

EPECTM-O

Education In **P**alliative And **E**nd-Of-Life **C**are For **O**ncology

Self-Study Module 10:
Clinical Trials

Module 10: Clinical Trials

Abstract	3
Introduction	3
Objectives	4
Why Patients Enroll in Trials	4
Research on Palliative Interventions	6
Opportunities in Clinical Trials	7
Patient Enrollment and Conflicts of Interest	8
Discussing Phase 1 Trials	8
Summary	14
Key Take-Home Points	14
References	16
Self-Assessment	19

Abstract

The participation rate in cancer clinical trials is low; 3% of patients with advanced cancer enroll in Phase 1 clinical trials. Patients with refractory symptoms are potential candidates for trials of new interventions. While it is important that patients who do enroll in these studies understand the minimal chance they have of meaningful personal benefit from a Phase 1 trial, it is also unfortunate for “fighters” to miss the opportunity to participate in clinical trials that could provide them with further hope, a sense of completion of all possible treatments, and the knowledge that their efforts may benefit others. Oncologists and members of the cancer care team can help patients recognize whether clinical trials are suitable for them. Importantly, oncologists can integrate attentive symptom management into their overall cancer care simultaneously with the clinical trial. This module presents an approach to structuring communication about participation in Phase 1 clinical trials based on the seven steps presented in EPEC™-O Module 7: Communicating Effectively.

Introduction

In the early 21st century, somewhat fewer than 1.5 million Americans are diagnosed with cancer and over 500,000 die of cancer each year. (Ref. 1) Clinical trials present a further opportunity for patients and families to:

- Try an additional therapy, even though the potential for benefit to them may be very low.
- Know they've tried everything possible and reasonable to prolong the patient's life.
- Give the patient and family further time to realize and adjust to their future.
- Provide a gift of knowledge to other patients who may benefit from their efforts.

It is estimated that 40,000 to 60,000 cancer patients will be enrolled in clinical research trials each year, and about 2,000 to 4,000 will be enrolled in Phase 1 studies. About one-half of these patients have advanced cancer. As a proportion of the total number of people living with cancer, these data indicate that <1% of all cancer patients actually enroll in clinical trials and about 3% of those with advanced cancer enroll in Phase 1 trials. Surveys suggest there are many reasons for this low participation rate: too few trials, restrictive eligibility criteria on the trials that are offered, physicians failing to offer eligible patients trials, and patients refusing enrollment in trials.

Objectives

After studying this module, oncologists and other members of the cancer care team will be able to:

- Describe the reasons why patients participate in clinical trials.
- Describe the opportunities for patients in Phase 1 clinical trials.
- Discuss Phase 1 clinical trials with patients and families using a seven-step protocol.

Why Patients Enroll in Trials

Caution has surrounded clinical trials for people with serious illness. Many people have concerns that cancer patients, especially terminally ill cancer patients who have exhausted conventional therapeutic options, enroll in research only because they have therapeutic misconceptions (i.e., “How could they sign up for a study with few or no prospects of benefits and many side effects unless they somehow had false hope that it would provide benefit?”)

It appears that many cancer patients who sign up for research trials hope they will benefit personally. Joffe et al. found that among cancer research participants:

- Seventy percent agreed with the claim that “the treatment being researched in my clinical trial has been proven to be the best treatment for my type of cancer”
- Sixty-three percent agreed with the claim that “compared with standard treatments for my type of cancer, my clinical trial does not carry any additional risks or discomfort.” (Ref. 2)

Similarly, Meropol et al. reported that 77% of Phase 1 trial participants hoped they would have a 50% or higher chance of benefit from the therapy. (Ref. 3)

These data indicate that most cancer patients believe their research interventions will be beneficial. But the situation is also more complex. Simultaneously with these responses, cancer research participants recognize that they might not personally benefit. For instance, in Joffe’s study:

Seventy-five percent of participants’ agreed that “there may not be direct medical benefit to me from my participation in this clinical trial.”

