New Hampshire
COMPREHENSIVE
CANCER
COLLABORATION
Together-Eliminating Cancer

Clinical Trials

By Nan Rollings RN, MEd CCRC Administrative Director, Office of Clinical Research, Norris Cotton Cancer Center and James R. Rigas MD, Professor of Medicine, Geisel School of Medicine at Dartmouth, Medical Director Office of Clinical Research, Dartmouth-Hitchcock Medical Center

More than 13 million Americans alive today have been diagnosed with cancer.[1] A patient facing this diagnosis has many decisions to make, including which treatment options are best and available, where to get treatment, and how to find needed care and support. While processing a cancer diagnosis a patient also may have the opportunity to take part in a clinical trial. Why should a cancer patient become a research participant, and how does a patient make the decision to enroll in a clinical trial?

CLINICAL TRIALS CONDUCTED IN PHASES

A clinical trial is defined, in general, by the National Cancer Institute as biomedical or health-related research studies in human beings that follow a pre-defined protocol.[2] There are various types of clinical trials, including treatment, screening and prevention, supportive care, and quality-of-life studies. Clinical trials are divided into phase categories dependent upon the focus of the work.

- *Phase I* studies enroll a small number of participants, usually 15-30 people, to determine safe dosing levels of an investigational product, side effects of the drug(s), and best route of administration.
- *Phase II* studies generally enroll 100 or less participants and take the data gathered from Phase I studies and expand the study scope to determine if the treatment has any effect on a specific cancer and further evaluates the side effects in the expanded cohort of study participants.
- *Phase III* studies are much larger, enrolling up to several hundred or thousands of participants to compare the new studied treatment with current standard of care treatments.
- *Phase IV* studies enroll thousands of people to evaluate the side effects, risks, and benefits of a drug over a longer period of time and in a larger number of people than in phase III clinical trials.

Only institutions with nationally approved set-ups are authorized to offer research trials, and individual trials undergo review for merit, safety, and relative promise compared to other studies under consideration.

WHY SHOULD A CANCER PATIENT ENROLL IN A CLINICAL TRIAL?

Patients decide to be part of a clinical study for various reasons. Joining a clinical trial may provide access to a new promising therapy before it is available on the open market. Receiving an investigational product through a clinical trial may be the only treatment option left for a cancer patient who has had many other treatments. Many people hope to extend their own lives with experimental treatments. Others without any treatment options enroll with the hope that their participation will lead to discoveries that could help future patients with the same disease. If disease progression or recurrence takes place, a clinical trial may provide a new avenue of treatment.

Current cancer therapies are possible because of those willing to participate in previous clinical trials. During the course of cancer treatment a clinical trial may provide supplementary treatment to standard care in order to improve supportive care or reduce toxicity,

Patients should talk to their doctors about participating in a clinical trial and get all their questions answered before deciding to enroll.

to test the most effective way to provide treatments, and to determine whether a new combination of standard treatment is more effective than current therapies. Patients enrolled in clinical trials have closely monitored care, and trials involving supplementary treatments typically add to a regimen currently deemed best available care.

RESEARCH ALLOWS FOR PERSONALIZED CANCER CARE

One recent advance made possible by participation in clinical trials is the development of personalized cancer care. Personalized cancer therapy includes all aspects of a patient's disease management including diagnosis, surgery, chemotherapy, targeted therapy, radiation therapy, and immunotherapy. For example, in a recent clinical trial, laboratory investigators identified a specific genetic rearrangement in patient tumor specimens. A new oral medication in development was found to target this genetic rearrangement. During a phase I clinical trial of this new oral targeted therapy, participants consented to receive this medication to define the safe dose to be administered for future studies. As soon as the safe dose was identified, the next participants, who also had the same genetic rearrangement, enrolled in the phase II portion of the clinical trial therapy. These individuals experienced remarkable shrinkage of their tumors with very manageable side effects. As a result of the willingness of individuals to participate in a clinical trial, this new targeted therapy was approved for treatment worldwide. We now know to identify patients with this specific genetic rearrangement and can offer them an approved oral targeted therapy specific for their cancer.

