

EPECTM-O

Education In Palliative And End-Of-Life Care For Oncology

Self-Study Module 8:

Clarifying Diagnosis and Prognosis

Module 8: Clarifying Diagnosis and Prognosis

Abstract	3
Introduction	3
Objectives	4
Determining Prognosis	4
Six Steps for Clarifying Diagnosis and Prognosis	11
Unrealistic Expectations	18
Summary	19
Key Take-Home Points	20
Appendix: Survival of Adult Patients by Type of Cancer in Phase III Trials	20
References	40
Self-Assessment	49

Abstract

Accurate prediction and disclosure of diagnosis and prognosis are essential for both treatment and personal decision making. Physicians tend to be overly optimistic in their survival estimates and even more optimistic when they relay prognostic information to patients. This module reviews physician prognostication skills, sources of prognostic information, and the role of integrated prognostic models and their limitations. It then presents a six-step protocol to guide the communication and clarification of diagnosis and prognosis. Approaches for handling unrealistic expectations and denial are also discussed.

Introduction

Module 8 - Video 1

It is customary for oncologists to convey information about prognosis. The vast majority of Americans want to know if they have a life-threatening illness and how long they have to live. (Ref. 1) (Ref. 2) Studies in other cultures yield surprisingly similar data. (Ref. 3) (Ref. 4) Although legitimate cultural variations are important, communicating diagnosis and prognosis in a direct and compassionate manner is likely to improve the patient's and family's ability to plan and cope; encourage realistic goals and autonomy; support the patient emotionally; strengthen the physician-patient relationship; foster collaboration among the patient, family, physicians, and other professionals; and be reassuring that the cancer care team will be honest, even when the news is not good.

Many patients ask about their prognosis. Others expect the oncologist will introduce the subject. Most want to have a sense of their future so they can plan their lives. Some are terrified and hope that you will reassure them that things are not so serious.

At times, understanding what a diagnosis and prognosis mean may be confusing to patients and families and challenging to oncologists. Patients and families do not always translate metastatic disease to incurable disease, which is usually though not always the full meaning of the situation. Furthermore, the word respond (as in "a certain percent of cancer patients respond to treatment") is often misinterpreted by patients and families as "are cured."

Module 8 - Video 2

As with communicating bad news, family members may not want you to tell the patient her or his prognosis. Some fear the news will be so distressing that it will affect the patient adversely or even lead to her or his death.

At times it may also be difficult for oncologists and members of the cancer care team, who want to be on the “hope” team, to share the information when they don’t want to believe the news either. To make this process easier, it may be helpful to reflect that information carefully shared is a gift to the patient and family who want it and minimizes the risk that patients will distrust the cancer care team. (Ref. 2)

Objectives

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

- Describe the difficulty inherent in prognostication.
- Contrast what is known with the limitations of current prognostic models.
- Apply the six-step protocol to communicate and clarify diagnosis and prognosis.

Determining Prognosis

At diagnosis, recognized tumor-specific prognostic factors (e.g., molecular markers, stage, grade, etc.), modified by treatment- and patient-specific factors (e.g., comorbid illness, performance status, and disease signs and symptoms), provide general prognostic information.

Overestimation

Prognostication for advanced cancer, based on a physician’s clinical experience and intuition (formulated prognosis), is generally inaccurate. Physician estimates of prognosis for patients in palliative care programs tend to be overly optimistic by a factor of three- to fivefold, according to Christakis and Lamont. (Ref. 5) (Ref. 6) Other studies bolster the finding that physicians tend to overestimate survival. In spite of this, physician estimates correlate with actual survival and are most accurate in patients with survival of less than 6 months. (Ref. 5) (Ref. 6) (Ref. 7) (Ref. 8)

In seven out of eight studies, physicians overestimated survival in patients with advanced disease. (Ref. 7) Actual survival (AS) and clinical predictions of survival (CPS) from the trials cited are shown in Table 1. The median CPS was 42 days, while the actual median survival was 29 days.

Table 1: Studies of Clinical Predictions of Survival vs Actual Survival

Study	# Patients	Median CPS (days)	Median AS (days)
Parkes, et al ¹	71	28 (45-56)	21 (9-34)
Evans, et al ²	42	81 (28-182)	120 (43-180)
Heyse-Moore, et al ³	50	56 (33-84)	14 (7-28)
Maltoni, et al ⁴	100	42 (28-56)	32 (13-63)
Maltoni, et al ⁵	530	42 (28-70)	32 (13-62)
Oxenham, et al ⁶	21	21 (14-35)	15 (9-25)
Maltoni, et al ⁷	451	42 (21-70)	33 (14-62)
Christakis, et al ⁸	325	77 (28-133)	24 (12-58)
Overall	1,591	42 (28-84)	29 (13-62)

A meta-analysis of these studies suggests that survival is generally 30% shorter than predicted by CPS. (Ref. 7) CPS was within 1 week of actual survival in 25% of cases and overestimated survival by 4 or more weeks in 27%.

In spite of the limited accuracy of physician estimates of prognosis, physician input adds accuracy and value to statistical models. (Ref. 6) (Ref. 8) (Ref. 9) Sources of prognostic information include physician predictions, stage-specific survival data, performance status, signs and symptoms, and integrated models of prognosis.

Stage of cancer

Survival data for specific cancers by stage are widely available but not very useful to assess the prognosis of an individual patient. Natural history studies, though generally

the experience of a single institution, provide insight into the variable course and prognosis of advanced cancer.

Similarly, randomized trials that include a “best supportive care” arm provide further natural history information—essential information to communicate to patients when relating the anticipated survival benefits from treatment for advanced disease.

For example, patients with untreated, advanced breast cancer have a median survival of more than 2 years, while those with untreated advanced head and neck cancer have a median survival of about 4 months. (Ref. 10) (Ref. 11)

Performance status

Karnofsky

Performance status is a measure to quantify the functional status of cancer patients, and with the Karnofsky performance scale, to measure medical care requirements. The Karnofsky performance scale, a reliable, valid, simple, and reproducible measure of patient function, is an independent predictor of survival. (Ref. 12) (Ref. 13) The predictability of the Karnofsky performance scale for survival is, however, valid only for patients with scores less than 50. (Ref. 14) (Ref. 15) Data from the 1,592 patients in the National Hospice Study identified the Karnofsky performance scale as the most important clinical factor estimating prognosis. (Ref. 16) The Karnofsky performance scale differentiated the survival time of three distinct patient groups: Karnofsky performance scale ≥ 50 (86.1 days), Karnofsky performance scale=30-40 (49.8 days), and Karnofsky performance scale=10-20 (16.8 days), see Table 2.

Table 2: Prognosis for Patients on Hospice Based on Karnofsky Performance Status

Definitions	Ratings	Criteria	Prognosis
Able to carry on normal activity and to work; no special care needed	100	Normal; no complaints; no evidence of disease; no special care needed	86.1 days
	90	Able to carry on normal activity; Minor signs or symptoms of disease	
	80	Normal activity with effort; some signs or symptoms of disease	

Definitions	Ratings	Criteria	Prognosis
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed	70	Cares for self; unable to carry on normal activity or do active work	
	60	Requires occasional assistance, but is able to care for most personal needs	
	50	Requires considerable assistance and frequent medical care	
Unable to care for self; requires equivalent of institutional or hospital care; diseases may be progressing rapidly	40	Disabled; requires special care and assistance	49.8 days
	30	Severely disabled; hospital admission is indicated although death not imminent	
	20	Very sick; hospital admission necessary; active supportive treatment necessary	16.8 days
	10	Moribund; fatal processes progressing rapidly	
	0	Dead	

Loprinzi et al. have also demonstrated the ability of the Karnofsky performance scale to define three advanced cancer patient populations with statistically distinct survival curves by univariate and multivariate analyses. (Ref. 17) The strength of the association between performance status and survival appears to be time dependent; the Karnofsky

performance scale is of greater prognostic value when the anticipated survival is less than 3 months. (Ref. 18)

ECOG/WHO

A simpler scale was developed by Zubrod and found to be as useful as the Karnofsky Score but more easily assessed by untrained observers. (Ref. 19) The Eastern Cooperative Oncology Group (ECOG) and the World Health Organization (WHO) have adopted this scale.

