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CML Study Links Imatinib Copayments to Adherence to Treatment

BY ROBERT H. CARLSON

There is nothing counterintuitive about this finding from a recent study of patients with chronic myeloid leukemia (CML): The higher their copayment for imatinib, the more likely they were to discontinue or be nonadherent to treatment.

In the analysis of insurance records for 1,541 CML patients—online as an Early Release article in the *Journal of Clinical Oncology* (***doi: 10.1200/JCO.2013.52.9123***)—17 percent of patients with higher copayments discontinued treatment with tyrosine kinase inhibitors (TKIs) during the first 180 days following initiation versus 10 percent of patients with lower copayments.

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Best Breast Cancer Research 2013

BY CYNTHIA X. MA, MD, PHD

With greater optimism in the fight against breast cancer, 2013 ended with discoveries that lend to a deeper understanding on the pathogenesis and progression of breast cancer. Highlighted here are a few examples of these studies that are likely to shape breast cancer research and ultimately patient care in the future.

HER2 Mutation as a Therapeutic Target in HER2 Non-amplified Breast Cancer

- *Bose R et al: Activating HER2 mutations in HER2 gene amplification negative breast cancer. **Cancer Discov 2013;3:224-237***: Bose et al demonstrated that HER2 somatic mutations in breast cancers that lack HER2 gene amplification are oncogenic and, importantly, are sensitive to treatment with the investigational irreversible HER-kinase inhibitor neratinib in preclinical models.

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PERIODICALS

Myeloma: Front-Line for Continuous 'Rd'

BY ROBERT H. CARLSON

NEW ORLEANS—Development of novel agents for multiple myeloma in recent years is bearing fruit, as treatment regimens move away from alkylating agents and toward immunomodulatory drugs and proteasome inhibitors.

Case in point: A plenary session report here at the American Society of Hematology Annual Meeting of the open-label Phase III "FIRST" (Frontline Investigations of Revlimid+Dexamethasone Versus Standard Thalidomide) trial (MM-020/IFM 07 01) showed lenalidomide plus low-dose dexamethasone to be superior in progression-free survival compared with the long-time standard of melphalan-prednisone-thalidomide (MPT), when given as front-line treatment for patients with newly diagnosed, transplant-ineligible myeloma.

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CML Study Links Imatinib Copayments to Treatment Adherence

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"Patients with higher copayments were 42 percent more likely to be nonadherent," the first author, Stacie B. Dusetzina, PhD, Assistant Professor in the Departments of General Medicine and Health Policy and Management at the University of North Carolina at Chapel Hill, said in an interview. "Given the importance of these therapies for patients with CML, our data suggest a critical need to reduce patient costs for the therapies."

High and low copayments were defined by two cutpoints: among all copays in a given year, the 75th percentile was the point above which a copayment was considered high; below the 25th percentile was considered low.

In 2011, the 75th percentile was $72.50. The 75th percentile for all copayments from January 1, 2002, and June 30, 2011 was $53, and the 25th percentile was $17. The median, or 50th percentile, for that period was $30.

Dusetzina noted that data on the impact of high copayments are all the more important given the increase in the use of oral medications to treat cancer and prevent recurrence.

The researchers used Truven Health MarketScan health plan claims from 2002 to 2011 to identify 1,541 adults (age 18 to 64) with CML who started imatinib therapy between January 1, 2002, and June 30, 2011, and had insurance coverage for at least three months before initiation through six months after.

ELLIN BERMAN, MD: "It's intuitive that when people have high copayments and times get tough and they have other bills, it's the drug that goes. This can be especially true for people with CML—if they are feeling relatively well, they may believe they can stop temporarily."

The database includes information from a selection of large employers, health plans, and government and public organizations and represents the health care experience of employees and their dependents enrolled in commercial health insurance plans sponsored by approximately 100 payers, the researchers noted. The data include monthly enrollment data, inpatient and outpatient medical claims, and outpatient prescription drug claims.

