A new test could save arthritis patients time, money and pain. But will it be used?

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Erinn Maury knew Remicade wasn't the right drug for Patti Schulte, a rheumatoid arthritis patient the physician saw at her Millersville, Maryland, practice. Schulte's swollen, painful joints hadn't responded to

Enbrel or Humira, two drugs in the same class.

But the insurer insisted, so Schulte went on Remicade. It didn't work either.

What's more, Schulte suffered a severe allergic reaction to the infusion therapy, requiring a heavy dose of prednisone, a steroid with grave side effects if used at high doses for too long.

After 18 months, her insurer finally approved Maury's drug of choice, Orencia. By then, Schulte's vertebrae, weakened by prednisone, had started cracking. She was only 60.

Schulte's story of pain, drug-hopping, and insurance meddling is all too common among patients with rheumatoid arthritis, who often cycle agonizingly through half a dozen drugs in search of one that provides a measure of relief. It's also a story of how doctors are steered by pharmacy benefit managers—the middlemen of the drug market—as well as by insurers.

Once people with inflammatory conditions such as rheumatoid arthritis reach a certain stage, the first prescription offered is typically Humira, the best-selling drug in history, and part of a class known as tumor necrosis factor inhibitors, or TNFis, which fail to significantly help about half of the patients who take it.

"We practice rheumatology without any help," said Vibeke Strand, a rheumatologist and adjunct clinical professor at Stanford. She bemoaned the lack of tools available to choose the right drug while bristling at corporate intervention in the decision. "We are told by the insurer what to prescribe to the patient. After they fail methotrexate, it's a TNF inhibitor, almost always Humira. And that's not OK."

If there's a shred of hope in this story, it's that a blood test, PrismRA, may herald an era of improved care for patients with rheumatoid arthritis and other autoimmune conditions. But first, it must be embraced by insurers.

PrismRA employs a predictive model that combines clinical factors, blood tests, and 19 gene patterns to identify the roughly 60% of patients who are very unlikely to respond to a TNFi drug.

Over the past 25 years, drug companies have introduced five new classes of autoimmune drugs. TNFis were the first to market, starting in the late 1990s.

Some 1.3 million Americans have rheumatoid arthritis, a disease in which a person's immune system attacks their joints, causing crippling pain and, if improperly treated, disfigurement. The newer drugs, mostly so-called biologics, are also used by some of the 25 million or more Americans with other autoimmune diseases, such as lupus, Crohn's disease, and psoriasis. Typically costing tens of thousands of dollars annually, the drugs are prescribed after a patient fails to respond to older, cheaper drugs like methotrexate.

Until recently, rheumatologists have had few ways to predict which of the new drugs would work best on which patients. Often, "it's a coin flip whether I prescribe drug A or B," said Jeffrey Curtis, a rheumatology professor at the University of Alabama-Birmingham.

Yet about 90% of the patients who are given one of these advanced drugs start on a TNFi, although there's often no reason to think a TNFi will work better than another type.

Under these puzzling circumstances, it's often the insurer rather than the doctor who chooses the patient's drug. Insurers lean toward TNFis such

as adalimumab, commonly sold as brand-name Humira, in part because they get large rebates from manufacturers for using them. Although the size of such payments is a trade secret, AbbVie is said to be offering rebates to insurers of up to 60% of Humira's price. That has enabled it to control 98.5% of the U.S. adalimumab market, even though it has eight biosimilar competitors.

PrismRA's developer, Scipher Medicine, has provided more than 26,000 test results, rarely covered by insurance. But on Oct. 15, the Centers for Medicare & Medicaid began reimbursing for the test, and its use is expected to rise. At least two other companies are developing drug-matching tests for rheumatoid arthritis patients.

Although critics say PrismRA is not always useful, it is likely to be the first in a series of diagnostics anticipated over the next decade that could reduce the time that autoimmune disease patients suffer on the wrong drug.

Academics, small biotechs, and large pharmaceutical companies are investing in methods to distinguish the biological pathways involved in these diseases, and the best way to treat each one. This approach, called precision medicine, has existed for years in cancer medicine, in which it's routine to test the genetics of patients' tumors to determine the appropriate drug treatment.