These responses seem contradictory and many have only commented on the interpretation that patients have misconceptions about research. An interpretation that is

true to the data also supports the view that participants are perfectly coherent and hold an understandably ambivalent perspective that works for their circumstances and dispositions. Patients recognize that there is only a chance that they will benefit, while they simultaneously hope they will benefit, i.e. they hope they will be among those who have tumor shrinkage or even cure. Holding these two views, knowing that you may not benefit but hoping you will be among those who do benefit, is characteristic of people who are “fighters” (i.e., not ready to give up), and “risk takers.” Indeed, it has been termed the “gambler’s” mentality. (Ref. 4)

One patient who wrote of his rationale for joining a Phase 1 cancer study characterized this personality and world view in the following way:

“Most patients do not ask to participate in protocols but rather are content to either let the disease follow its natural course or adhere to the advice of their health care providers (who in turn may be somewhat fatalistic). Patients who seek to participate in protocols are those who question the status quo and who are most eager to alter it...We who are struggling to escape cancer do not, obviously, want to die of it. We do prefer death in the struggle to life under cancer’s untenable rule. The enemy is not pain or even death, which will come for us in any eventuality. The enemy is cancer, and we want it defeated and destroyed...better that a few fall in the storming of the bastion, than no storming be attempted.” (Ref. 5)

Patients may also find meaning and value in knowing that they are providing data that may someday benefit someone else.

Reasonable hope

While the odds of a clinically important antitumor response are low, they are not zero. The perceived hope is not a false hope but the best hope for life that is available. Denying the possibility of therapeutic benefit from early-phase cancer trials is untrue. In some cases (e.g., imatinib mesylate [Gleevec]), there have been long-lasting and clinically meaningful responses. On the basis of Phase 1 data, the drug was approved by the Food and Drug Administration. In rare cases there have been cures on Phase 1 trials. Many patients with testicular cancer were cured in the Phase 1 trials of platinum in the 1970s. Indeed, every antineoplastic agent currently approved was first tested in a Phase 1 trial. It is important for the oncologist to be realistic and neither overly optimistic nor nihilistic. Patients must understand the risks and benefits of the trial and their alternatives.

Alternatives

Another concern is that terminally ill cancer patients who enroll in Phase 1 trials may not know about their alternatives, especially palliative care and hospice. Reviews of Phase 1 consent forms indicate that almost none mention hospice as an alternative. (Ref. 6) However, 56% mention palliative or supportive care, and 26% mention relief of symptoms. Indeed, among “classic” Phase 1 studies in which a single chemotherapeutic

agent that has never been tried in humans before is assessed for safety, 69% of informed consent documents mention palliative or supportive care, and 42% mention relief of symptoms.

Some patients who participate in Phase 1 trials may be fully aware of the availability of palliative care or hospice as alternatives but may not see them as interventions they want at the time of enrollment in Phase 1 trials. In as yet unpublished data, Agrawal and colleagues found that 80% of 90 patients participating in Phase 1 studies at five centers were aware of hospice and 89% were aware of palliative care as alternatives. However, only 5% “seriously considered” hospice for themselves and 9% “seriously considered” palliative care as an alternative for themselves. The problem is not awareness of these options; rather, it is that people who enroll in Phase 1 oncology trials do not want these interventions at this time in the course of their illness.

In part, this finding underscores the misperception that palliative care is end-of-life care as opposed to a component of optimal cancer care, whether curative, palliative, or experimental in intent. It is important that patients not suffer needlessly and palliative care should be part of both control and intervention arms in a clinical trial. The potential of palliative care to manage adverse effects may even allow use of higher doses of the new agent in Phase 1 trials.

Adverse effects of Phase 1 agents

A full understanding of the risks and benefits of participation in a clinical trial is an essential component of informed consent. For Phase 1 trials, the goal of the study, i.e. to determine at what dose adverse effects occur, should be clear to the potential subject.

At the same time, it is also important to recognize that in the last decade or so the nature of early-phase oncology research has changed. Vaccines, antiangiogenesis factors, immunological agents, protein kinase inhibitors, as well as other agents have been introduced into the antitumor armamentarium. Research with these agents accounts for approximately 40 to 50% of all Phase 1 trials. This is important because, compared with traditional chemotherapeutic agents, many of these agents have fewer adverse effects and no maximum tolerated dose is encountered in the early-phase studies. Thus, with many newer agents the risk profile may be smaller, enhancing the risk-benefit ratio for patients with advanced disease.

Research on Palliative Interventions

Research on palliative interventions presents a new area of clinical research. With the development of new interventions to treat symptoms and side effects, clinical research is required on these interventions. For the most part, clinical trial design applies for palliative care agents in the same way as for other agents. The standard of care clinical

trial arm should use full palliative therapies, and the new intervention should add or replace one of those in the clinical trial arm.