In all studies, a score of 3 correlates with a prognosis of less than 3 months. A score of 4 correlates with a prognosis of less than 1 month. (Ref. 20)

Table 3: Prognosis by ECOG/WHO Performance Status

Grade	Criteria	Median Prognosis
0	Fully active, able to carry on all predisease performance without restriction	
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (e.g., light house work, office work)	
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours	
3	Capable of only limited self-care, confined to bed or chair more than 50% of waking hours	<3 months
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair	<1 month
5	Dead	—

Clinical signs and symptoms

Integrating the impact of various physical symptoms with performance status improves its predictive capability. A systematic review of prognostic factors in advanced cancer from 24 studies examined more than 100 variables and identified cognitive factors, weight loss, dysphagia, xerostomia, anorexia, and dyspnea as independent survival factors for patients with advanced cancer. (Ref. 18)

Palliative Prognostic Index

Prognostication is both art and science, and is imperfect at best. Integration of data from multiple sources of prognostic information improves one's ability to predict outcome. (Ref. 21) (Ref. 22) The Palliative Prognostic Index (PPI) is a validated model to predict prognosis for patients with advanced cancer. (Ref. 23) (Ref. 24) This model incorporates performance status, CPS, and specific clinical symptoms and signs. The model is able to predict 3- and 6-week survival in a cohort of advanced cancer patients with a sensitivity and specificity of 83% and 85% at 3 weeks and 79% and 77% at 6 weeks, respectively. (Ref. 23)

A prognostic model for patients continuing on treatment that includes integration of signs and symptoms is not available, and the PPI has not been evaluated in patients earlier in their disease course.

Module 8 - Video 2

Advanced or metastatic solid tumors receiving antineoplastic therapy

A review of the median survival for patients with advanced or metastatic solid tumors reported in published Phase III treatment trials during the last 5 years provides a broad view of the prognosis for patients receiving treatment for advanced or metastatic disease (see Appendix for trial details). A summary of the common tumors and their reported median survival is shown in Table 4.

For patients with an anticipated survival of 6 months or more, survival data from recent trials provide little more than general information about prognosis. What factors help refine prognosis for these patients? Prognostic modifiers for patients felt to have “chronic” metastatic disease include: performance status, hypercalcemia, brain metastases, and pleural effusions.

Hypercalcemia

Hypercalcemia is one of the most common metabolic complications of cancer and usually occurs during the last weeks of life. A review of the effects of antihypercalcemic treatment on morbidity and mortality in cancer-associated hypercalcemia reported a

median survival of 30 days. (Ref. 25) For the subset of patients for whom specific therapeutic interventions were directed at the cancer, survival was improved to 135 days. These data predate the widespread use of bisphosphonates for patients with osteolytic bone metastases from solid tumors. The poor prognosis for hypercalcemia does not appear to have changed, though anecdotally its incidence is reduced.

Table 4: Survival of Adult Patients Receiving Antineoplastic Therapy

-	Disease Status	Median Survival (months)
Bladder (TCC)	Advanced/metastatic	9-15
Brain – glioblastoma multiforme	Newly diagnosed	10-11
Breast	Metastatic	15-22
Cervix – squamous	Recurrent	6-8
Colon/rectum	Advanced/metastatic	12-22
Esophagus	Advanced/metastatic	3-6
Gastric	Advanced	7
Head and neck	Advanced/recurrent	5-12
Kidney	Metastatic	12-13
Liver	Advanced	3-10
Nonsmall-cell lung	Advanced	6-11
Small-cell lung	Extensive	9-14
Melanoma	Metastatic	5-12
Ovaries	Advanced	10-36
Pancreas	Advanced	5-6
Prostate	Refractory	9-14
Sarcoma	Advanced	12-14
Unknown primary	Metastatic	8-13

Brain metastases

The incidence of brain metastases has increased as treatment options for systemic disease have improved. In addition, a multimodal approach to brain metastases can prolong survival in some patients, though for the majority, this is a life-limiting site of metastases. Gaspar et al. analyzed 1,200 patients enrolled in 3 consecutive RTOG brain metastases trials to identify prognostic factors for survival. (Ref. 26) Using recursive partitioning analysis, best survival (median 7.1 months) was observed in patients <65 years old with a Karnofsky performance scale ≥ 70 and controlled primary tumor; worst survival (median 2.3 months) was observed in patients with a Karnofsky performance scale <70 (Group 3). All other patients fell into an intermediate prognostic group with a median survival of 4.2 months (Group 2). When a similar analysis was applied to patients who underwent surgical resection of brain metastases (with or without radiotherapy), the overall survival was improved. (Ref. 27) However, the survival varied based on the patient characteristics defined by the three groups, with a median survival of groups 1, 2, and 3 of 14.8, 9.9, and 6 months, respectively. In a highly selected group of patients, those with a Karnofsky performance scale >70 and the absence of extracranial disease, prolonged survival (>1 year) can be anticipated.

Malignant pleural effusions

Symptomatic malignant pleural effusions generally portend a poor prognosis, with a median survival of less than 4 months. (Ref. 28) (Ref. 29) As with other manifestations of advanced disease, prognosis is modified by the Karnofsky performance scale. (Ref. 29) Patients with recurrent, symptomatic pleural effusions and a Karnofsky performance scale score of ≥ 70 have a median survival of 13 months, while those with a Karnofsky performance scale ≤ 30 have a median survival of 1 month. While some series have failed to identify primary tumor site as a significant prognostic variable, others note a markedly worse survival for patients with nonsmall-cell lung cancer and a malignant effusion (median survival 2.9 months) and a better outcome for those with breast cancer (median survival 10 months) or ovarian cancer (median survival 9 months). (Ref. 28) (Ref. 29) (Ref. 30)

There are inadequate data to provide accurate prognostic information for most patients with metastatic disease and months to years of projected survival. However, when complications such as hypercalcemia or brain metastases—among others—occur, the prognosis can be more clearly defined and inform both treatment and personal decisions.

Six Steps for Clarifying Diagnosis and Prognosis

It is difficult to predict prognosis for an individual patient, and it can be difficult to present this information.

This module adapts the six-step protocol, SPIKES, presented in EPEC™-O Module 7: Communicating Effectively, to guide the communication and clarification of diagnosis and prognosis. (Ref. 31) (Ref. 32) (Ref. 33)

During the first three steps, prepare to share the information. Start by gathering the facts. Then sit down comfortably and assess the patient's understanding. Inquire what the patient knows, and what he or she would like to know about the diagnosis and/or prognosis.

Some of these first three steps can be completed before the session at which you actually discuss the news.

During the last three steps, manage the information carefully. Deliver the news clearly and succinctly and without using jargon. Once the facts have been stated, stop talking. Allow time for the patient's reactions and respond to them. Once the patient is settled, plan for follow-up.

