercial insurance plans. "The major challenge that we see for people is they get denied, and then they don't understand they have a right to appeal those denials," she said.

For example, the Affordable Care Act (ACA) requires insurance companies to inform patients why they deny a claim and how patients can appeal it. If the appeal is denied, patients can challenge the decision again with an external reviewer, which is binding on both the patient and the insurance company. However, less than 0.1 percent of claims denied by commercial insurers are appealed, even though once it gets to the level of the external reviewer, appeals are successful 39 percent to 59 percent of the time. "If you generalize that, it means half the time when the insurance company is saying, 'No,' the external reviewer is saying the insurance company was wrong and they should have paid," said Bryant.

For cancer patients like Mitchell who know to keep appealing and have the stamina to do so, this is "absolutely an added burden" on them and their families as well as on healthcare providers, Bryant acknowledged.

Even when interventions are "covered," the out-of-pocket costs can still be staggering. "If I have a plan with a $9,000 out-of-pocket maximum and I'm barely making ends meet, how can I possibly pay that?" she said.

Bryant often encourages patients insured through commercial plans to take advantage of open enrollment periods and to sign up for plans with better coverage. The first year that cancer

patients are diagnosed, they may have a plan that doesn't offer much coverage. However, at open enrollment, there's an opportunity to consider alternatives, and Triage Cancer helps patients compare insurance policies and choose plans that are cost-effective for their cancer treatment. "Thanks to the ACA, we are not locked into our insurance policies year after year," Bryant said.

While pharmaceutical companies often provide direct copayment assistance to patients with commercial insurance, legally, they cannot provide that assistance to Medicare recipients. According to Bryant, when it comes to prescription drug coverage under Medicare Part D, after meeting the deductible, the patient pays 25 percent of the costs up to a threshold of about $8,000. After that, the patient is still responsible for 5 percent of drug costs.

The list price for a three-week dose of the immunotherapy Keytruda (pembrolizumab), according to manufacturer Merck, is $10,897, and is $21,794 for a six-week course. Five percent of that is more than $500 and $1,000, respectively. "[That's] a lot of money, especially when you think about who Medicare beneficiaries are. They are seniors who often have a fixed income, and individuals with disabilities so severe they cannot work," said Bryant. "Where are these people coming up with the extra money to pay for five percent of an expensive drug?"

Andrew Hertler, chief medical officer at New Century Health, a specialty care management company, also highlighted the challenges for Medicare patients. "If you have Medicare and don't have a companion plan, you may well be hit with a 20 percent copay, and 20 percent of $20,000 a month is still $4,000," he said. "That's beyond the budget of many families in this country."

Financial toxicity is an especially heavy burden on the largely Haitian, Spanish-speaking cancer patients who are often on Medicaid that oncologist Andrew Schneider treats in his South Florida practice. Sorting out patients' financial challenges consumes a great deal of his office's time.

"Whenever I want to prescribe a medication like Keytruda, the first thing I have to do is go to my office staff and look at the benefits that the patient has. What is their out-of-pocket [cost]?" said Schneider. In the past, his office has been able to help patients cover copayments with funds available through grants, but Schneider said those are becoming scarce.

In the absence of grants and other financial assistance, Schneider's practice might set up a payment plan or offer a less expensive alternative. He said rebates of up to 30 percent are available on some drugs like Keytruda. Still, if the rebate offered by the manufacturer only allows Schneider's practice to break even, he said he can't assist the patient. "If they're going to be on it for a long time and I have enough margin and [a] rebate on a drug, then I might do it," he said.

Fear of financial hardship

A study of 9.5 million cancer patients who were at least 50 years old, diagnosed between 2000 and 2012, revealed that 42 percent totally depleted their assets, and more than 30 percent racked up debt by the second year of their diagnosis. The fear of financial hardship keeps many patients from getting treated at all, and Hertler from New Century Health has seen this firsthand during his time as an oncologist. When he first started practicing in 1985, he never encountered patients who refused therapy. More recently, he has had patients refuse treatment that in some cases could have cured them or significantly prolonged their lives. When he asked why they didn't want these drugs, the patients said they didn't want to leave their families bankrupt.

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Hertler's observation of cancer patients refusing necessary treatment parallels the market entry of more high-cost precision cancer treatments: first the availability of targeted agents, then biomarker-informed drugs, followed by immunotherapies, and now, highly individualized n-of-1 CAR T-cell therapies. Most cancer drugs commercialized between 2009 and 2014 cost more than $100,000 per year. CAR T-cell therapies launched in the past few years can cost almost $500,000 annually.

Hertler pointed out, however, that for all the "precision" touted in these newer drugs, advanced cancer patients may only experience marginal benefits, which complicates the cost-benefit calculation. "We've got these very, very expensive drugs, some of which are substantial steps forward [scientifically]. But we know that all patients don't benefit," said Hertler. For example, he pointed out that while checkpoint inhibitors like Bristol Myers Squibb's Opdivo (nivolumab) and Keytruda have significantly changed the treatment for a number of cancers, most patients don't experience enduring benefits on them. And while newer biomarker-informed therapies are allowing patients to live longer, most of these drugs aren't curative.

Thirty-eight years ago, "the median survival [for metastatic NSCLC] was six months, and now it's getting up over two years," said Hertler, adding that over that same period of time, there have been several logs of increase in drug price. Given the relatively "modest" gains in survival and the fact that most of the newer cancer drugs still don't cure metastatic cancer patients, Hertler wondered: "Is that progress?"

Part of the solution, Hertler hopes, will come from better screening and diagnostic tools and moving many of the newer precision medicines to the early-stage setting, when patients have a better shot at a cure. "Cancer is a genetic disease. It's mutation-driven. That's what's going to be the key both in screening and in determining who is most likely to benefit from these different therapies," said Hertler.

Mitchell, whose cancer continues to respond well to Enhertu, pointed out that it's not just one factor that leads to financial toxicity for patients receiving biomarker-driven therapies, but a combination of drug pricing, payor resistance, and hospital billing. "The insurance companies are trying to do a lot of things to mitigate these really high drug prices, and I don't blame them," Mitchell said.

"The hospitals are also part of the problem," she added, noting that copayments on costly imaging and other services add to patients' financial burden.

Ultimately, what works against patients is that they don't have the knowledge or resources or they're too sick to keep pushing for advanced cancer care when denied coverage. For many patients, Mitchell said that "the idea of fighting an insurance company or going through appeals is just more than they can handle." PMQ

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Catherine has been a reporter with *Precision Oncology News* since 2022 where she focuses on the latest advances in genomics and drug discovery as they relate to the development of personalized medicines for cancer. Prior to that, she covered science and biotechnology for a number of other publications, including *Genetic Engineering and Biotechnology News, Nature Biotechnology,* and *BioWorld Today*, as well as on-air regional news for NPR affiliate WUOM in her hometown of Ann Arbor, Michigan. Catherine is also an award-winning science fiction author. Her stories have appeared in numerous magazines and anthologies *Analog* and *Nature's Futures*. Catherine has a bachelor's degree in biochemistry from Michigan State University and a master's in biological chemistry from the University of Michigan.