INFORMING STUDY VOLUNTEERS OF THE BENEFITS AND HARMS OF CLINICAL TRIALS

By definition, services still in research development cannot guarantee benefit, and there may be unanticipated side effects of investigational drugs. Where interventions benefit some, but not all, subjects, participation in trials helps better define the factors at diagnosis most likely to predict benefit from a given available intervention, while also identifying characteristics that might indicate those who are unlikely to benefit and should be spared the risks of enrollment. All clinical trial investigators are required to receive training on research and ethical treatment of research participants as well as Good Clinical Practice

(GCP) in Research. Before entering into a study, a patient must be informed about all aspects of the trial, including risks vs. benefits, costs, and other options to study participation. Participation in a clinical trial is always voluntary and may be offered as an alternative to other standard treatments. Clinical trial participation cannot be a prerequisite for receiving care from a provider, and clinical trial participants can withdraw from a clinical trial at any time without compromising the commitment of the provider to their ongoing care off-study.

QUALITY, SAFETY AND OVERSIGHT

As part of a study, a patient should expect to receive excellent standard of care treatment and the additional oversight of the research protocol. However, additional financial and time expectations may impact a patient's ability to participate in a clinical trial.

REIMBURSEMENT ISSUES

As of July 9, 2007, Medicare covers the routine costs of qualifying clinical trials (as such costs are defined below) as well as reasonable and necessary items and services used to diagnose and treat complications arising from participation in a clinical trial. Routine costs of a clinical trial include all items and services that are otherwise generally available to Medicare beneficiaries (i.e., there exists a benefit category, it is not statutorily excluded, and there is not a national non-coverage decision).[3] This Medicare policy has become a standard for how other insurers define coverage as well. In New Hampshire, coverage is required for clinical trials that are approved by:

- National Institutes of Health (NIH)
- NIH cooperative group or center
- U.S. Food and Drug Administration
- U.S. Department of Veterans Affairs
- U.S. Department of Defense
- An Institutional Review Board of an institution in New Hampshire with a Multiple Project Assurance (MPA) from the U.S. Department of Health and Human Services' Office for Human Research Protections

Trials are covered when standard treatment has been or would be ineffective or does not exist, or when there is no clearly superior non-investigational therapy.[4]

OBSTACLES TO CLINICAL RESEARCH

One major issue hampering the effectiveness of cancer clinical trials is low participation. Adult clinical trial participation in the U.S. remains under 3 percent of eligible individuals, with enrollment rates among minorities and people over 65 even lower.[5] Approximately one-third of phase III clinical trials closed with insufficient enrollment to address the primary question being addressed.[6] New Hampshire has a large rural population, and often participants in clinical trials need to travel long distances. In some cases, travel concerns can be eased by arranging for ongoing and follow-up care with collaborating physicians in a local community. In cases of rare cancers, multiple institutions collaborate on the same clinical trial to allow for better access to the study.

Still, accrual is a challenge. Reasons for poor accrual vary but some factors include:

- prolonged length of time to approve and open a clinical trial (from concept to opening at a clinical site)
- very narrow eligibility criteria
- lack of standardized procedures to inform patients about clinical trials as a treatment option[7]

The Institute of Medicine reported that 40 percent of Cancer Therapy Evaluation Program (CTEP)-approved phase III clinical trials failed to achieve minimum accrual goals,[8] Dr.S.Cheng states "In an era when patient participation in clinical trials is low, it is critically and ethically imperative to best allocate our patient participants to studies that are most likely to succeed."[8]

Curesearch for Children's Cancer reports that while less than five percent of adults with cancer are enrolled in clinical trials, 60 percent of patients under age 29 diagnosed with cancer are enrolled in trials. Given the severity of childhood cancers and the intensity of their standard care, the complexities added by enrollment in a clinical trial are relatively limited. This has led to a huge advance of survival rates for childhood cancers from 10 percent to 78 percent in the past 40 years.[9]

DRIVING CHANGES IN PATIENT CARE

Clinical trials change how cancer treatments are delivered. Standard practice by physicians is determined by the scientific findings from clinical research studies, and they must be completed in a timely manner to provide better treatments for all cancer patients. Cancer therapies are being developed at the molecular level, and the need for cancer clinical trial participants is critical to bringing novel treatments to the public. Participating in a trial gives teams of doctors in local institutions, approved to do research, the opportunity to test promising approaches to known current concerns.

New Hampshire medical practices participating in multi-institutional studies give residents access to trials testing promising leads from around the world. Participation in a trial helps doctors with small practices evaluate the efficacy of available treatments based on outcomes across many cases in a wide variety of similar situations, rather than just their own isolated experiences. Clinical trials are accessible in many communities and participation in a study can be part of the conversation a patient holds with their providers over the course of their treatment.

Information on the availability of clinical trials, and some background information on patient eligibility, can be obtained from the National Cancer Institute at 1-800-4-CANCER or cancer.gov.

References:

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