Table 5: SPIKES

SPIKES	Six-step protocol to clarify diagnosis and prognosis
S etting. Getting started.	1. Getting Started.
P erception. What does the patient know?	2. What does the patient know?
I nvitation. How much does the patient want to know?	3. How much does the patient want to know?
K nowledge. Sharing the information.	4. Share the information.
E motion. Responding to feelings.	5. Respond to feelings.
S ubsequent. Planning and follow-up.	6. Plan next steps and follow up.

Don't consider this protocol to be a script to be followed rigorously. Use it as a tool to guide important aspects of an interaction in which difficult information is shared.

Step 1: Getting Started

Before starting to communicate any news, plan what will be discussed. Confirm the medical facts of the case (i.e., the diagnosis, prognosis, etc.). Ensure that all needed information is available. If this is an unfamiliar task, rehearse what you will say. Don't delegate the task. If several team members will be present, it may be helpful for the team to meet to plan the communication in advance.

Create an environment that is conducive to effective communication. Ensure privacy and adequate seating. Ensure that a box of facial tissues and a glass of water are handy.

Allot adequate time for the discussion. Do not slip this into a short interval between other critical tasks. Prevent interruptions. Arrange to hold telephone calls and pages.

Determine who else the patient would like to have present for the discussion. This might include family, significant others, surrogate decision makers, and/or key members of the interdisciplinary team (e.g., nurse, social worker, chaplain, etc.).

Step 2: What does the patient know?

Start the discussion by establishing what the patient and family know about the patient's health. With this information, ascertain whether the patient and family will be able to comprehend the information.

Questions might include:

- "What do you understand about your diagnosis and its prognosis?"
- "How would you describe the change in your medical situation?"
- "Have you been worried about your illness or treatment?"
- "What did you think might be causing symptom x?"
- "When you developed new symptoms, what did you think might be going on?"
- "What are your expectations from treatment?"
- "Did you think something serious was going on when you developed new symptoms?"
- "How do you expect your diagnosis to affect your survival?"

Occasionally a patient will fall silent and seem completely unprepared or unable to respond. To ease the situation and stimulate discussion, try to clarify what the patient understands about his or her medical history and recent investigations. Identify absent family members or others on whom the patient relies. If this is ineffective and the patient

remains silent, or if it appears the patient requires more support, it may be better to reschedule the meeting for another time.

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

Next, establish what and how much each patient wants to know.

People handle information differently, depending on their race, ethnicity and culture, religion, and socioeconomic class. Each person has the right to voluntarily decline to receive any information and may designate someone else to communicate on his or her behalf. Ask the patient and family how they would like to receive information. If the patient prefers not to receive critical information, establish to whom information should be given.

Possible questions include the following:

- “If the tests turn out to show something serious, do you want to know?”
- “Are you the kind of person who likes to know all the facts?”
- “Would you like me to tell you the full details of your treatment and prognosis? If not, is there somebody else you would like me to talk to?”
- “Some people really do not want to be told how the cancer will affect survival, but would rather their families be told instead. What do you prefer?”
- “Do you want me to go over the anticipated results of the treatment now, and explain exactly how I think it will affect you?”
- “Who would you like me to talk to about these issues?”

Before introducing the subject of prognosis, or directly answering questions about prognosis, consider starting with questions like:

- “Many patients want to know the prognosis. Is this true for you?”
- “What are you expecting to happen?”
- “How specific do you want me to be?”
- “What experiences have you had with others with cancer?”
- “What experiences have you had with others who have died?”
- “What are you afraid will happen?”

The way the patient answers the questions will give clues to her or his educational level, verbal fluency, and family dynamics. Listen carefully and observe everyone’s responses to your questions. Use this experience to influence how you deliver your news.

Advance preparation

All of the discussion to this point is about preparation to give the diagnosis and prognosis. Some of that preparation might best occur well before the information is actually given. The initial assessment and subsequent discussions that prepare the patient for critical tests provide opportunities to determine what the patient already knows and how he or she would like to have information handled.

Provide periodic information and cautions that the news might not always be good. With this incremental approach and periodic “warning shots,” the patient and family may be better prepared for bad news.

When the family says “don’t tell”

Many times, family members will ask the physician not to tell the patient the diagnosis, prognosis, or other important information. While it is the physician’s legal obligation to obtain informed consent from the patient, an effective therapeutic relationship requires a congenial alliance with the family.

Rather than confronting their request with, “I have to tell the patient,” inquire why they are concerned. Possible questions include:

- “Why don’t you want me to tell the patient?”
- “What is it that you are afraid I will say?”
- “Tell me about your past experience with cancer.”
- “Is there a personal, cultural, or religious context that I should know about?”

Suggest that you go to the patient together to ask how much he or she wants to know about his or her health and what questions there might be. Share anecdotes and talk about the pain of secrecy and the opportunities that come with open communication.

These situations may require significant negotiation. In particularly difficult cases, support from the institutional ethics committee may be helpful. Ultimately, it may be decided, after discussion with the patient, that details of diagnosis and prognosis and treatment decisions will be discussed only with the family. However, unless the patient has previously indicated that he or she wants no information, hiding the diagnosis or important information about prognosis or treatment from the patient is neither ethical nor legally acceptable.

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. The patient should be asked about general preferences for handling of medical information and decision making early in the clinical relationship before significant information needs to be shared. This will help the clinician avoid making a misstep.

Step 4: Share the information

Before sharing the information, consider the implications of the prognostic information you provide. Patients who wish to plan their lives want information that is more detailed. Those who are terrified may do better with answers that are more general. Definitive answers (e.g., “You will be cured,” or “You have 6 months to live,”) run the risk of producing disappointment if the time proves to be less, and anger or frustration if you underestimate the patient’s lifespan.

Consider responding by giving a range of time that encompasses an average life expectancy, such as “hours to days,” “days to weeks,” “weeks to months,” “months to years,” etc. Alternatively, indicate averages such as “one-third of people will be alive and well a year from now; half will live about 6 months. Exactly what will happen for you, I don’t know.” After giving a range, it may help to emphasize the limits of prediction by saying something like, “What this will mean for you I can’t tell. We need to hope for the best, while we plan for the worst. We can’t predict surprises and should plan in case something happens. We’ll have a better sense over time how things will evolve for you.”

Once you are ready, deliver the information in a sensitive but straightforward manner.

Start by letting the patient know that you have news, then share the facts about the patient’s diagnosis and prognosis. Say it, and then stop. Avoid delivering all of the information in a single, steady monologue. Use simple language that is easy to understand. Avoid technical jargon or euphemisms. Pause frequently. Check for understanding. Use silence and body language as tools to facilitate the discussion.

Do not minimize the severity of the situation. Well-intentioned efforts to “soften the blow” may lead to vagueness and confusion.

You might choose to tell the diagnosis and prognosis by using language like:

- “I feel badly to have to tell you this, but your cancer has recurred and you only have a few months left to live.”
- “I’m afraid the news is not good. The CT showed that your colon cancer has spread to your liver. This is a treatable, but not curable disease.”
- “Unfortunately, there’s no question about the CT scan: the cancer has spread to your liver.”
- “The report is back, and it’s not as we had hoped. It showed that there is cancer in your liver. I’m afraid this is not curable disease.”
- “I’m afraid I have bad news. The CT scan shows your husband has cancer throughout his liver.”

