To the editor:

The purposes of studies involving human subjects are many and vary according to the stakeholder. The sponsor's goal is to achieve marketing approval and make a profit, the physician and patient consider clinical trials as therapeutic options, the FDA's role is closest to the view of Dr. Annas: to test a clinical hypothesis – the assessment of risks and benefits in to protect the public interest.

However, what the study was “designed to test” is not the main issue. Consider the most appropriate action of a man who has created a new boat design, and during the test sees a child alone and in distress, caught in rip tide. Similarly, access to investigational drugs are case-based decisions, and FDA has done a good job of making it easier for sponsors and doctors to understand what to do when the need arises.

Clearly, progress against cancers depends on reliable answers that can only come from well-design controlled clinical trials; and an important obstacle to progress is low patient enrollment in clinical trials, which has been estimated as less than 5% of available patients with cancers.

The circumstances prompting patients to consider trials are as variable as the diseases, but it is rarely if ever done for the selfless concern for the welfare of others. It has been found that “patients rely heavily on their physicians to inform and advise them about treatment options, physicians are often the most influential factor in a patient’s decision to participate in a clinical trial.” Thus clinical trials involving human subjects can and should often “equates with Good Medicine”; and lacking the potential to meet each of these purposes will raise serious questions about the ethics of the study.

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1 Cancer and the Constitution — Choice at Life's End: “the Abigail Alliance court, the Congress, and the FDA all seem to be suffering from the "therapeutic illusion" in which research, designed to test a hypothesis for society, is confused with treatment, administered in the best interests of individual patients.”

2 Proposed Rules for Charging for Investigational Drugs and Expanded Access to Investigational Drugs for Treatment Use http://www.fda.gov/cder/regulatory/applications/IND_PR.htm

3 The ODAC Chronicles 2005 ~ Antonio J. Grillo-Lopez, MD Chairman, Neoplastic and Autoimmune Diseases Research Institute


5 Cancer therapy and the randomized clinical trial good medicine? Dwight Kaufman, M.D., Ph.D. *Cancer Volume 72, Issue S9*, Pages 2801 – 2804
That clinical trials are considered treatment decisions by patients and physicians is reinforced by IRB guidelines and the consent process, which requires “disclosure of any appropriate alternative procedures or courses of treatment that might be advantageous to the subject”  

It’s sad but true that there are many times when the patient and family do need to know when to let go, but "Life's End" is not always so easy to predict.

How realistic the hope of benefiting from a clinical trial can vary significantly, as can the setting in which patients may seek compassionate use of agents that are awaiting regulatory assessment for marketing approval. We have seen evidence that even advanced blood cancers can be reversed completely by administration of agents with a unique mechanism of action - notably Gleevec for advanced CML. Similarly, patients with diseases refractory to standard protocols have achieved complete and durable remissions with radioimmunotherapy in expanded access trials prior to marketing approval.

We might call promising new active agents that have a unique mechanism and well understood toxicities "exceptional new agents (ENAs)." Patient demand apparently driving the installment of expanded access programs for ENAs, Bexxar and Gleevec, some few years ago. Thus, concern about the influence of compassionate use on trial enrollment will not often apply to ENAs; and providing a case-based pathway for access is unlikely to do any harm to society.

It should be noted that the gatekeepers for compassionate access include the patient's licensed physician, an IRB, the FDA, and the drug sponsor – which points to the challenge of utilizing these programs, when appropriate, in a timely manner. Dr. Annas correctly points out that FDA cannot compel the sponsor to make their agent available, and that this appears to be the main obstacle to access in deserving cases: when the patient is ineligible for a clinical trial and his or her doctor believes an investigational agent provides a reasonable best hope for clinical benefit.

The potential liability to the sponsor when providing expanded access is also a point well taken by the author. But it might well be a problem that some sponsors will welcome, as the demand would speak to the clinical and financial potential of their product. If the ENA is what it appears to be, the benefits of providing expanded access could many times exceed the risks to the company. So there could be a need to help the sponsors in these exceptional circumstances to see the entire picture, and not focus on the liabilities and costs.

~ Karl Schwartz

6 Guidelines For Writing Informed Consent Documents, National Institute of Health

President, Patients Against Lymphoma