"You wouldn't give Herceptin to a breast cancer patient without knowing whether her tumor was HER2-positive," said Costantino Pitzalis, a rheumatology professor at the William Harvey Research Institute in London. He was speaking before a well-attended session at an American College of Rheumatology conference in San Diego in November. "Why do we not use biopsies or seek molecular markers in rheumatoid arthritis?"

It's not only patients and doctors who have a stake in which drugs work best for a given person.

When Remicade failed and Schulte waited for the insurer to approve Orencia, she insisted on keeping her job as an accountant. But as her prednisone-related spinal problems worsened, Schulte was forced to retire, go on Medicaid, and seek disability, something she had always sworn to avoid.

Now taxpayers, rather than the insurer, are covering Schulte's medical bills, Maury noted.

Precision medicine hasn't seemed like a priority for large makers of autoimmune drugs, which presumably have some knowledge of which patients are most likely to benefit from their drugs, since they have tested and sold millions of doses over the years. By offering rebate incentives to insurers, companies like AbbVie, which makes Humira, can guarantee theirs are the drugs of choice with insurers.

"If you were AbbVie," Curtis said, "why would you ever want to publish data showing who's not going to do well on your drug, if, in the absence of the test, everyone will start with your drug first?"

What testing could do

Medicare and commercial insurers haven't yet set a price for PrismRA, but it could save insurers thousands of dollars a year for each patient it helps, according to Krishna Patel, Scipher's associate director of medical affairs.

"If the test cost $750, I still only need it once, and it costs less than a month of whatever drug is not going to work very well for you," said Curtis, a co-author of some studies of the test. "The economics of a

biomarker that's anything but worthless is pretty favorable because our biologics and targeted drugs are so expensive."

Patients are enthusiastic about the test because so many have had to take TNFis that didn't work. Many insurers require patients to try a second TNFi, and sometimes a third.

Jen Weaver, a patient advocate and mother of three, got little benefit from hydroxychloroquine, sulfasalazine, methotrexate, and Orencia, a non-TNFi biologic therapy, before finding some relief in another, Actemra. But she was taken off that drug when her white blood cells plunged, and the next three drugs she tried—all TNFis—caused allergic reactions, culminating with an outbreak of pus-filled sores. Another drug, Otezla, eventually seemed to help heal the sores, and she's been stable on it since in combination with methotrexate, Weaver said.

"What is needed is to substantially shorten this trial-and-error period for patients," said Shilpa Venkatachalam, herself a patient and the director of research operations at the Global Healthy Living Foundation. "There's a lot of anxiety and frustration, weeks in pain wondering whether a drug is going to work for you and what to do if it doesn't."

A survey by her group found that 91% of patients worried their medications would stop working. And there is evidence that the longer it takes to resolve arthritis symptoms, the less chance they will ever stop.

How insurers will respond to the availability of tests isn't clear, partly because the arrival of new biosimilar drugs—essentially generic versions—are making TNFis cheaper for insurance plans. While Humira still dominates, AbbVie has increased rebates to insurers, in effect lowering its cost. Lower prices make the PrismRA test less appealing to insurers, since widespread use of the test could cut TNFi prescriptions by up to a third.

However, rheumatologist John Boone in Louisville, Kentucky, found to his surprise that insurers mostly accepted alternative prescriptions for 41 patients whom the test showed unlikely to respond to TNFis as part of a clinical trial. Boone receives consulting fees from Scipher.

Although the test didn't guarantee good outcomes, he said, the few patients given TNFis despite the test results almost all did poorly on that regimen.

Scientists from AbbVie, which makes several rheumatology drugs in addition to Humira, presented a study at the San Diego conference examining biomarkers that might show which patients would respond to Rinvoq, a new immune-suppressing drug in a class known as the JAK inhibitors. When asked about its use of precision medicine, AbbVie declined to comment.

Over two decades, Humira has been a blockbuster drug for AbbVie. The company sold more than $3.5 billion worth of Humira in the third quarter of 2023, 36% less than a year ago. Sales of Rinvoq, which AbbVie is marketing as a treatment for patients failed by Humira and its class, jumped 60% to $1.1 billion.