Pazdur's Cancer Rules

Many observers—including some on Congressional oversight committees—are still puzzled by the Food and Drug Administration's recent decision to effectively pull a good lung cancer treatment called Iressa from the U.S. market. Let us suggest that the best way to look at it is as an all-too-predictable case of bureaucratic revenge.

The FDA's oncology chief gets his revenge.

Forgive us for getting personal, but in this case the personal is the political is the policy. FDA oncology drugs chief Richard Pazdur is the most important person in the U.S. government when it comes to cancer drugs, and he has never made a secret that he dislikes the accelerated approval process under which Iressa got the green light. Nor has he been shy about suggesting that the agency was railroaded in this drug's case.

The truth is that Iressa-maker AstraZeneca simply refused to play by Dr. Pazdur's rules. In 2002—knowing it had plenty of data to qualify for accelerated approval—the company rebuffed his requests for more trials and appealed directly to something called the Oncologic Drugs Advisory Committee (ODAC).

That September, the practicing cancer doctors on ODAC agreed with AstraZeneca, voting 11-3 to recommend Iressa's approval. "Ten percent [response] is pretty substantial," remarked ODAC chairwoman Donna Przepiorka. "I've never seen a lung cancer patient whose cancer went away by itself. Very clearly there are patients whose cancer went away with Iressa." Dr. Pazdur tried his best to find reasons to reject the ODAC recommendation, but eventually the FDA relented, granting approval in May 2003.

What's changed since? Not much about the data on Iressa's effectiveness. We still know it helps only about 10% of lung victims—nothing to sneeze at for such a deadly cancer. There is now even a genetic test to help predict in advance which patients will respond.

What has changed is the politics. For starters, Dr. Pazdur no longer labors under the reform-minded former FDA Commissioner Mark McClellan. Dr. Pazdur has also since stacked ODAC with people who share his anti-industry views. Most importantly, the unrelated panic over painkiller safety last fall has created the political cover for Dr. Pazdur to punish AstraZeneca for disobeying his wishes.

Some readers may find it hard to believe that life and death decisions about drug approvals and withdrawals would be made for political reasons. So it's worth pointing out that Dr. Pazdur has admitted doing so before. In 2002, the FDA rejected Erbitux, with Dr. Pazdur admitting it was a "good drug" but that it had a "bad development plan." Erbitux later became a clinical success against colon cancer.

But later that same year when the FDA approved a colon cancer chemotherapy called Eloxatin, Dr. Pazdur approvingly remarked "we want to send a message" about "the value in doing randomized trials." In other words, the less revolutionary drug (Eloxatin) got approved first because its makers had jumped through the right bureaucratic hoops.

The Iressa move is Dr. Pazdur's way of sending another "message" about the necessity of doing things his way. It isn't so much a withdrawal as a relabeling of the product. Patients currently on the drug will be able to continue with it. But come September no new patients will be able to start on it outside FDA-approved clinical trials. In other words, the option to use Iressa freely as a front-line cancer treatment will disappear.

That prospect doesn't sit well with patients like Sandy Britt, who believes Iressa saved her life after she was diagnosed with metastatic, stage 4 lung cancer late last year. "The first doctor gave me a death sentence," the 46-year Alameda, California, resident tells us. "She wasn't even going to treat me." But another doctor administered a genetic test that indicated she would be one of the 10% who respond to Iressa. "I've had an amazing response to it. They predicted I'd be dead now. Instead, I just got back from three weeks in Italy." As for Dr. Pazdur's decision, Ms. Britt asks a common-sense question: "This is a drug that works amazingly well for some people, so why take it off the market?"

The only possible excuse is that there is now an alternative non-chemo lung-cancer treatment called Tarceva with marginally better clinical-trial results. But remember that such results are only averages for the population, and that the responses of individual patients differ widely. Dr. Pazdur's decision to give future cancer patients—even those with the Iressa-response gene—only the option of Tarceva could well amount to a death sentence for many. Dr. Bruce Johnson of the Dana-Farber Cancer Institute points out that there is little data supporting the efficacy of Tarceva in patients who have the mutation for which Iressa is believed to be effective.

Dr. Pazdur and his allies like to suggest that accelerated-approval advocates risk throwing science out the window. But in truth, there's no scientific reason to believe that large placebo-controlled trials—in which treatments are tested against nothing, i.e., the proverbial sugar pill—should be considered the "gold standard," as Dr. Pazdur believes. Withholding treatment is unethical in terminal diseases, and we have enough historical data about how cancer patients fare to judge new treatments without the need for placebo control groups.

This was the philosophy that the practicing doctors of ODAC implicitly endorsed when they approved Iressa; it was the philosophy promoted by former Commissioner McClellan; and it is the philosophy that Dr. Pazdur and his fellow FDA bureaucrats are challenging by pulling Iressa now that there is a politically opportune moment for them to do so. Never since the creation of the accelerated approval process in 1992 have the regulatory barriers to cancer research looked so oppressive.