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Why should cancer patients participate in clinical trials?

ABSTRACT

Primary care physicians can help their cancer patients decide whether to enter a clinical trial of an experimental treatment by frankly discussing the pros and cons. Phase 1 trials pose difficult emotional issues for patients and ethical issues for physicians.

FOR MOST CANCER PATIENTS, the decision to enter a clinical trial of an experimental therapy is fraught with fear and anxiety.

At such difficult times, cancer patients often turn to the physician they know best—their primary care physician—to help them decide what to do. Primary care physicians can help these patients by frankly and openly discussing the pros and cons of getting involved in experimental cancer treatment protocols (TABLE 1).

TABLE 1

Pros and cons of participating in cancer clinical trials

Pros

- Patients receive state-of-the-art treatment
- Treatment protocol is designed by experts
- Experimental protocols carefully define necessary dose modifications
- Potential for improved outcome
- Innovative treatment approach (phase 1 trials)
- Absence of evidence that the research strategy is ineffective treatment; this gives the patient hope for a better outcome
- Results of trials provide benefits for future cancer patients

Cons

- Therapy selected by random chance (phase 3 trials), rather than by the physician the patient trusts to make the best decision
- Patient feels like a guinea pig
- Benefits and toxicities of treatment (phase 1 trials) are unknown
- Potential for excessive toxicity from experimental therapy
- Greater time and effort involved for patient and family (eg, requirement for additional testing and monitoring compared to standard treatment programs)

PATIENTS' CONCERNS: TWO SCENARIOS

The following scenarios illustrate what physicians often hear from patients faced with entering into a clinical trial of an experimental cancer treatment:

Scenario 1

"The oncologist you sent me to suggested I participate in what he calls a 'randomized phase 3 trial,' comparing standard chemotherapy to an experimental drug. When you sent me to this doctor, you said he was 'the best.' If this is true, why doesn't he know the best treatment for me? I am so confused."

Scenario 2

"My oncologist just informed me that my cancer is not responding to the chemotherapy and suggested I consider being treated on what he calls a 'phase 1 clinical trial.' I don't understand what this means. Can this therapy really help me, or will I just be a guinea pig?"

These cases are fictional, but the situations are real. When confronted with such questions from patients, what do you tell them?

In the pages that follow I outline the information that the patient and family should consider before deciding about entering a clinical trial, the common misconceptions that patients have about the goals, benefits, and risks of clinical research, and why it is often in the best interests of the patient to enter a clinical trial.

WHY SHOULD PATIENTS ENTER CLINICAL TRIALS?

For nearly all forms of cancer, we seek to devise therapy that is less toxic or more effective. The only way to do this is through clinical trials. But how does an individual patient personally benefit from being in a clinical trial? TABLE 1 presents the pros and cons.

Clinical trials are ethical

A well-conceived, well-conducted trial should offer a therapeutic strategy that the physician believes is at least as effective as other options. Otherwise, the trial would be unethical, and asking a patient to participate in it would undermine the trust that is the basis of the doctor-patient relationship.

However, clinical trials carry no guarantees that the experimental treatment will be more effective or less toxic than standard treatment. There is also no reason to believe that the results will be worse.

Patients often participate in trials to help future patients

Trial patients receive good care

Often, patients in clinical trials receive state-of-the-art care—in terms of receiving the most up-to-date therapy and careful monitoring of their condition. This is particularly important in cancer care, in which chemotherapeutic agents can be highly toxic and have a narrow therapeutic index, requiring careful attention to dosage.

Clinical trials are carefully monitored for adverse events

Clinical research protocols usually contain detailed information about how patients will be monitored for adverse reactions, and how treatment will be modified should these occur. They also contain detailed information about modifying the dosage on the basis of therapeutic effect and toxicity, including excessive bone marrow suppression and gastrointestinal side effects.

Patients can withdraw at any time

Patients are always free to withdraw from a clinical trial at any time, for any reason. Physicians should emphasize this point in discussions with patients, as it may alleviate patients' concerns about potential side effects of treatment.

However, the anxiety and fear that patients usually feel about the toxicity of an experimental therapy when deciding whether to participate in a trial often far exceed the actual toxicities encountered. Once patients find that the side effects of the experimental treatment are acceptable, they feel less emotional distress and find it easier to continue.

Participating may help other patients

Often when a patient perceives no particular advantage or disadvantage to participating in a clinical trial, he or she may opt to participate because of altruistic motives. These patients participate because of a desire to help future cancer patients even if the trial fails to benefit them personally. Such motivations can be powerful. And, of course, today's patients benefit from information gained from the participation of patients in previous studies. However, the importance of altruism as a motive can only be determined by the individual patient.

WHAT INFORMATION SHOULD THE PATIENT CONSIDER?

In all clinical trials, patients must sign an informed consent document, which must spell out, in plain language, the following points:

- What the trial is supposed to accomplish
- What will happen to the patient
- Whether alternate therapy is available
- The benefits and possible risks of participating
- Whom to call with further questions

The patient must be satisfied in all these particulars before signing. Ultimately, patients must decide whether the potential benefits of participating in a cancer clinical trial outweigh their concerns about entry into a treatment protocol.

Physicians should encourage patients to ask questions, because for many patients a thorough discussion of the pros and cons of a trial will relieve any anxiety associated with being a research subject. It is particularly important to stress that participation in a clinical trial is entirely voluntary and that patients can withdraw from the study at any time, without compromising their relationship with the treating physician.

THE DILEMMAS OF PHASE 1 TRIALS: IS HOPE UNREALISTIC?

As the question in scenario 2 above illustrates, phase 1 cancer clinical trials pose especially difficult and complex issues for patients.

Phase 1 trials are designed to determine the maximally tolerated dose—not the effectiveness—of new, highly experimental cytotoxic agents with as yet unknown activity against any cancer, or novel combinations of established drugs known to possess only limited activity when used as single agents.

In general, patients are invited to participate in phase 1 trials after standard treatment has failed or when the effectiveness of currently available therapies is uncertain. Information about safety, toxicity, and efficacy of the experimental regimen is minimal in phase 1 trials. Thus, it is impossible to present the patient with an objective assessment of the potential risks and benefits associated with phase 1 clinical trials. No wonder patients believe they are "guinea pigs" if they enter into a phase 1 trial.

Despite the best efforts of an investigator to present the limited scientific objectives of a phase 1 trial, with its focus on gaining information on toxicity and pharmacology, and only secondarily on efficacy, patients asked about why they have agreed to enter a phase 1 trial commonly report it is to treat the cancer.[1]

When cancer patients have no useful treatment options, they often seek experimental treatment, even if the only realistic potential benefits that the experimental treatment can provide are hope and a positive outlook toward the future.

In this situation, the physician must understand the particular vulnerability of the patient and be certain the proposed study provides a reasonable compromise between an individual's desire to continue to fight the cancer and the potential toxicities and negative impact the regimen may have on the patient's quality of life. Alternatives such as palliative treatment and hospice care should be discussed along with experimental treatments.

REFERENCES

1. **Daugherty C. Ratain MJ, Grochowski E, et al.** Perceptions of cancer patients and their physicians involved in phase 1 trials. J Clin Oncol 1995; 13:1062–1072.

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