American Society of Clinical Oncology Developing First Clinical Trial

By Vicki Brower

At its June 1 annual meeting, the American Society of Clinical Oncology (ASCO) announced its first clinical trial. The trial aims to offer advanced cancer patients off-label access to approved targeted drugs based on genetic driver mutations and to gather information on efficacy and toxicity across cancer types. ASCO stated that it seeks to broaden access to drugs for patients in community settings who have exhausted standard-of-care therapies and to collect “real world” outcomes data in a prospective registry.

The study, called TAPUR (Targeted Agent and Profiling Utilization Registry), will include patients with advanced solid cancers, multiple myeloma, and non-Hodgkin lymphoma whose tumors have a genomic variation or mutation known to be a drug target, such as the epidermal growth factor receptor and B-RAF. Five companies are supplying at least 13 drugs, free to participants, which target more than 15 genomic variants. ASCO is writing the protocol for the study and hopes to begin patient enrollment in January 2016. It is not yet releasing figures on cost of the study, or its length, but expects that more information will become public when the protocol is finalized.

Implementing Personalized Medicine

“TAPUR springs from the challenges of implementing personalized medicine in clinical medicine and has been in development since 2013,” said Richard Schilsky, M.D., chief medical officer of ASCO. “A major challenge for oncologists who aim to provide personalized medicine to their patients is obtaining drugs predicted to be beneficial based on genomic testing of the tumor but which would be off-label and, as such, only available through a clinical trial or not at all,” Schilsky said. Clinical reports suggest that 30%–80% of advanced solid tumors harbor potentially actionable genomic variants, but outcomes of patients treated on the basis of such tests remain largely anecdotal or unknown, he said. That is the reason for the registry.

TAPUR is one of several recent biomarker-driven clinical “basket” trials designed to advance personalized, or precision, medicine and expedite the clinical trial process. They share the principle that cancers should be grouped by and tested for genetic mutations, rather than solely by tissue of origin. Another such trial is the National Cancer Institute’s MATCH, a phase II trial now enrolling patients, which will sequence the DNA of 3,000 advanced cancer patients for actionable mutations. Patients will be grouped into cohorts of 20–30 according to mutation, rather than anatomical site of tumor, and treated with approved or investigational targeted drugs. Another recent innovative trial is the Lung Cancer Master Protocol, in which five companies test their targeted drugs in squamous cell lung cancer. For this study, researchers are using one genomic test to screen patients’ tumors, and drugs are not compared with each other. Rather, they are compared with the standard of care, according to Roy Herbst, M.D., Ph.D., Ensign Professor of Medicine and chief of medical oncology at Yale University in New Haven, Conn., who is directing the study. An earlier trial, I-SPY2, which began in 2010, tested multiple drugs in newly diagnosed breast cancer patients before surgery who were stratified according to 10 biomarkers. This trial revealed, among other findings, that veliparib, a poly(ADP–ribose) polymerase inhibitor, is effective in triple-negative breast cancer.

“By changing the treatment paradigm to the genotype-to-phenotype approach, we are advancing translational research at a much faster pace than ever, and TAPUR [and other trials] will help to hasten that process even further,” said Arturo Loaiza-Bonilla, M.D., assistant professor of clinical medicine in the division of hematology–oncology at the University of Pennsylvania in Philadelphia. “The new treatment paradigm in translational and personalized genomic oncology is to look first at the genetic makeup of the cancer (genotype), target the driving mutations, and then use the phenotype mostly for classification and less for treatment purposes,” he said.

Unlike NCI, ASCO has no established clinical trial mechanisms, “so we’ve had to build them from the ground up,” Schilsky said. NCI has an extensive infrastructure of thousands of designated clinical sites around the country and is opening MATCH at many of these sites. By contrast, TAPUR will open initially at only three sites: the Michigan Cancer Research Consortium, the Cancer Research Consortium of West Michigan, and the Carolinas Healthcare System. Those sites conduct clinical trials for NCI and the pharmaceutical industry.

TAPUR will accept tumor biopsy samples processed through any CLIA (Clinical Laboratory Improvement Amendments)-certified lab, rather than a central lab with uniform assays. ASCO will collaborate and share data with The Netherlands Center for Personalized Cancer Treatment, a Utrecht-based coalition of three Dutch cancer centers, using a protocol similar to what ASCO is developing for TAPUR.

Broad Patient Inclusiveness

“The TAPUR trial will be more open than a traditional clinical trial and will include more rare cancers, both of which could lead to approvals of targeted drugs in new indications,” said Jane Perlmutter, Ph.D. (She is a psychologist, breast cancer
Scientists Journey Into Genomes Via CRISPR-Cas9

By Delthia Ricks

Cancer researchers are testing an evolving gene-editing technology that lets them manipulate DNA. Cold Spring Harbor Laboratory (CSHL) in New York is one of dozens of institutions using the technique—clustered regularly interspaced short palindromic repeats (CRISPR)–Cas9—to investigate genomes.

The revolutionary technology has drawn a spotlight in and out of cancer research because of the simplicity, precision, and speed with which researchers can manipulate the basic chemical components of life. But even as this potent form of gene editing has stirred the research community with its promise, the technology is coming under scrutiny. A group of influential scientists convened in California earlier this year to discuss ethical concerns that CRISPR-Cas9 raised and called for a moratorium on using it in germ-line research.

Investigators at CSHL, however, along with a growing number of cancer