

Questions to the Committee

June 7, 2001

Single Patient Use of Non-approved Oncology Drugs and Biologics

Single Patient Treatment Use of Investigational Drugs and Biologics

As discussed in the briefing document, the FDA strongly endorses participation in clinical trials because it is in the best interest of the patient and the American public. Individual patients benefit by receiving the best available treatment and the American public benefits by sound development of new therapies. However, sometimes patients are ineligible for clinical trials or are unable or unwilling to participate.

The FDA is seeking advice from the committee to help FDA in its role of assessing the risk to benefit ratio of treatment use with an experimental drug in an individual patient.

When determining the apparent risk to benefit ratio, the following are important considerations:

- How thoroughly has the drug been studied in humans?¹
- What do the preliminary results from these studies suggest about the safety and efficacy (or activity) of the drug?
- What are the other therapeutic options available to the patient?

At any stage of development, evidence from ongoing trials may suggest that the drug is effective or ineffective, or that it is toxic or non-toxic.

The appropriateness of treatment use of experimental therapy also depends upon the patient's medical history, especially whether the patient has already received standard therapy. The following are scenarios that FDA may encounter. They are listed according to the benefit available from standard therapy in the particular clinical situation.

¹ For the purpose of our discussion, the degree to which a drug has been studied may be categorized as follows:

0: The drug has not yet been tested in humans.

1: The drug has been tested in Phase 1 studies to evaluate toxicity.

2: The drug has been tested in Phase 2 studies to evaluate whether it can reduce tumor size in some patients.

3: The drug has been tested in Phase 3 studies and we have some knowledge about whether it affects survival or other endpoints indicating clinical benefit.

Questions to the Committee

- 1. For each of the following clinical scenarios describing standard therapy, please discuss the following question:**

FDA receives a request from an investigator to use Drug X under a single patient IND. The commercial sponsor (manufacturer) of drug X has granted permission for the investigator to use the drug and also has provided written permission for FDA to refer to the commercial IND. The patient's medical history is outlined in each of the scenarios below.

The investigator states that the patient is aware of the benefits of standard therapy but wants to receive investigational treatment with Drug X instead. The patient is ineligible or unable to participate in a clinical trial using Drug X.

When would single patient treatment with Drug X be appropriate?

In your discussion, consider:

- The drug's **stage of development** (0-3 above), and
- The **level of efficacy and toxicity** of Drug X that would be acceptable in the following standard therapy cases.

Standard Therapy Cases

- A. There is no standard therapy available.**

EXAMPLE: A patient with metastatic nonsmall cell lung cancer has received all available therapy.

- B. Available treatment shows a marginal survival benefit.**

EXAMPLE: A patient has metastatic nonsmall cell lung cancer. Standard chemotherapy produces a 1-2 month median survival benefit and produces moderate toxicity.

C. Standard therapy provides a substantial prolongation of median survival.

EXAMPLE: A patient has advanced ovarian cancer. Standard chemotherapy produces a 1 to 2 year median survival benefit but is generally not curative.

D. Standard therapy provides a substantial rate of cure.

EXAMPLE: A patient with acute leukemia does not want to receive chemotherapy that is associated with a 40% rate of cure with substantial acute toxicity but that produces few lasting toxic effects.

E. Available therapy provides cure in most patients, but treatment involves permanent morbidity.

EXAMPLE: A 60 year old man has recurrent superficial bladder cancer that has recurred despite treatment with all available intravesical chemotherapy agents. Recently, a muscle-invasive bladder tumor (Stage T2) was removed during cystoscopy. Cystectomy (surgical removal of the bladder) is standard therapy and is associated with a high cure rate. The patient does not want to undergo cystectomy despite counseling about various surgical techniques that can be used to provide a substitute for the urinary bladder after it is removed. He also refuses radiation therapy.

2. As noted above, FDA strongly endorses participation in clinical trials. Patients should first consider entering a clinical trial before pursuing treatment under a single patient IND. If a patient is eligible and able to receive drug X as part of a clinical trial but is unwilling to do so, should that patient be allowed to receive drug X under a single patient IND?

3. If FDA has sufficient evidence to conclude that a drug is ineffective for treatment of a particular cancer, discuss under what circumstances, if any, single patient treatment use should be permitted.