Discontinuation of therapy was defined as a gap in supply of more than 60 days following the exhaustion of drug supply. "We chose 60 days because treatment breaks are rarely for 60 days or more," Dusetzina said.

Adherence was defined by using the proportion of days covered, representing the number of days that a patient had medication available divided by the number of days in the period. Patients were considered adherent to TKIs if they had more than 80 percent of days with TKIs available during the 180-day period after initiating imatinib; otherwise they were considered nonadherent.

STACIE B. DUSETZINA, PhD: "Given the recent increase in the use of oral medications for cancer treatment and recurrence prevention, it is important to develop rational policies that do not inhibit patient access to highly effective, life-extending treatments."

Financial 'Toxicity': Best Case Scenario

This analysis, she noted, may represent only the best-case scenario of the impact of cost sharing on adherence to TKIs. It included privately insured patients with relatively generous employer-sponsored insurance (median copayment was $30 per fill) who filled at least one imatinib prescription. Patients with very high copayments that resulted in primary nonadherence—not filling the first prescription at all—were not represented.

Dusetzina cited a recent study that showed noncompliance from a different angle, a pilot study on the "financial toxicity" of cancer treatment (***Zafar et al: The Oncologist 2013;18:381-390***). In that survey of 254 insured cancer patients, 75 percent had applied for drug copayment assistance; 42 percent reported a significant or catastrophic subjective financial burden; 68 percent cut back on leisure activities; 46 percent reduced spending on food and clothing; and 46 percent used savings to defray out-of-pocket expenses.

And to save money, 20 percent of those surveyed said they took less than the prescribed amount of medication, 19 percent only partially filled their prescriptions, and 24 percent avoided filling prescriptions altogether.

Blood Editorial about 'Unsustainable' Drug Prices

Dusetzina said the study was initiated after the publication of a much-publicized editorial in *Blood* last year, signed by 116 oncologists and hematologists, decrying the extremely high cost of treating CML with TKIs such as imatinib (***OT 5/25/13 issue***).

"There really wasn't any good information about what patients actually paid, so we thought to look at information available on what insurance companies are paying, what patients

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"The way most other costs are controlled in our society—people making rational decisions of whether it's worth it to them or not—that's the model under which one would like to see drugs and health care managed, but that's not what we have."

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are paying, and then look at the downstream effects on patients for having higher cost sharing," she said.

Ellin Berman, MD, Attending Physician in the Leukemia Service of Memorial Sloan-Kettering Cancer Center, was one of the 116 physicians signing the article in *Blood*. She said she did so because she was outraged by the alarmingly high cost of imatinib.

The potential effect on patients is obvious, she said. "It's intuitive that when people have high copayments and times get tough and they have other bills, it's the drug that goes," Berman said in a telephone interview. "It can be especially true for people with CML—if they are feeling relatively well they may believe they can stop temporarily. Even when we tell people that stop-start-stop-start with these TKIs may be a breeding ground for a resistant clone, it most of the time does not penetrate."

The price of imatinib and the other TKIs should at least be stable, she said. "The price of Gleevec has gone up terribly, and we do have people we refer to patient-assistance programs. To my knowledge we have not had anyone stop the drug due to high copays, but the highest monthly copay I have seen is $500."

Whether patients are compliant or not is difficult to say, she said. "If patients say they take the drug every day, I take them at their word. Some will say they missed a day or two, and some come in and tell us they stopped for a few weeks—most people don't hide that."

Nonetheless, PCR levels in peripheral blood will eventually show if the patient with CML has not been compliant.

Berman added that Novartis has sponsored two clinical trials looking at whether patients with CML can safely stop therapy: "I think it interesting that Novartis sponsored these trials. I suspect there are a proportion of people who can safely discontinue imatinib."