“I’m sorry”

The phrase “I’m sorry” may be interpreted to imply that the physician is responsible for the situation. It may also be misinterpreted as pity or aloofness. If you use the phrase, adjust it to show empathy. For example, “I’m sorry to have to tell you this.” The phrase, “I wish things were different” may be equally effective at communicating empathy without conveying responsibility for the condition. (Ref. 34)

Step 5: Respond to feelings

Patients and families respond to bad news in a variety of ways. Some respond emotionally with tears, anger, sadness, love, anxiety, relief, or other strong emotions. Others experience denial, blame, guilt, disbelief, fear, or a sense of loss or shame, or may even intellectualize why the situation is happening. A few may demonstrate reflexive psychophysiologic responses such as “fight or flight” and may even try to bolt from the room or totally withdraw into themselves.

Outbursts of strong emotion make many oncologists and other physicians uncomfortable. (Ref. 35) Give the patient and family time to react. Be prepared to support them through a broad range of reactions.

Listen quietly and attentively. Acknowledge their emotions. Ask them to describe their feelings:

- “I imagine this is difficult news...”
- “You appear to be angry. Can you tell me what you are feeling?”
- “Does this news frighten you?”
- “Tell me more about how you are feeling about what I just said.”
- “What worries you most?”
- “What does this news mean to you?”
- “I wish the news were different.”
- “I’ll try to help you.”
- “Is there anyone you would like me to call?”
- “I’ll help you tell your son.”

Remind them that their responses are normal. Make a box of facial tissue available. Nonverbal communication may also be helpful. Consider touching the patient in an appropriate, reassuring manner. Offer a drink of water, a cup of tea, or something else that might be soothing.

Allow time for the patient and family to express all of their immediate feelings. Don't rush them. Once the emotion is spent, most people will be able to move on. This usually lasts only a few minutes. The most frequent physician error is to talk. (Ref. 36) Yet, this is counter-productive. A shared understanding of the news and its meaning enhances the physician-patient relationship and facilitates future decision making and planning.

Step 6: Plan next steps and follow-up

Establish a plan for the next steps. This may include gathering additional information or performing further tests. Treat current symptoms. It may include helping parents tell their child about the illness and what treatment will be like. Arrange for appropriate referrals. Explain plans for additional treatment. Discuss potential sources of emotional and practical support (e.g., family, significant others, friends, social worker, spiritual counselor, peer support group, professional therapist, hospice, home health agency, etc.).

Always caution patients and families that unexpected surprises can happen. Suggest that they get their affairs in order so they won't be vulnerable if something unexpected does occur. Reassure them that you will be available to them to deal with issues and support them throughout the illness, whatever happens. Help clarify what can be realistically expected and distinguish this from what might be wished for or what is most feared. Identify the miraculous for what it is—something outside of usual experience that happens exceedingly rarely.

Reassure the patient and family that they are not being abandoned and that you will be actively engaged in an ongoing plan to help. Indicate how the patient and family can reach you to answer additional questions. Establish a time for a follow-up appointment.

Ensure that the patient will be safe when he or she leaves. Is the patient able to drive home alone? Is the patient distraught, feeling desperate, or suicidal? Is there someone at home to provide support?

At future visits, elements of this protocol may need to be revisited. Many patients and families require repetition of the news to gain a complete understanding of their situation.

Unrealistic Expectations

Despite the communication of accurate information, a survey of surgical, medical, pediatric, and radiation oncologists showed that 29% thought patients' unrealistic expectations were a challenge; 50% thought families' unrealistic expectations were a challenge.

Apply the six-step protocol in cases where unrealistic expectations are expressed. In particular, focus on step 2.

- “What is it that the patient and family know?”
- “What are they expecting?”
- “What have they heard the oncologist say?”
- “What other information do they have?”

Try to “suspend belief” and form a mental image of the patient’s or family’s point of view. What may have initially appeared to be an unrealistic expectation may seem less bizarre once the point of view is understood.

Differences in values frequently occur (i.e., “it’s important to try anything, no matter how small the chance” or “it’s important to be a fighter,”) will emerge. Differences in values are not resolved by scientific data.

Once a common understanding is developed, explore how the conflict can be resolved. This is discussed further in EPEC™-O Module 12: Conflict Resolution.

Summary

The six-step protocol for communicating effectively (see EPEC™-O Module 7: Communicating Effectively) provides a tool to guide the communication and confirmation of diagnosis and prognosis.

Prognostication is an inexact science, and physicians are often overly optimistic with their survival estimates. There are multiple sources of prognostic information (e.g., clinician estimates of survival, signs and symptoms, the Karnofsky performance scale, stage-specific survival data, and integrated models). The Karnofsky performance scale is an independent prognostic factor that is highly predictive of survival when the Karnofsky performance scale is under 50. For patients with very advanced disease and an anticipated survival of less than 3 months, some symptoms (e.g., dyspnea) are highly predictive of survival less than 1 month.

Prognosis is more difficult to predict for patients with advanced disease and a longer anticipated survival. Some cancer complications redefine prognosis for this group. There remains inadequate prognostic information for many of these patients and further research is needed.

Key Take-Home Points

1. Physicians are often overly optimistic with their survival estimates.
2. Inquire why the patient and family are asking about prognosis in order to have a sense of their context for the question.
3. Give as accurate an estimate of prognosis as you can, when requested.
4. The six-step protocol for communicating effectively provides a tool for clarification of diagnosis and prognosis.

Pearls

1. The shorter the anticipated survival, the more accurate physician predictions of survival tend to be.
2. Hypercalcemia, pleural effusion, and brain metastasis portend a poor prognosis.
3. 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. Trying to “soften the blow”; the patient and family may not understand the significance of the message.
2. Failing to clarify terms: be sure patients and families understand how response does and does not relate to cure.

Appendix: Survival of Adult Patients by Type of Cancer in Phase III Trials

Below is the list of cancer types that are addressed in the Phase III Trails. The complete table with detailed information can be viewed by clicking the link below or to the right.

- Bladder
- Brain
- Breast
- Cervix
- Colorectal
- Esophagus
- Gastric

- Head and neck
- Kidney
- Liver
- Lung - Nonsmall cell
- Lung - Small cell
- Melanoma
- Myeloma
- Ovarian
- Pancreas
- Prostate (hormone refractory)
- Sarcoma
- Unknown Primary