Patients with refractory symptoms may enroll in a Phase 1 trial rather than resign to uncontrolled suffering or choose terminal sedation. To be sure patients are refractory to palliative interventions and not just poorly managed, it may be important to require assessment by a pain and palliative care service prior to enrollment in a clinical trial. Once an intervention is proven safe and efficacious, trying it as a supplement or substitute for other palliative options can be ethical.

Outcome measures are challenging since outcomes are subjective in many instances of palliative care and patients may have reduced awareness. However, progress is being made in this area, with improved quality-of-life assessments for this population. Further challenges are presented by the often short lifespan of the patient population, which makes prospective studies difficult. However, progress is being made in this area, too. Oncologists will want to remain alert to palliative care clinical trials that may be available to their patients.

Opportunities in Clinical Trials

What do these data mean for the oncologist and the cancer care team who are working with patients with advancing cancer who are not responding to conventional therapies?

Ensure that everyone knows that a clinical trial is an option: As part of disclosing reasonable alternatives in a truly informed consent process, let every patient know that existing clinical trials, including Phase 1 trials, are options. At this time, provide a brief overview. You do not need to discuss the details.

Expect that only a few patients will inquire about a Phase 1 trial: Phase 1 trials will probably appeal only to the “fighters” or “risk takers.”

Explain what is known; what is not known: For the patient who expresses an interest, explain the purpose of the trial, including:

- The experimental nature of the study.
- The potential for the trial to benefit the patient (close to zero in Phase 1 trials).
- The fact that in Phase 1 trials we do not know the risk of adverse events, and that the trial is designed to establish the risk. Explain clearly that some interventions may have adverse effects.
- Estimate the burden for the patient and family to participate in the trial.

If the patient remains interested, a full informed consent discussion is the next step.

Patient Enrollment and Conflicts of Interest

Oncologists, like other clinicians, sometimes engage in both clinical practice and research. It is possible that motivations to enroll patients in clinical trials may be driven by incentives, i.e. financial, career advancement, or aspirations to advance research, that go beyond the patient's interests. To protect against perceptions of or actual coercion, oncologists should be clear about their role when they discuss trials with their patients. This may take special care since patients are often emotionally vulnerable and easily swayed because of the circumstances of their illness.

The patient's clinician should keep the obligations of his or her clinical role rather than investigator role paramount. In addition, clinicians should enroll patients in a trial only if enrollment meets criteria of free informed consent. The patient should also understand the clinician's role in the trial, whether the clinician is a little-acquainted colleague of the investigator or is a participating investigator. Reassurances that nonparticipation in a trial will not adversely affect care must be real and credible, especially if the clinician is involved in the study.

Module 10 - Video 1

Discussing Phase 1 Trials

The Seven-Step Protocol, adapted from *How To Break Bad News: A Guide For Health Care Professionals* by Robert Buckman, known by its acronym, SPIKES, can be modified to provide a structure to discuss Phase 1 clinical trials. (Ref. 7) (Ref. 8) The adaptation is illustrated here for discussion of a Phase 1 trial.

SPIKES +

SPIKES+	Seven-step protocol to communicate
Setting. Getting started.	1. Set the stage.
Perception. What does the patient know?	2. Determine what the patient/family knows.
Invitation. How much does the patient want to know?	3. How much does the patient want to know? Sufficient desire for information to meet informed consent standards is necessary.
Knowledge. Sharing the information.	4. Discuss the patient's situation and the Phase 1 clinical trial; information sharing must meet informed consent standards.
Emotion. Responding to the feelings of the patient and family.	5. Respond to emotions.
Subsequent. Planning and follow-up.	6. Plan next steps and follow-up.
+ Review. Reassess and revise periodically.	7. Review and revise periodically

The first three steps deal with preparatory activities, some of which could be completed before the session at which you actually discuss the trial. At the fourth step, the news is delivered. The following two steps permit you to respond to the patient's reactions and constructively plan for follow-up.

Step 1: Set the stage

Before initiating a discussion about a Phase 1 clinical trial, familiarize yourself with:

- The details of the patient's diagnosis, history, and prognosis.
- The details of the protocol, the known facts about the study medication and its potential for benefit, risk of adverse events, and burden to the patient and family to participate in the trial.

- Alternative treatment options.

