

# ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

Section Editor: Mark J. Ratain, MD

---

## The Role of the National Cancer Institute in Drug Development

James Doroshow, MD  
Director, Division of Cancer Treatment  
and Diagnosis  
Chairman, Clinical Trials Working Group  
National Cancer Institute

**H&O** What is the Division of Cancer Treatment and Diagnosis? What are its components and what do they do?

**JD** The Division of Cancer Treatment and Diagnosis (DCTD) is the largest division of the National Cancer Institute (NCI), and is composed of 6 interrelated programs that span a wide range of cancer research. The Cancer Diagnosis Program oversees grants and contract programs for tissue acquisition, including the archiving and banking of tumor specimens from around the country. The Radiation Oncology Sciences Program funds research in radiation biology and radiation oncology. The Biometrics Program is the major biostatistics program at the NCI. The rapidly growing Cancer Imaging Program oversees the development of new molecules for imaging, from laboratory-based preclinical activities through clinical trials in imaging. Through the Cancer Therapy Evaluation Program (CTEP), the NCI supports national clinical trials, from phase I through phase III. Every year, over 30,000 patients enroll in clinical trials supported by the NCI. The Developmental Therapeutics Program supports a range of drug development-related activities, such as the discovery of new compounds from marine sources and, more so, the screening of new molecules identified by academic investigators, small biotechnology companies, and pharmaceutical companies for anticancer activity.

Many services are provided for investigators, in particular those who are being supported by NCI grants, including the development of high-throughput screening procedures and assays. In addition, the Rapid Access to Intervention and Development (RAID) program was initiated to help academic investigators further their research after identifying possible therapeutic advances.

**H&O** How does the RAID program work?

**JD** As an example, an investigator who is conducting research in an academic laboratory might identify a new target for therapy, and may even have a hypothesis about what molecules might block that target and thus lead to tumor cell death. However, the investigator might not be able to further those initial studies. There may be no way to produce enough of the potential drug to test it in animal models. Alternatively, if animal model studies are done, there may not be a way to conduct toxicity studies, which almost no universities have the resources to do. If the compound seems promising in animal studies and is found to have a side effect profile that supports further testing in humans, the RAID program develops assays for testing the level of the compound in patients and provides the resources to produce enough of the molecule for initial pilot studies that the investigator can conduct at his or her home university. Finally, the program assists investigators in filing a new drug application with the US Food and Drug Administration. The program also funds the development of antibodies and vaccines for investigators who have developed ideas in the laboratory but do not have the facilities to produce enough material for an early pilot study in humans. In essence, we provide services that pharmaceutical companies provide but are only available in a small number of universities.

**H&O** Were these programs developed specifically for investigators whose research was not pursued by a pharmaceutical company?

**JD** Actually, when these programs began, there were many fewer pharmaceutical firms that were interested in producing anticancer drugs. For this reason, many of the initial anticancer drugs were developed at the NCI in the late 1950s, 1960s, and into the 1970s. In more recent years, the pharmaceutical industry has grown increasingly interested in anticancer drugs and now has many of its own drug development programs. Therefore, the NCI programs have turned their focus to providing resources for, in particular, investigators who may or may not be able to develop their ideas and research findings to the point where a pharmaceutical firm will take them into clinical studies. There might be issues of intellectual property that

prevent pharmaceutical industry investment, and also there are more academic investigators than there are firms willing to invest in ideas that might not yet have a large amount of data supporting them. Part of our job is to help academic investigators develop the data that would then allow them to pursue filing a new drug application or industry-based sponsorship, with the ultimate goal of developing new drugs for patients.

### **H&O** Are academic investigators able to keep ownership of their ideas and research when working with the NCI?

**JD** Yes. In my view, one of the strongest aspects of the NCI's drug development programs is that the investigators and their universities retain the intellectual property rights to anything they develop with NCI support.

### **H&O** Does this approach help spur drug development?

**JD** If the investigators did not maintain this ownership, further development would be almost impossible. As an example, what if an investigator has a possible drug or target that proceeds through an initial clinical trial with positive results and he or she does not possess the rights to the compound and its intellectual property? It is unlikely that a for-profit company would further develop the compound without some ability to negotiate for those rights.

### **H&O** How does the NCI interact with pharmaceutical companies?

**JD** Large pharmaceutical firms approach CTEP when a compound has been developed and manufactured and is ready for testing. Frequently, companies ask the NCI to participate in this development through our cooperative group networks. There may often be interest in evaluating an agent in a few diseases, but not in what are termed "orphan diseases," those with a very low incidence rate. The development of new treatments for orphan diseases is an NCI mandate; the NCI takes the responsibility to test compounds in these settings. Over the past 20 years, it has occurred with some regularity that the broader setting in which the NCI studies an agent turns out to be more fertile than the setting in which the pharmaceutical company had initially chosen to focus.

### **H&O** How is the landscape of anticancer drug development and the NCI's role changing?

**JD** Right now, the area in which there is the most focused interest is in the identification of molecular correlates that will enable the development of predictive tests that can

define which subset of patients are likely to benefit from a particular therapy. In the past, drug development efforts were focused on safely delivering new therapies, mainly through studies to determine the maximum tolerated dose and the efficacy of the new treatment. Starting approximately 5 years ago, with the increasing development of molecules that target a smaller number of proteins or other molecules in tumor cells, the possibility of developing assays to determine the likelihood of therapeutic benefit in advance became more apparent.

Developing these assays is more difficult than, say, measuring the concentration of a drug in a patient. As cancer research moves toward the era of more personalized oncologic therapy, a major part of the NCI's role is to assist in the funding and support of expensive and sometimes difficult laboratory work necessary to develop these correlative markers of response and resistance. This research will greatly facilitate drug testing in the future.

### **H&O** What changes can be expected in the clinical trial process for new anticancer drugs?

**JD** The NCI's Clinical Trials Working Group has been attempting to evaluate and update the clinical trials process. This June, the Group will make recommendations to the National Cancer Advisory Board. While these recommendations are not yet finalized, they address the development of systems to better prioritize what studies to pursue, and making resources available that would allow clinical trial investigators to have access to correlative laboratory studies that are needed for the development of more personalized medicine.

### **H&O** In your opinion, does the general public understand what the NCI does?

**JD** I think there is some confusion in the public's mind about the role of the NCI and also that of the National Institutes of Health (NIH). Surveys including this question have found that most people do not know what the NCI is. Most people know that there is an agency called the NIH, but anyone I've met who has seen the NIH for the first time is amazed to find this enormous campus, and to learn that it is probably the largest biomedical research campus in the world, just a few miles from downtown Washington, DC.

### **Suggested Reading**

Takimoto CH. Anticancer drug development at the US National Cancer Institute. *Cancer Chemother Pharmacol.* 2003;52(suppl 1):S29-S33.

Sausville E. Indifferently pursued or unowned drugs: who should lead where companies do not treat? *J Clin Oncol.* 2005;23:1-3.