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
Bladder	Transitional Cell		9				Popov I, Jelic S, Radosavljevic D, Nikolic-Tomasevic Z. Amsacrine and cisplatin in poor prognosis patients with metastatic transitional cell carcinoma of the urothelium: A phase-II study. <i>Eur Urol.</i> 2001 Sep;40(3):324-329. PMID: 11684850; full text.	
			15/14		35/25		Sternberg CN, de Mulder PH, Schornagel JH, et al. Randomized phase III trial of high-dose-intensity methotrexate, vinblastine, doxorubicin, and cisplatin (MVAC) chemotherapy and recombinant human granulocyte colony-stimulating factor	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							versus classic MVAC in advanced urothelial tract tumors: European Organization for Research and Treatment of Cancer Protocol no. 30924. <i>J Clin Oncol.</i> 2001 May 15;19(10):2638-2646. PMID: 11352955; full text.	
			14/15	58			von der Maase H, Hansen SW, Roberts JT, et al. Gemcitabine and cisplatin versus methotrexate, vinblastine, doxorubicin, and cisplatin in advanced or metastatic bladder cancer: Results of a large, randomized, multinational, multicenter, phase III study. <i>J Clin Oncol.</i> 2000 Sep;18(17):3068-3077. PMID: 11001674; full text.	
Brain	Glioblastoma multiforme (GBM)	Newly diagnosed	11/11	45/44			Grossman SA, O'Neill A, Grunnet M, et al. Phase III study comparing three cycles of infusional carmustine and cisplatin followed by radiation therapy with radiation therapy and concurrent carmustine in patients with newly diagnosed supratentorial glioblastoma multiforme: Eastern Cooperative Oncology Group Trial 2394. <i>J Clin Oncol.</i> 2003 Apr 15;21(8):1485-1491.	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							PMID: 12697871; full text.	
		Newly diagnosed	11/11				Buckner JC, Schomberg PJ, McGinnis WL, et al. A phase III study of radiation therapy plus carmustine with or without recombinant interferon-alpha in the treatment of patients with newly diagnosed high-grade glioma. <i>Cancer</i> . 2001 Jul 15;92(2):420-433. PMID: 11466698; full text.	
		Newly diagnosed	10/10.5				Prados MD, Wara WM, Sneed PK, et al. Phase III trial of accelerated hyperfractionation with or without difluoromethylornithine (DFMO) versus standard fractionated radiotherapy with or without DFMO for newly diagnosed patients with glioblastoma multiforme. <i>Int J Radiat Oncol Biol Phys</i> . 2001 Jan 1;49(1):71-77. PMID: 11163499; full text.	
Breast	Adenocarcinoma	IV	17.4/16				Milla-Santos A, Milla L, Portella J, et al. Anastrozole versus tamoxifen as first-line therapy in postmenopausal patients with hormone-dependent advanced breast cancer: A prospective, randomized, phase III study. <i>Am J Clin Oncol</i> . 2003 Jun;26(3):317-322.	ER+