Have written information about the trial, including the consent, available for the patient and family to take away and read.

Determine who else the patient would like to have present for the discussion. This might include family members, significant other(s), or other health professionals or caregivers who are involved with the patient's care.

Find a quiet place for the discussion. Ensure the comfort of everyone who is present. To minimize interruptions, turn off mobile phones and pagers, or give them to someone outside the meeting.

Step 2: Determine what the patient and family know

Start the discussion by establishing what the patient and family know about the patient's diagnosis and prognosis, their goals of care, and their expectations about treatment. Ascertain what else they are hoping to achieve in the time that remains (particularly if prognosis is limited). Ask what they know about Phase 1 clinical trials. Questions might include:

- "What do you understand about your illness?"
- "How would you describe your medical situation?"
- "What do you expect from your future?"
- "What do you hope for from future treatment?"
- "Tell me what you know about clinical trials."
- "Tell me what you know about Phase 1 clinical trials."
- "What do you expect from a Phase 1 clinical trial?"

Step 3: How much does the patient want to know?

Next, establish how much and what each patient wants to know; determine who is a "fighter," and who is not. Everyone handles information differently. Some patients want to hear all of the details related to toxicity and expectations for the future, while others prefer generalities. If there is critical information that needs to be communicated during the trial, establish to whom information should be given.

As in any situation where information is to be shared and decisions undertaken, there are ethnic and cultural differences in the preferred handling of information. While knowledge of such differences is useful as a background, global conclusions about them rarely help with decision making for an individual. Ask a patient about general preferences for handling of medical information and decision making early, before

significant information needs to be shared. This will help you avoid making a misstep. Possible questions include:

- “Would you like me to tell you the full details of what you might expect? From the experimental drug? For your future?”
- “If not, is there somebody else you would like me to talk to?”

Use the responses to these queries to assess the potential to complete informed consent discussions. In order to comply with standards for informed consent, the patient must be comfortable with receiving all information relevant to that process, and with making his or her rational, autonomous decisions.

If the patient wants decisions to be made by another person, proceed with participation in a clinical trial only with great caution. It may be possible to establish a Durable Power of Attorney for Health Care to make decisions if the patient strongly wants to participate yet not handle information. However, counseling against participation for such a patient may be wiser.

Module 10 - Video 2

Step 4: Discuss the patient’s situation and the Phase 1 clinical trial

When the patient and those present are ready, review the facts about the patient’s situation, i.e. the diagnoses and prognosis, experience with anticancer therapy, and the potential for any other anticancer therapy to be of any benefit.

Deliver information in a straightforward manner about the intent of Phase 1 trials, the scientific background of the investigational agent, its potential toxicity, and the burden that the patient and family will face to participate in the trial. Don’t minimize the potential toxicity or the time commitment to participate in the trial. Speak in simple terms first. Avoid using medical jargon. Pause frequently. Check for understanding. Encourage questions. Evolve to more complex concepts once you verify understanding.

Ensure that everyone who enrolls in a Phase 1 trial understands that they are taking a risk of side effects with a low chance of personal benefit.

Data suggest that most patients who enroll in Phase 1 studies understand that they may not personally benefit: they have hope while still being realistic. However, oncologists should reinforce this point while not being nihilistic, probably by saying something like:

“We are all hoping for the best and that your tumor responds to the experimental drug (or agent), but we also need to recognize that you may not benefit at all. Since this is the first time the drug is being used in people, this is a long shot and not even close to a guarantee of benefit.”

Emphasize that participation, or not, will not compromise standard care. It is very important for patients and families to know the alternatives available to them, including hospice care. Emphasize that whatever the patient's choice:

- The oncologist and the cancer care team will not abandon the patient.
- Enrollment is not mutually exclusive with treatment of pain or nausea, or any other appropriate palliative care. (Ref. 9)

Too often both oncologists and patients seem to think that palliative care is an alternative to chemotherapy or enrollment in clinical research trials. It does not have to be an either/or choice: palliative care **or** anticancer treatment.

