



Drug Czars

By STEVEN WALKER

May 4, 2007; Page A15

The Food and Drug Administration recently argued in the D.C. Court of Appeals that it has the power to ban meat and vegetables without violating anyone's fundamental rights. The agency chose this bizarre position in an attempt to counter arguments made by patients and their advocates in *Abigail Alliance v. von Eschenbach*. This groundbreaking case challenges the agency's refusal to grant access to investigational drugs, even as a last resort for terminally ill patients.

Last year, a three-judge panel decided that the FDA is violating the due-process rights of terminally ill patients by denying them access to promising investigational drugs. In response the FDA moved for a rehearing by the full court, hoping to prevent a lower court-supervised examination of whether its draconian policies actually serve a narrowly tailored compelling governmental interest. In layman's terms, this means the FDA would have to show its policies toward terminal patients are so critical to the well-being of society that they supersede (in broad and highly imperfect fashion) the fundamental right of an individual to pursue life free of undue government interference. The FDA knows their policies will not survive this test, and doesn't want the question asked.

Consider the FDA's handling of Genasense, a new drug for melanoma and chronic lymphocytic leukemia (CLL), two often terminal forms of cancer. The drug is being developed by Genta, a small, innovative company with only one approved drug and limited financial resources. Despite compelling evidence that Genasense is making progress in fighting both diseases, the FDA appears determined to kill the drug. In the case of the melanoma application, instead of reviewing the clinical-trial data in accordance with usual methods (which showed positive results), the FDA chose a nonstandard statistical approach aimed at discrediting the results. The agency used this analysis in its briefing to its advisory committee, claiming that the drug might not be effective. The committee then relied on that information to vote against approval. Now, Genta has found a serious mathematical error in the FDA's analysis, rendering its results meaningless. Genta is filing a complaint under the Federal Data Quality Act to correct the record. But in the meantime, the drug remains unapproved and melanoma patients continue to wait.

Genasense was also shown in a well-run, randomized clinical trial (the FDA's gold standard) to cause a complete disappearance of disease in 17% of patients with advanced CLL when combined with two older drugs. Just 7% of patients in a control group who received only the older drugs experienced similar benefit. The responders to Genasense have seen their relief last an average of 36 months, while those using other drugs saw their cancer return, on average, in 22 months.

Following these results, the Director of the FDA's cancer division, Dr. Richard Pazdur, again convened a public meeting of his advisory committee. After an agency presentation designed to elicit a negative outcome, the panel voted 7 to 3 against approval, triggering an immediate reaction of surprise and dismay among many CLL experts.

But the committee vote is less surprising if one knows that the FDA appointed several voting consultants to the committee (none of them CLL experts), and recused from the meeting the only sitting member of the committee who is an expert in CLL. Perhaps even more troubling, two of the voting committee members worked behind the scenes as undisclosed consultants for the FDA on Genasense, then without disclosure voted in the open meeting.

A shocked Genta quickly requested a meeting with the FDA to seek clarity on the agency's position, and to present additional information from patient follow-up. On the referral of an eminent leukemia expert, Genta asked if we would attend the meeting as witnesses in our capacity as patient advocates. No compensation was offered, requested or received.

Most of the meeting was consumed by getting the FDA to admit the obvious: The long-lasting, complete disappearance of CLL and its symptoms constituted "clinical benefit." Making these arguments were two cancer-medicine professors at M.D. Anderson Cancer Center, the recused ODAC member and an immediate past president of the American Society of Hematology -- all experts in CLL. None were

employees of Genta and collectively represented a far more qualified advisory committee than the one that the FDA had convened.

The FDA's inane answer to the CLL experts was that the long-lasting disappearance of disease in patients taking Genasense was a "theoretical construct" and not grounds for approval.

The experts explained to the FDA that complete responses in advanced CLL patients are the medical equivalent of the Holy Grail. The FDA finally agreed, but was unimpressed with emerging data showing responders to Genasense living longer than responders in the control group.

The experts were unanimous in advising that Genasense should be approved, but the FDA was unmoved. The agency's Dr. Pazdur suggested that Genta could make the drug available as an unapproved treatment through an expanded access program -- this from a regulator fond of stating that the best way to get a drug to patients in need is through approval! In this case the agency was saying to Genta: We are not going to approve your drug, but any patient who needs it can have it so long as you give it away.

Genta responded that nonapproval would be a denial of patient access to Genasense because they could not afford to give it away in an expanded access program. Twice, Dr. Pazdur referred to that logic as a "business decision."

Less than 48 hours later, the FDA rejected Genasense. Within days Genta made a "business decision," laying off a third of its staff in a cost cutting move aimed at keeping the doors open long enough to appeal the FDA's decision. The appeal was filed in early April. Genta's announcement of the filing included a statement from one of the expert physicians: "It is puzzling that they would deny approval to a drug that met its primary and key secondary endpoint, especially since these findings were observed in the only randomized controlled trial that has ever been conducted in patients with relapsed CLL."

The FDA's handling of Genasense lays bare the all too common, aggressive incompetence of the FDA's cancer-drug division and should lead to an immediate examination of its policies and leadership, followed by swift corrective action.

As for the FDA's belief that their power to control us and even deny us the pursuit of life itself is unlimited under the Constitution, we can only hope the appeals court disagrees. An agency that blocks progress against deadly diseases -- while arguing that its power to do so is above challenge -- is in dire need of a court supervised review.

Mr. Walker is co-founder and chief adviser for the Abigail Alliance for Better Access to Developmental Drugs . He receives no compensation for his work as an advocate, nor has he ever received compensation from any private or public-sector entity involved in drug development, approval or marketing.