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							PMID: 12796608; full text.	
		IV	1.7 yr				Parnes HL, Cirrincione C, Aisner J, et al. Phase III study of cyclophosphamide, doxorubicin, and fluorouracil (CAF) plus leucovorin versus CAF for metastatic breast cancer: Cancer and Leukemia Group B 9140. <i>J Clin Oncol</i> . 2003 May 1;21(9):1819-1824. PMID: 12721259; full text.	
		IV	18.9/22.2				Sledge GW, Neuberg D, Bernardo P, et al. Phase III trial of doxorubicin, paclitaxel, and the combination of doxorubicin and paclitaxel as front-line chemotherapy for metastatic breast cancer: An intergroup trial (E1193). <i>J Clin Oncol</i> . 2003 Feb 15;21(4):588-592. Sledge GW, Neuberg D, Bernardo P, et al. Phase III trial of doxorubicin, paclitaxel, and the combination of doxorubicin and paclitaxel as front-line chemotherapy for metastatic breast cancer: An intergroup trial (E1193). <i>J Clin Oncol</i> . 2003 Feb 15;21(4):588-592. PMID: 12586793; full text.	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
		IV	16/15				Bonneterre J, Roche H, Monnier A, et al. Docetaxel vs 5-fluorouracil plus vinorelbine in metastatic breast cancer after anthracycline therapy failure. <i>Br J Cancer</i> . 2002 Nov 18;87(11):1210-5. PMID: 12439707; full text.	Second-line therapy
		IV	22.5/21.7				Nabholtz JM, Falkson C, Campos D, et al. Docetaxel and doxorubicin compared with doxorubicin and cyclophosphamide as first-line chemotherapy for metastatic breast cancer: Results of a randomized, multicenter, phase III trial. <i>J Clin Oncol</i> . 2003 Mar 15;21(6):968-975. PMID: 12637459; full text.	
Cervix	Squamous Cell	IV	8/6				Kumar L, Pokharel YH, Kumar S, Singh R, Rath GK, Kochupillai V. Single agent versus combination chemotherapy in recurrent cervical cancer. <i>J Obstet Gynaecol Res</i> . 1998 Dec;24(6):401-409. PMID: 10063235.	
Colorectal	Adeno-carcinoma	IV	22/21				Tournigand C, Andre T, Achille E, et al. FOLFIRI followed by FOLFOX6 or the reverse sequence in advanced colorectal cancer: A randomized GERCOR study. <i>J Clin Oncol</i> . 2004 Jan 15;22(2):229-237.	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
		IV	11/13/13				Kohne CH, Wils, J, Lorenz M, et al. Randomized phase III study of high-dose fluorouracil given as a weekly 24-hour infusion with or without leucovorin versus bolus fluorouracil plus leucovorin in advanced colorectal cancer: European Organization of Research and Treatment of Cancer Gastrointestinal Group Study 40952. <i>J Clin Oncol</i> . 2003 Oct 15;21(20):3721-3728.	
		IV	13/12				Van Cutsem E, Twelves C, Cassidy J, et al. Oral capecitabine compared with intravenous fluorouracil plus leucovorin in patients with metastatic colorectal cancer: Results of a large phase III study. <i>J Clin Oncol</i> . 2001 Nov 1;19(21):4097-5106.	
Esophagus		IV	4				Govindan R, Read W, Faust J, et al. Phase II study of docetaxel and irinotecan in metastatic or recurrent esophageal cancer: A preliminary report. <i>Oncology</i> . 2003 Sep;17(9 Suppl 8):27-31.	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
		IV	6				Muhr-Wilkenshoff F, Hinkelbein W, Ohnesorge I, Wolf KJ, Riecken EO, Zeitz M. A pilot study of irinotecan (CPT-11) as single-agent therapy in patients with locally advanced or metastatic esophageal carcinoma. <i>Int J Colorectal Dis.</i> 2003 Jul;18(4):330-334.	
		IV	3				Macdonald JS, Jacobson JL, Ketchel SJ, et al. A phase II trial of topotecan in esophageal carcinoma: A Southwestern Oncology Group study (SWOG 9339). <i>Invest New Drugs.</i> 2000 May;18(2):199-202.	
		IV	6				Stahl M, Wilke H, Meyer HJ, et al. 5-Fluorouracil, folinic acid, etoposide and cisplatin chemotherapy for locally advanced or metastatic carcinoma of the oesophagus. <i>Eur J Cancer.</i> 1994;30A(3):325-328.	
Gastric	Adeno-carcinoma	IV	7/7/7				Vanhoefer U, Rougier P, Wilke H, et al. Final results of a randomized phase III trial of sequential high-dose methotrexate, fluorouracil, and doxorubicin versus	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							etoposide, leucovorin, and fluorouracil versus infusional fluorouracil and cisplatin in advanced gastric cancer: A trial of the European Organization for Research and Treatment of Cancer Gastrointestinal Tract Cancer Cooperative Group. <i>J Clin Oncol.</i> 2000 Jul;18(14):2648-2657.	
Head and neck	Squamous Cell	IV	7	29			Forastiere AA, Leong T, Rowinsky E, et al. Phase III comparison of high-dose paclitaxel + cisplatin + granulocyte colony-stimulating factor versus low-dose paclitaxel + cisplatin in advanced head and neck cancer: Eastern Cooperative Oncology Group Study E1393. <i>J Clin Oncol.</i> 2001 Feb 15;19(4):1088-1095.	Unresectable, recurrent or metastatic
			12				Okuno SH, Mailliard JA, Suman VJ, et al. Phase II study of methotrexate, vinblastine, doxorubicin, and cisplatin in patients with squamous cell carcinoma of the upper respiratory and alimentary passages of the head and neck. <i>Cancer.</i> 2002 Apr 15;94(8):2224-	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							2231.	
			5/8	26/33			Argiris A, Li Y, Murphy BA, Langer CJ, Forastiere AA. Outcome of elderly patients with recurrent or metastatic head and neck cancer treated with cisplatin-based chemotherapy. <i>J Clin Oncol.</i> 2004 Jan 15;22(2):262-268.	
Kidney	Carcinoma	IV	13/12	55/47			Figlin RA, Thompson JA, Bukowski RM, et al. Multicenter, randomized, phase III trial of CD8(+) tumor-infiltrating lymphocytes in combination with recombinant interleukin-2 in metastatic renal cell carcinoma. <i>J Clin Oncol.</i> 1999 Aug;17(8):2521-2529.	
Liver	Hepatocellular carcinoma		10/3				Cheng AL, Yeh KH, Fine RL, et al. Biochemical modulation of doxorubicin by high-dose tamoxifen in the treatment of advanced hepatocellular carcinoma. <i>Hepatogastroenterology.</i> 1998 Nov-Dec;45(24):1955-1960.	
Lung	Nonsmall cell	IIIb/IV	10/9	45/35			Wachters FM, Van Putten JW, Kramer H, et al. First-line gemcitabine with cisplatin or epirubicin in	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							advanced non-small-cell lung cancer: A phase III trial. <i>Br J Cancer</i> . 2003 Oct 6;89(7):1192-1199.	
		IIIb/IV	11/11		21/14		Fossella F, Pereira JR, et al. Randomized, multinational, phase III study of docetaxel plus platinum combinations versus vinorelbine plus cisplatin for advanced non-small-cell lung cancer: The TAX 326 study group. <i>J Clin Oncol</i> . 2003 Aug 15;21(16):3016-3024.	
		IIIb/IV	9/7	38/28			Gridelli C, Perrone F, Gallo C, et al. Chemotherapy for elderly patients with advanced non-small-cell lung cancer: The Multicenter Italian Lung Cancer in the Elderly Study (MILES) phase III randomized trial. <i>J Natl Cancer Inst</i> . 2003 Mar 5;95(5):362-372.	
		IIIb/IV	9/8	24/20			Gebbia V, Galetta D, Caruso M, et al. Gemcitabine and cisplatin versus vinorelbine and cisplatin versus ifosfamide + gemcitabine followed by vinorelbine and cisplatin versus vinorelbine and cisplatin followed by ifosfamide and gemcitabine in stage	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							IIIB-IV non small cell lung carcinoma: A prospective randomized phase III trial of the Gruppo Oncologico Italia Meridionale. <i>Lung Cancer</i> . 2003 Feb;39(2):179-189.	
		IV	6/8/8	23/33/35	11/14/17		Sculier JP, Lafitte JJ, Lecomte J, et al. A three-arm phase III randomised trial comparing combinations of platinum derivatives, ifosfamide and/or gemcitabine in stage IV non-small-cell lung cancer. <i>Ann Oncol</i> . 2002 Jun;13(6):874-882.	
Lung	Small cell		14/10		14/6	5/2	Sundstrom S, Bremnes RM, Kaasa S, et al. Cisplatin and etoposide regimen is superior to cyclophosphamide, epirubicin, and vincristine regimen in small-cell lung cancer: Results from a randomized phase III trial with 5 years' follow-up. <i>J Clin Oncol</i> . 2002 Dec 15;20(24):4665-4672.	
			10	28/25			Schiller JH, Adak S, Cella D, DeVore RF. Topotecan versus observation after cisplatin plus etoposide in extensive-stage small-cell lung cancer: E7593—a phase III trial of the Eastern Cooperative	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							Oncology Group. <i>J Clin Oncol.</i> 2001 Apr 15;19(8):2114-2122.	
			10/9	40/29			Pujol JL, Daures JP, Riviere A, et al. Etoposide plus cisplatin with or without the combination of 4'-epidoxorubicin plus cyclophosphamide in treatment of extensive small-cell lung cancer: A French Federation of Cancer Institutes multicenter phase III randomized study. <i>J Natl Cancer Inst.</i> 2001 Feb 21;93(4):300-308.	
			12/11	51/40	16/7		Hanna NH, Sandier AB, Loehrer PJ Sr, et al. Maintenance daily oral etoposide versus no further therapy following induction chemotherapy with etoposide plus ifosfamide plus cisplatin in extensive small-cell lung cancer: A Hoosier Oncology Group randomized study. <i>Ann Oncol.</i> 2002 Jan;13(1):95-102.	
Melanoma			12/9				Eton O, Legha SS, Bedikian AY, et al. Sequential biochemotherapy versus chemotherapy for metastatic melanoma: Results from a phase III randomized trial. <i>J</i>	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							<i>Clin Oncol.</i> 2002 Apr 15;20(8):2045-2052.	
			8/6				Middleton MR, Grob JJ, Aaronson N, et al. Randomized phase III study of temozolomide versus dacarbazine in the treatment of patients with advanced metastatic malignant melanoma. <i>J Clin Oncol.</i> 2000 Jan;18(1):158-166.	
			7	25			Agarwala SS, Ferri W, Gooding W, Kirkwood JM. A phase III randomized trial of dacarbazine and carboplatin with and without tamoxifen in the treatment of patients with metastatic melanoma. <i>Cancer.</i> 1999 May 1;85(9):1979-1984.	
			9				Falkson CI, Ibrahim J, Kirkwood JM, Coates AS, Atkins MB, Blum RH. Phase III trial of dacarbazine versus dacarbazine with interferon alpha-2b versus dacarbazine with tamoxifen versus dacarbazine with interferon alpha-2b and tamoxifen in patients with metastatic malignant melanoma: An Eastern Cooperative	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							Oncology Group study. <i>J Clin Oncol.</i> 1998 May;16(5):1743-1751.	
			5/9				Agarwala SS, Glaspy J, O'Day SJ, et al. Results from a randomized phase III study comparing combined treatment with histamine dihydrochloride plus interleukin-2 versus interleukin-2 alone in patients with metastatic melanoma. <i>J Clin Oncol.</i> 2002 Jan 1;20(1):125-133.	
			10/11				Ridolfi R, Chi. Cisplatin, dacarbazine with or without subcutaneous interleukin-2, and interferon alpha-2b in advanced melanoma outpatients: Results from an Italian multicenter phase III randomized clinical trial. <i>J Clin Oncol.</i> 2002 Mar 15;20(6):1600-1607.	
Myeloma		Relapsed	31				Schenkein DP, Koc Y, Alcindor T, et al. Treatment of primary resistant or relapsed multiple myeloma with high-dose chemoradiotherapy, hematopoietic stem cell rescue, and granulocyte-macrophage colony-	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							stimulating factor. <i>Biol Blood Marrow Transplant.</i> 2000;6(4A):448-455.	
Ovarian	Adeno-carcinoma		10				Bodurka DC, Levenback C, Wolf JK, et al. Phase II trial of irinotecan in patients with metastatic epithelial ovarian cancer or peritoneal cancer. <i>J Clin Oncol.</i> 2003 Jan 15;21(2):291-297.	
			15				Thigpen JT, Blessing JA, Olt G, Lentz SS, Bell J. Cisplatin as second-line therapy in ovarian carcinoma treated initially with single-agent paclitaxel: A Gynecologic Oncology Group Study. <i>Gynecol Oncol.</i> 2003 Sep;90(3):581-586.	Progressive, persistent after first-line treatment
			36/26				Piccart MJ, Bertelsen K, James K, Cassidy J, Mangio. Randomized intergroup trial of cisplatin-paclitaxel versus cisplatin-cyclophosphamide in women with advanced epithelial ovarian cancer: Three-year results. <i>J Natl Cancer Inst.</i> 2000 May 3;92(9):699-708.	
			27/18				Gordon AN, Fleagle JT, Guthrie D, Parkin DE, Gore ME, Lacave AJ. Recurrent epithelial	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							ovarian carcinoma: A randomized phase III study of pegylated liposomal doxorubicin versus topotecan. <i>J Clin Oncol.</i> 2001 Jul 15;19(4):3312-3322.	
			13/12				Omura GA, Brady MJ, Look KY Ave. Phase III trial of paclitaxel at two dose levels, the higher dose accompanied by filgrastim at two dose levels in platinum-pretreated epithelial ovarian cancer: An intergroup study. <i>J Clin Oncol.</i> 2003 Aug 1;21(15):2843-2848.	
		III/IV	24				Belpomme D, Krakowski I, Beauduin M, et al. Gemcitabine combined with cisplatin as first-line treatment in patients with epithelial ovarian cancer: A phase II study. <i>Gynecol Oncol.</i> 2003 Oct;91(1):902-910.	
Pancreas	Adeno-carcinoma	IV	5/6				Colucci G, Giuliani F, Gebbia V, et al. Gemcitabine alone or with cisplatin for the treatment of patients with locally advanced and/or metastatic pancreatic carcinoma: A prospective,	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							randomized phase III study of the Gruppo Oncologia dell'Italia Meridionale. <i>Cancer</i> . 2002 Feb 15;94(4):902-910.	
Prostate (hormone refractory)	Adeno-carcinoma	IV	12/14				Levine EG, Halabi S, Roberts JD, et al. Higher doses of mitoxantrone among men with hormone-refractory prostate carcinoma: A Cancer and Leukemia Group B study. <i>Cancer</i> . 2002 Feb 1;94(3):665-672.	
		IV	10/9				Small EJ, Meyer M, Marshall ME, et al. Suramin therapy for patients with symptomatic hormone-refractory prostate cancer: Results of a randomized phase III trial comparing suramin plus hydrocortisone to placebo plus hydrocortisone. <i>J Clin Oncol</i> . 2000 Apr;18(7):1440-1450.	
Sarcoma	Soft tissue	IV	14/14	53/57	24/26		LeCesne A, Judson I, Crowther D, et al. Randomized phase III study comparing conventional-dose doxorubicin plus ifosfamide versus high-dose doxorubicin plus ifosfamide plus recombinant human granulocyte-macrophage colony-stimulating factor in	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							advanced soft tissue sarcomas: A trial of the European Organization for Research and Treatment of Cancer/Soft Tissue and Bone Sarcoma Group. <i>J Clin Oncol.</i> 2000 Jul;18(14):2676-2684.	
	Bone	IV	12/13				Antman K, Crowley J, Balcerzak SP, et al. An intergroup phase III randomized study of doxorubicin and dacarbazine with or without ifosfamide and mesna in advanced soft tissue and bone sarcomas. <i>J Clin Oncol.</i> 1993 Jul;11(7):1276-1285.	
Unknown Primary	Carcinoma	IV	11				Guardiola E, Pivot X, Tchicknavorian X, et al. Combination of cisplatin-doxorubicin-cyclophosphamide in adenocarcinoma of unknown primary site: A phase II trial. <i>Am J Clin Oncol.</i> 2001 Aug;24(4):372-375.	
		IV	8				Voog E, Merrouche Y, Trillet-Lenoir V, et al. Multicentric phase II study of cisplatin and etoposide in patients with metastatic carcinoma of unknown primary. <i>Am J Clin Oncol.</i> 2000	