Another of the 116 authors of the *Blood* article, Elias Jabbour, MD, Associate Professor in the Department of Leukemia at the University of Texas MD Anderson Cancer Center, said

ELIAS JABBOUR, MD: "Pharma may have patient assistance plans, but obviously they are not working. The copayments should be reasonable."

LEONARD SALTZ, MD, called imatinib a poster child for a highly efficacious, elegantly scientifically designed drug that completely transformed several diseases. "It is unacceptable to us as clinicians and members of society for such a drug to be unavailable to someone who could benefit."

compliance is a major cornerstone for long-term outcome in CML.

He cited a study showing that adherence is the critical factor for achieving molecular responses in patients with CML who achieve complete cytogenetic responses on imatinib (***Marin D et al: JCO 2010;28:2381-2388***). Those researchers concluded that in patients with CML treated with imatinib for some years, poor adherence may be the

> "There is no easy solution to the problem or somebody would have thought of it."

predominant reason for inability to obtain adequate molecular responses.

"In this new study, most of these patients have good private insurance, but for those with high copayments, there was a high rate of discontinuation and bad adherence to therapy" Jabbour said. "That is critical, because these patients could have a normal life span if they adhered to therapy. The benefit of a normal lifespan, the product of years of research, should not be lost because patients cannot afford the drug anymore."

Some pharma companies do offer patients assistance with the cost of their drugs, Jabbour said, but that is a transient solution that covers the drug for only a short period of time and cannot be considered the answer.

Jabbour related his experience trying to get patient assistance from one manufacturer for a patient who could not make the copayment: "I spent two hours on the phone but couldn't get the assistance, and I'm a physician," he said, suggesting that patients themselves would have worse luck. Pharma may have patient assistance plans but obviously they are not working. The copayments should be reasonable."

No Easy Fix

Getting rid of copayments entirely would only be a short-term solution to a problem that needs a long-term solution, said Leonard Saltz, MD, Chief of the Gastrointestinal Oncology Service and Head of the Colorectal Oncology Section at Memorial Sloan-Kettering Cancer Center, also asked to comment for this article.

"The main problem is the egregiously high price of many of these drugs, and the need to come up with a more sustainable and reasonable pricing schedule," he said.

Saltz, who has been vocal in criticizing the enormously high cost of cancer drugs, said our society today has no mechanism for controlling those costs. "The way most other costs are controlled in our society—people making rational decisions of whether it's worth it to them or not—that's the model under which one would like to see drugs and health care managed, but that's not what we have. We have a situation where once a drug is approved by the FDA, another arm of the government, CMS, is required to pay whatever price that company sets and is forbidden by law from negotiating from that price.

"So if there is no limit to what the cost of the drug could be, and if there is no copay, that is no solution—that is a short-term fix."

Saltz called imatinib a poster child for a highly efficacious, elegantly scientifically designed drug that completely transformed several diseases. "It is unacceptable to us as clinicians and members of society for such a drug to be unavailable to someone who could benefit," he said. "But there are many stakeholders involved here, and to say that the pharmaceutical company that markets the drug should be immune from everybody else's problem of how to pay for it, and to set any price it wishes, is not looking at the whole picture."

He said that on a simple level it is untenable for Medicare, the largest purchaser of pharmaceuticals, to be forbidden from negotiating drug prices.

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Imatinib is not part of the armamentarium in the GI clinic, but Saltz said there are similar cases where high copayments are a problem. For example, a patient with a pancreatic neuroendocrine tumor may be prescribed sunitinib or everolimus, which are useful but are quite expensive "and copays are sometimes quite problematic, and we don't necessarily have an easy solution for that," he said.

"It is very rare that we have been able to get a patient into any of the patient assistance programs—most of the time our patients don't meet the criteria."

Saltz reiterated that there is no easy answer: "If I had a simple Solomonic solution I would have proposed it a long time ago and the problem would have gone away. There is no easy solution to the problem or somebody would have thought of it."