Personalized Medicine in Cancer: Matching Patients and Drugs

By Kate Ruder

For the first time in quite a while, physicians who treat cancer are genuinely excited about the possibility that “personalized medicine” may soon become a reality for some lung cancer patients.

It has been a year and a half since the drug Iressa came on the market, which works spectacularly in about ten percent of lung cancers patients and fails to help the rest. No one could figure out why.

Last spring, two groups of researchers figured out that most people who respond to Iressa have similar genetic mutations in their tumors. A later study extended the findings to a related drug, Tarceva, which is awaiting approval by the U.S. Food and Drug Administration.

Now that scientists can explain the drugs’ effectiveness in some cases, there is hope that they can better predict who will respond to them in the future and that lessons from Iressa and Tarceva can be applied to other cancers.

Just a few months ago, two research hospital laboratories began offering a test to detect the mutations, which occur in a gene called EGFR. The tests have been used in fewer than 200 patients so far, but scientists speculate they could become widely available in three to six months.

“The simple fact is it’s all about matching the right patient with the right drug,” says Brian Druker of Oregon Health Science University in Portland, who was a pioneer in developing another drug, Gleevec.

“We’re in a transition phase where we don’t know all the options,” says Druker, “but the era of matching patients to drugs is not far away.”

One of the problems is that all of the patients don’t fit into neat boxes, and perhaps they never will. For example, people without the mutations also respond to Iressa for reasons that are not known, but scientists are expanding their search for key mutations that could explain this.

“We are looking for mutations in other genes that could explain why some tumors respond to Iressa in the absence of EGFR mutations, and also looking at how and why tumors may eventually become resistant to Iressa,” says Daniel Haber of Massachusetts General Hospital in Boston.

Haber’s colleague at Mass General Thomas Lynch is doing work on Iressa too. He has a clinical trial that is testing patients for the mutations as a predictor of their response to Iressa as an initial treatment. Iressa isn’t usually the first option; it’s typically given to lung cancer patients who haven’t responded to chemotherapy.

Iressa and Tarceva are part of a relatively new class of drugs known as targeted drugs, which are different from traditional chemotherapy drugs because they are designed to specifically hit cancer cells. Unlike chemotherapy, which kills healthy and cancerous cells, targeted drugs are supposed to kill only cancer cells.

The vision for these types of drugs was that they would be “magic bullets” against cancer, but they’ve had their downs.
Iressa didn’t work in most people in clinical trials, but it had marvelous, undeniable benefit for a small percentage of people, and for this reason the U.S. Food and Drug Administration approved it in May 2003.

It’s approved for patients with the most common type of lung cancer, non-small-cell lung cancer, which is also the biggest killer among cancers in the United States with 140,000 new cases each year. AstraZeneca makes Iressa.

It took a year for researchers to begin to unravel the reasons behind Iressa’s erratic success.

Two groups of Harvard researchers painstakingly sequenced the EGFR gene, for Epidermal Growth Factor Receptor, in lung tumors from patients who responded to Iressa and those who did not. Most responders had the mutations. Non-responders did not.

Both Haber and Lynch were researchers on the study from Mass General. The other study was done by scientists at Dana-Farber Cancer Institute.

“The studies generated significant buzz,” says Daniela Gerhard of the Office of Cancer Genomics at the National Cancer Institute. “It was very important and encouraging for everyone who was trying to use genomics to develop targets for cancer treatments.”

It was a buzz for some patients too. After the studies were published, the scientists received calls from patients who wanted to find out if their tumors had mutations and whether Iressa would work for them.

The problem was the scientists did not have the time or the facilities to do the sequencing.

That’s when Harvard Partners stepped in. Harvard Medical School-Partners Healthcare Center for Genetics and Genomics (HPCGG) is a Harvard-affiliated institute with DNA sequencers, and they developed a genetic test that could be done “at cost” for doctors at Massachusetts General and Dana-Farber.

The test was up and running in August, and the center now screens up to 50 tumors a month for roughly $850 per sample.

“The discovery [of the EGFR mutations] was made and in a relatively short time we had turned it around into a test,” says Randall Mason of HPCGG.

At the same time, scientists at City of Hope National Medical Center in Duarte, California, saw the two Harvard studies and set to work on a genetic test for Iressa. It also had a test ready in August and has done fourteen tests to date, for doctors at City of Hope Hospital. Their turnaround is about two weeks.

“We were pretty excited by the papers and we thought the data was significant, so we immediately started to develop a test to detect the mutations,” says Juan-Sebastian Saldivar, co-director of the laboratory at City of Hope.

He says that some of the requests for tests have been patient-driven. For example, two patients asked their doctors at City of Hope for the test because they were concerned about a side effect of Iressa, a sometimes fatal kind of pneumonitis called interstitial lung disease.

“At this point in time we are not advocating that the test should be used to decide who does and who doesn't get the drug, says Saldivar. “But we think it is a useful prognostic tool and can be a valuable instrument for making decisions about treatments.”

These tests raise more questions than answers right now, and they’re not even widely available yet. Who should test? How should the information be used?

The other question that remains is why certain groups of patients such as nonsmokers and women are more likely to have the mutations and respond to Iressa and Tarceva. While most lung cancer patients are smokers, a small percentage of lung tumors occur in people who have never smoked—and they tend to respond to Iressa.

It could take a long time to answer these and other questions about why drugs work for some people and not others. Doing so will be critical if medicine is to reach the goal of matching the right drugs with the right patients.


Pao, W. et al. EGF receptor gene mutations are common in lung cancers from "never smokers" and are associated with sensitivity to gefitinib and erlotinib. Published online in Proceedings of the National Academy of Sciences on August 23, 2004.

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