Cancer	Histology	Stage	Median Survival* (months)	1-Year Survival* (months)	2-Year Survival* (months)	5-Year Survival* (months)	Reference	Notes
Note: Numbers quoted are survival times in months from time of study enrollment of the 1, 2, or 3 arms of the Phase III trial.								
							Dec;23(6):614-616.	
		IV	13				Hainsworth JD, Erland JB, Kalman LA, Schreeder MT, Greco FA. Carcinoma of unknown primary site: Treatment with 1-hour paclitaxel, carboplatin, and extended-schedule etoposide. <i>J Clin Oncol.</i> 1997 Jun;15(6):2385.	Single institution

References

Module 8: Clarifying Diagnosis and Prognosis

- 1 Field MJ, Cassel CK, eds. Approaching Death: Improving Care at the End-of-Life. Washington, DC: National Academy Press; 1997:59-64. ISBN: 0309063728; full text.
- 2 Hagerty RG, Butow PN, Ellis PM, et al. Communicating with realism and hope: Incurable cancer patients' views on the disclosure of prognosis. J Clin Oncol. 2005;23:1278-1288. PMID: 15718326; full text.

In a survey of terminally ill patients, 126 (58% response rate) reported the following: 98% said they wanted their oncologists to be realistic, provide an opportunity to ask questions, and acknowledge them as individuals when discussing prognosis. Physician behaviors associated with hope were: providing up-to-date treatment (90%), appearing knowledgeable about the patient's cancer (87%), and assuring that pain would be controlled (87%). Behaviors not instilling hope were appearing nervous or uncomfortable (91%), providing the prognosis to the family first (87%), and using euphemisms (82%).

- 3 Sekimoto M, Asai A, Ohnishi M, et al. Patients' preferences for involvement in treatment decision making in Japan. BMC Fam Pract. 2004;5(1):1. PMID: 15053839.
- 4 Jadalla A, Sharaya H. A Jordanian view about cancer knowledge and attitudes. Cancer Nurs. 1998 Aug;21(4):269-273.

An assessment of Jordanian knowledge and attitudes about cancer is provided; 81.5% of the participants wanted to know their diagnosis if they had cancer.

- 5 Christakis N, Lamont E. Extent and determinants of error in doctors' prognoses. *BMJ*. 2000;320:469-473; full text.

To describe doctors' prognostic accuracy in terminally ill patients and evaluate the determinants of that accuracy, 343 doctors provided survival estimates for 468 terminally ill patients at the time of hospice referral. Doctors overestimated survival by a factor of 5.3. Few patient or physician characteristics were associated with prognostic accuracy. Doctors in the upper quartile of practice experience were the most accurate. As duration of doctor-patient relationship increased and time since last contact decreased, prognostic accuracy decreased.

- 6 Vignano A, Doran M, Bruera E, Suarez-Alzamor ME. The relative accuracy of the clinical estimation of the duration of life for patients with end-of-life cancer. *Cancer*. 1999;86:170-176; full text.

The authors prospectively evaluated the accuracy of clinical estimation of survival (CES) in an inception and population-based cohort of 233 cancer patients who were seen at the onset of their terminal phase. They systematically review the literature on CES in advanced or end-stage cancer patients. Treating physicians overestimate the duration of life of terminally ill cancer patients, particularly those patients who die early in the terminal phase and who may potentially benefit from earlier participation in palliative care programs.

- 7 Glare P, Virik K, Jones M, et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. *BMJ*. 2003;327:195-200; full text.

Cochrane Library, Medline (1996-2000), Embase, Current Contents, and Cancerlit databases as well as hand searching were utilized to systematically review the accuracy of physicians' clinical predictions of survival in terminally ill cancer patients. The authors conclude that although clinicians consistently overestimate survival, their predictions are highly correlated with actual survival.

- 8 Justice AC, Covinsky KE, Berlin JA. Assessing the generalizability of prognostic information. *Ann Intern Med*. 1999;130:515; full text.