- Let the patient know that the clinical trial team personnel and you are committed to providing both palliative care and anticancer treatment simultaneously.
- Explain that the study will use anticancer therapy to kill tumor cells and palliative care to help the patient eat well, sleep well, minimize stress, and maintain function, self-esteem, and quality of life while on a Phase 1 trial. Almost all clinical research studies, including Phase 1 trials, permit both therapeutic approaches simultaneously. It is the very rare clinical trial that contains exclusion of some palliative care options, usually to avoid specific drug-drug interactions, and none contain blanket exclusions of all palliative interventions.
- Emphasize that utilizing palliative care is not “giving up” or implying that there is nothing else to do. Let the patient know that it may even help to minimize the impact of adverse events from trial medications and facilitate a more expeditious and successful outcome for the trial.

With this perspective, oncologists should reassure patients considering Phase 1 trials, saying something like:

“We are also going to use standard interventions to relieve your symptoms and support you. We know this doesn't interfere with getting the full effect of the experimental drug. We will try to eliminate suffering while still trying to beat your cancer.”

Review the consent form with the patient and family. Offer them time to review the form and ask you or study personnel any questions.

Again, reassure the patient and family that:

- You will not abandon them.
- They will continue to have access to comprehensive cancer care no matter what their choice.
- The patient can withdraw from the clinical trial at any time.

Step 5: Respond to emotions

Respond calmly and with understanding to any emotions the patient and family may express. To the question, “Are you using me as a guinea pig?” you might respond with language like the following:

“Well, that’s one way to put it. Another is that we need people like you to help us develop the drugs of the future: just as other patients participated in past clinical trials so you could benefit from the treatment you’ve already had. It is the case that a very small number of patients in these trials have improvements in their cancer. It’s important that you understand that the main purpose of the trial is to see how human beings tolerate the drug.”

To the exclamation, “I’m going to go through all of this for nothing!” you might respond as follows:

“It is true that you may receive no personal gain and no improvement in your tumor or prognosis from this treatment. However, we may learn things from this trial that will help other people. It has been through clinical trials and the evaluation of new treatments that we have improved the outcome for some cancer patients.”

To the concern, “I’m going to give up all of the good time I have left,” you might respond:

“There is a loss of personal time associated with participation in this study. You might spend your time differently if you were not participating in this study. Some patients, when they look back, feel like they would rather have gone on a trip or spent more time with their kids than coming to the doctor’s office.”

If participation in a clinical trial will jeopardize the patient’s chance to complete life goals (e.g., if he or she is approaching the end-of-life and has little time left to complete important relational work or other tasks), the trial may not be appropriate for the patient.

Step 6: Plan next steps and follow-up

Establish a plan for next steps. For the patient who consents to participate in a clinical trial, explain plans for any needed evaluations. Review and provide a written schedule of planned tests, office visits, and treatment. Introduce the patient and family to study personnel that may interact with the patient. Be sure the patient knows how to access supportive care. Reassure the patient that you will continue to be available.

For the patient who declines to participate in a Phase 1 trial, discuss alternate treatment choices, including hospice referral. Make a commitment to continued symptom management, and plan follow-up. Reassure the patient that you will continue to be available for questions. Establish the time for the next appointment.

Step 7: Review and revise periodically

As patients and families sometimes change their goals for care and treatment and life priorities, review their understanding of the clinical trial and how it is going periodically. Make sure they continue to understand the intent of the clinical trial. Answer any questions. It is comforting for patients and families to know that the plan can change at any time.

Summary

Participation in cancer clinical trials, especially Phase 1 trials for advanced disease, is low. The reasons for low enrollment include lack of appropriate trials, restrictive enrollment criteria, physicians' failure to offer the trials, and patient refusal to participate. Patients who choose to enroll in Phase 1 studies usually recognize the small potential for personal gain, but as "fighters," hope for a response from the treatment. Oncologists need to present clinical trial options, follow the steps for good communication and informed consent, and integrate symptom management into cancer care.

Key Take-Home Points

1. Participation in adult clinical trials is low.
2. Use a modification of the seven-step approach, particularly when learning this skill, to present Phase 1 clinical trials.

Step 1: Set the stage

3. Familiarize yourself with the trial and prepare what you are going to say.
4. Determine who else should be present.

Step 2: Determine what the patient and family know

5. Establish what the patient (and family) knows about the patient's disease status. Establish what the patient expects from treatment and his or her understanding of clinical trials/Phase 1 studies.

Step 3: How much does the patient want to know?

6. People handle information differently.
7. Find out how much information the patient wants to receive.
8. Ensure that informed consent standards can be met.

Step 4: Discuss the patient's situation and the Phase 1 clinical trial

9. Deliver the information in a straightforward manner. Avoid jargon and encourage questions.
10. Adhere to informed consent requirements.

