Investigational Drug Access
Taken To Task in Lawsuit Against FDA

Frank Burroughs was understandably heartbroken when his daughter, Abigail, a 21-year-old college senior and his only child, died of head and neck cancer in June 2001. But the grief-stricken father was also outraged by what had happened after it had become clear the previous March that standard treatments for her illness were not working.

Abigail was a patient at Johns Hopkins University Hospital, Baltimore, where one of her doctors had tempered the bad news with the suggestion that a drug that targeted the epidermal growth factor receptors (EGFRs) of her tumor just might prolong her life. Either AstraZeneca’s Iressa (gefitinib) or ImClone Systems’ Erbitux (cetuximab), the oncologist had said, would be appropriate.

However, neither drug was on the market because both were investigational. Abigail could, in principle, have been able to get one of the drugs through an expanded access or compassionate use program, in which drug companies, with the blessing of the U.S. Food and Drug Administration, can at their discretion supply investigational drugs to eligible patients outside of a clinical trial. But AstraZeneca’s compassionate use program refused to accommodate her because Iressa was in trials only for lung cancer, and ImClone Systems had no compassionate use program.

Thus, the seeds were sown for the Abigail Alliance for Better Access to Developmental Drugs, a nonprofit organization in Arlington, Va., which Burroughs founded and continues to head. It has crafted a plan called Tier 1 Initial Approval, which aims to make it financially profitable for a drug (or biotechnology) company to provide that “better access” to terminally ill patients whose only other option is, as an Alliance press release put it, “to wait for death.”

From the FDA’s perspective, a drug’s approval, or the agency’s authorization for the company to market a drug, normally comes after data are available from phase III clinical trials. Under the Tier 1 proposal, however, candidate drugs for use by patients with life-threatening illnesses who have no approved treatment options would be eligible for FDA approval after they had passed muster in nothing more than a phase I trial. In other words, drugs that have been evaluated in only a preliminary human trial would be salable commodities.

The Abigail Alliance is pushing Tier 1 to the extent that it has joined with the Washington Legal Foundation (WLF), a public interest law firm best known for championing deregulation and libertarian causes, to sue the FDA and its parent agency (the Department of Health and Human Services), seeking to force the federal government to adopt it. The suit, filed in July, has yet to be resolved, but has been highly publicized in the meantime by, among other things, a large and prominently displayed advertisement that the WLF recently ran in the New York Times.

At press time, the institutional stakeholders in the lawsuit were not discussing the case. The Pharmaceutical Research and Manufacturers of America, the industry’s largest trade group, declined comment, as did the American Society of Clinical Oncology, which is composed largely of oncology professionals who conduct clinical trials. Likewise, the FDA and HHS did not comment. Still, there are stakeholders who eagerly speak up.

Mark Thornton, M.D., Ph.D., president of the Sarcoma Foundation of America, Damascus, Md., is one of them. Although he and his group are not involved in the Abigail Alliance–WLF lawsuit (they regard it as “unfortunate”), they like the Tier 1 concept principally because, like head and neck cancer, sarcomas are rare.

“Rare cancers are not profitable cancers for drug companies,” said Thornton. “So companies hoping for FDA approval of a new cancer drug...
usually arrange to have the clinical trials done in a population of patients with a cancer that occurs more frequently. Essentially all sarcoma patients (and by extension patients with other rare cancers) thus find themselves at the back of the bus if they want to obtain a drug (under compassionate use) that has shown some promise in a trial. It takes critical months for them to get it, if they can get it at all. We think Tier 1 would fix that.”

Thornton and the Alliance are persuaded that the formal clinical trials system and the Tier 1 system could peaceably coexist. Others doubt it. They fear that Tier 1 would make it harder than it often already is to recruit patients for trials, particularly those in which a patient could be randomly assigned to a placebo group and thus not receive a new drug. Musa Mayer, a New Yorker and breast cancer survivor, is a patient representative on the FDA’s Oncologic Drugs Advisory Committee. She saw precisely this scenario play out at its March 2003 meeting when the committee focused on seven cancer drugs (for eight indications) which had been granted accelerated approvals several years earlier.

Such drugs are said to be “fast tracked” because they are approved on the basis of their performance in phase II studies. However, that is on the condition (which the FDA requires their manufacturers to agree to) that they will be tested further for safety and effectiveness in phase III trials; that is, in trials that are randomized and controlled, which phase I and phase II studies are not. For none of the seven drugs was this requirement met. Said Mayer, in an article she wrote for the *Journal of Clinical Oncology* (published in the Oct. 15, 2003 issue): “… repeatedly, during the 2-day meeting, it was clear that enrolling patients onto randomized trials when a drug is available on the marketplace is next to impossible.”

Critics of Tier 1 also cite as pertinent the enthusiasm during much of the 1990s for high-dose chemotherapy facilitated by stem cell or bone marrow transplants for breast cancer patients with metastatic or otherwise exception-
Erwin also contends that introducing the profit motive into the experimental situation could be all but sure to corrupt it. “You have only to look at the world of unproven nutritional products and dietary supplements,” he said, “to realize that Tier 1 approvals would give pharmaceutical firms less incentive to invest in research and a lot of incentive to engage in misleading advertising and promotion.” Moreover, the designation of investigational drugs as FDA-approved, Erwin and others noted, could open up the issue of insurance coverage for their use. Indeed, the WLF and the Abigail Alliance have stated publicly that they have exactly that in mind and plan to start by doing battle with the federal government’s Center for Medicare and Medicaid Services, where it is now policy to reimburse for only some forms of FDA-approved cancer chemotherapy.

—Judith Randal