Step 5: Respond to emotions

11. Respond calmly to patients' concerns about clinical trial participation.

Step 6: Plan next steps and follow-up

12. Establish a plan for next steps.

Step 7: Review and revise periodically

13. Check understanding and goals of care periodically. Ensure that the patient is comfortable with continued participation in the trial.

Pearls

1. Allow enough time for the information to sink in.
2. Ask for the patient to repeat back what he or she has understood.
3. Patients may take more risks and want to enter a clinical trial, even a Phase 1 trial, when established therapeutic options have run out.
4. "Fighters" may hope for amelioration of their cancer even when the odds are against them, if this small chance is the best they have. It can be rational to enter a trial and not a misconception on their part.
5. Make a partnership with your patient and the family caregiver; draw them into the interdisciplinary team and foster their active participation in the care plan.

Pitfalls

1. Letting other considerations (promotion, publications, enthusiasm, limited time) influence a balanced presentation of risks and benefits. This would be a mistake.
2. Imagining that all participants in Phase 1 studies are involved because of a therapeutic misconception.
3. Believing that research on palliative care is precluded on ethical grounds. This would be misguided. Palliative care research is necessary and can be done in full compliance with ethical requirements.
4. Failing to alert patients to the option of participation in a clinical trial. This deprives patients of important options and slows the progress of research.

References

Module 10: Clinical Trials

- 1 Jemal A, Murray T, Ward E, et al. Cancer statistics, 2005. *CA Cancer J Clin*. 2005 Jan-Feb;55(1):10-30. PMID 15661684; full text.

The article provides a summary of the most recent data on cancer incidence, mortality, and survival using incidence data from the National Cancer Institute and mortality data from the National Center for Health Statistics.

- 2 Joffe S, Cook EF, Clearly PD, et al. Quality of informed consent in cancer clinical trials: A cross-sectional survey. *Lancet*. 2001;358:1772-1777.

The purpose of this survey was to measure the quality of understanding among participants in clinical trials of cancer therapies, identify correlates of increased understanding, and assess providers' beliefs about clinical research. A standard questionnaire was administered to 287 adult patients with cancer who had recently enrolled in a clinical trial. The provider who obtained each patient's consent was also surveyed. Only 46% of providers recognized that the main reason for clinical trials is benefit to future patients. Frequent misconceptions about cancer clinical trials among trial participants are identified and discussed. Efforts to educate providers and participants about the underlying goals of clinical trials are needed.

- 3 Meropol NJ, Weinfurt KP, Burnett CB, et al. Perceptions of patients and physicians regarding Phase 1 cancer clinical trials: Implications for physician-patient communication. *J Clin Oncol*. 2003;13:2589-2596; full text.

To describe and compare the perceptions of cancer patients and their physicians regarding Phase 1 clinical trials, both were asked to complete questionnaires with domains including perceptions of potential benefit and harm from treatment (experimental and standard), relative value of quality and length of life, and perceived content of patient-physician consultations. Cancer patients offered Phase 1 trial participation had expectations for treatment benefit that exceeded those of their physicians. The discordant perceptions of patients and physicians may possibly be explained by patient optimism and confidence; however, the discrepancies in reports of consultation content raise the possibility that communication in this context is suboptimal.

- 4 Yoder LH, O'Rourke TJ, Etnyre A, et al. Expectations and experiences of patients with cancer participating in Phase 1 clinical trials. *Onc Nurs Forum*. 1997;24:891-896.

To describe the expectations and experiences of patients entering Phase 1 clinical trials, a descriptive, exploratory, prospective study was undertaken. Interviews using structured entry and exit questionnaires evaluated expectations and experiences of patients in Phase 1 clinical trials. Patients expected slightly increased support from family members and received more support than expected. Patients' expectations for tumor response and increased communication with their physicians were not met. The implications for nursing practice are discussed.

- 5 Daugherty CK, Siegler M, Ratain MJ, Zimmer G. Learning from our patients: One participant's impact on clinical trial research and informed consent. *Ann Intern Med*. 1997;125:892-897; full text.

This perspective includes an essay on modifying Phase 1 clinical trials written by George Zimmer, a cancer patient who participated in the Phase 1 clinical trial program at the University of Chicago, and a professor of English. A commentary on his essay is included.

- 6 Horng S, Emanuel EJ, Wilfond B, et al. Description of benefits and risks in consent forms for Phase 1 oncology trials. *N Engl J Med*. 2002;347:2134-2140.

To evaluate the written description of direct benefit as well as risk, consent forms for 1,999 Phase 1 cancer trials were compiled from 80% of the National Cancer Institute-designated cancer centers and from six of eight large pharmaceutical developers of anticancer drugs. Consent forms for Phase 1 oncology studies almost never promise direct benefit, rarely mention cure, and usually communicate the seriousness and unpredictability of risk. The consent forms are unlikely to be the primary source of misunderstanding by subjects in Phase 1 oncology trials.

- 7 Buckman R. *How to Break Bad News: A Guide for Health Care Professionals*. Baltimore, MD: The Johns Hopkins University Press; 1992:65-97. ISBN: 0-8018-4491-6.

- 8 Baile WF, Buckman R, Lenzi R, Glober G, Beale EA, Kudelka AP. SPIKES—A six-step protocol for delivering bad news: Application to the patient with cancer. *Oncologist*. 2000;5:302-311.

A protocol for disclosing unfavorable information—"breaking bad news"—to cancer patients about their illness is presented. Directions for continuing assessment of the protocol are suggested.

- 9 Agrawal M, Danis M. End-of-life care for terminally ill participants in clinical research. *J Palliat Med.* 2002;5:729-737.

This paper focuses attention on and offers an analysis of how to meet the needs of participants in clinical research who are terminally ill. Two important tasks are reconciled: providing optimal end-of-life care and conducting clinical research. The inherent tension between the goals of medicine and the goals of science are examined. Suggestions to address this tension are presented.

Self-Assessment

Module 10: Clinical Trials

1. Mrs. Kuzel is a 43-year-old nurse who has recurrent acute myelogenous leukemia after transplant. The most likely reason why she would not participate in a clinical trial is:
 - a). too many clinical trials
 - b). eligibility criteria too vague
 - c). the oncologist won't offer the trial
 - d). the trial will be too expensive

2. Ms. Shega is a 21-year-old woman with a diagnosis of BRCA-1 positive breast cancer that is refractory to standard therapy. She is eligible for a Phase I clinical trial. Her view of why she would participate is most likely to be:
 - a). hoping she will have no side effects
 - b). knowing that she is likely to benefit personally from experimental therapy
 - c). hoping to benefit, but knowing that is unlikely
 - d). ensuring that her mini-mental status shows she has capacity

3. If Mrs. Shega's oncologist were to offer clinical trials to all of her patients, she should expect that:
 - a). a majority of patients would enroll
 - b). only a few patients would enroll
 - c). she will need to provide financial incentives for enrollment
 - d). she will need to tell them they are likely to benefit

4. If Mrs. Shega enrolls in the clinical trial, she will need to understand that palliative care:
- a). will have to wait until the trial is over
 - b). can be offered concurrently with the clinical trial
 - c). will only be offered if covered by her insurance plan
 - d). can only be provided once she elects hospice care
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Self-Assessment Answers

Question 1. The correct answer is: c)

This question gets at why clinical trial participation is low. Surveys suggest there are many reasons for this low participation rate: too few trials, restrictive eligibility criteria on the trials that are offered, physicians not offering eligible patients trials, and patients refusing enrollment in trials. Physicians not offering the trials is the most often cited reason.

Question 2. The correct answer is: c)

This question gets at the reasons patients say they participate in clinical research. Patients recognize that there is a chance, even a high chance, that they will not benefit, while simultaneously hoping they will benefit—hoping they will be among the few who will have tumor shrinkage or even cure.

Question 3. The correct answer is: b)

This question gets at what oncologists should expect when offering clinical trials. Oncologists should expect that only a few patients will opt for such trials; participating in such trials will probably appeal only to the “fighters” or “risk takers.” Oncologists should make a special effort to delineate to such patients the full range of trials that are available and the kinds of risks they may confront.

Question 4. The correct answer is: b)

Enrolling in early-phase trials is not mutually exclusive with treating pain, nausea, or any other appropriate palliative care. Too often, both oncologists and patients seem to think that palliative care is an *alternative* to chemotherapy or enrollment in clinical research trials. This is not and should not be an either/or choice. It is not palliative care **or** anti-cancer treatment. Both can and should be provided simultaneously.