This paper describes an approach for evaluating prognostic systems based on the accuracy (calibration and discrimination) and generalizability (reproducibility and transportability) of the system's predictions.

- 9 Oxenham D, Cornbleet MA. Accuracy of prediction of survival by different professional groups in a hospice. *Palliat Med.* 1998;12:117-182.

This article examines the accuracy of prediction of prognosis by different professional groups in hospice. Importance of length of patient survival; necessity for health workers to make accurate predictions for probable short survival; and analysis of the predictions of patients are described.

- 10 Johnstone PAS, Norton MS, Riffenburgh RH. Survival of patients with untreated breast cancer. *J Surg Oncol.* 2000;73:273-277; full text.

This article analyzes historical survival data of >1,000 patients with untreated breast cancer. Five- and 10-year survival rates were about 18% and 4%, respectively.

- 11 Kowalski LP, Carvalho AL. Natural history of untreated head and neck cancer. *Eur J Cancer.* 2000;36:1032-1037; full text.

This paper describes the characteristics and natural history of the largest reported group of patients with untreated head and neck cancer. The overall survival ranged from 1 day to 53.8 months (median 3.82 months). Performance status was the most significant predictor of survival. Approximately 50% of untreated head and neck cancer patients die within 4 months of their diagnosis.

- 12 Yates JW, Chalmer B, McKegney P. Evaluation of patients with advanced cancer using the Karnofsky performance status. *Cancer.* 1980;45:2220-2224.

An investigation of the reliability and validity of the Karnofsky Performance Status Scale (KPS) is presented. The authors conclude that the KPS has considerable validity as a global indicator of the functional status of patients with cancer.

- 13 Mor V, Laliberte L, Morris JN, Wiemann M. The Karnofsky performance status scale: An examination of its reliability and validity in a research setting. *Cancer.* 1984;53:2002-2007.

The reliability and validity of the Karnofsky Performance Status Scale (KPS) as a measure of the functional status of cancer patients are reported. The KPS was found to be strongly related to two other independent measures of patient functioning. The relationship of the KPS to longevity in a population of terminal cancer patients documents its predictive validity.

- 14 Maltoni M, Pirovano M, Scarpi E, et al. Prediction of survival of patients terminally ill with cancer. *Cancer*. 1995;75:2613-2622.

This article describes a prospective multicentric study to verify those clinical factors predictive of survival in 540 patients with terminal cancer. Multiple regression analysis revealed that only clinical prediction of survival, anorexia, dyspnea, palliative steroidal treatment, Karnofsky performance status, and hospitalization were independent predictors of survival.

- 15 Evans C, McCarthy M. Prognostic uncertainty in terminal care: Can the Karnofsky index help? *Lancet*. 1985;i:1204-1206.

Members of a terminal care support team recorded upper and lower estimates of prognosis based on KPS. Just over half of the actual survivals were within the estimate limits, and the estimates tended to be overoptimistic. For the initial observations on each patient, the Karnofsky index gave a closer correlation with actual survival than the estimates.

- 16 Reuben DB, Mor V, Hiris J. Clinical symptoms and length of survival in patients with terminal cancer. *Arch Intern Med*. 1988;148:1586-1591.

Using data from the National Hospice Study, the correlation of 14 easily assessable clinical symptoms with survival in patients with terminal cancer was examined. Performance status was the most important clinical factor in estimating survival time, but five other symptoms had independent predictive value as well (shortness of breath, problems eating or anorexia, trouble swallowing, dry mouth, and weight loss).

- 17 Loprinzi CL, Laurie JA, Wieand HS, et al. Prospective evaluation of prognostic variables from patient-completed questionnaires. *J Clin Oncol*. 1994;12:601-607.

A detailed questionnaire was administered to 1,115 patients with advanced colorectal or lung cancer. Data generated by the patient-completed questionnaire provided important prognostic information independent from that obtained by other physician-determined prognostic factors.

- 18 Vigano A, Dorgan M, Buckingham J, et al. Survival prediction in terminal cancer patients: A systemic review of the medical literature. *Palliat Med*. 2000;14:363-374; full text.

This paper evaluates the published medical literature concerned with the survival of patients with terminal cancer and identifies potential prognostic factors. On the basis of 24 studies, performance status, cognitive failure, weight loss, dysphagia, anorexia, and dyspnoea appear to be independent survival predictors. Clinical estimation of survival by the treating physician appeared to be independently associated with survival but the magnitude of the association was small.

- 19 Zubrod CG, Sheiderman MA, Frei E. Appraisal of methods for the study of chemotherapy in man: Comparative therapeutic trial of nitrogen mustard and triethylene thiophosphoramide. *J Chron Dis*. 1960;11:7-33.
- 20 Miller RJ. Predicting survival in the advanced cancer patient. *Henry Ford Hosp Med*. 1991;39:81-84. PMID: 1890012.

This report presents available data for predicting survival for patients with advanced common cancers. The impact of performance status, sites, and number of metastasis and response are considered.

- 21 Bruera E, Miller MJ, Kuehn N, et al. Estimate of survival of patients admitted to a palliative care unit: A prospective study. *J Pain Symptom Manage*. 1992;7:82-86.

This was a prospective open study of 61 consecutive patients with advanced cancer admitted to a palliative care unit who underwent survival estimation by two independent physicians after a complete medical exam. An independent research nurse also assessed each patient. The assessment included activity, pain, nausea, depression, anxiety, anorexia, dry mouth, dyspnea, dysphagia, weight loss, and cognitive status. Logistic regression showed a significant correlation between survival and dysphagia, cognitive failure, and weight loss. These three simple determinations can predict survival more or less than 4 weeks as well as the assessments of two skilled physicians.

- 22 Llobera J, Esteva M, Rifa J, et al. Terminal cancer: Duration and prediction of survival time. *Eur J Cancer*. 2000;36:2036; full text.

The objective of this study was to determine the duration of the terminal period, the prognostic ability of health care professionals to predict this terminal period, and the factors that may improve prognostic accuracy. In the final model, clinical prognosis ($P=0.0094$), asthenia ($P=0.0257$), and the Hebrew Rehabilitation Centre for Aged Quality of Life (HRCA-QL) Index ($P=0.0002$) were shown to be independent predictors of survival.

- 23 Maltoni M, Nanni O, Pirovano M, et al. Successful validation of the palliative prognostic score in terminally ill cancer patients. *J Pain Symptom Manage*. 1999;17:240-247; full text.

This work validates a previously constructed prognostic score for terminally ill cancer patients—the Palliative Prognostic Score (PaP Score).

- 24 Pirovano M, Maltoni M, Nanni O, et al. A new palliative prognostic score: A first step for the staging of terminally ill cancer patients. *J Pain Symptom Manage*. 1999;17:231-239.

This study describes the construction of a simple prognostic score, the Palliative Prognostic Score, which includes the following variables: Clinical Prediction of Survival (CPS), Karnofsky Performance Status (KPS), anorexia, dyspnea, total white blood count (WBC), and lymphocyte percentage.

- 25 Ralston SH, Gallacher SJ, Patel U, et al. Cancer-associated hypercalcemia: Morbidity and mortality. Clinical experience in 126 treatment patients. *Ann Intern Med*. 1990;112:499-504.

This retrospective study reviews the effects of antihypercalcemic treatment on morbidity and mortality in cancer-associated hypercalcemia.

- 26 Gaspar L, Scott C, Rotman M, et al. Recursive partitioning analysis (RPA) of prognostic factors in three Radiation Therapy Oncology Group (RTOG) brain metastases trials. *Int J Radiat Oncol Biol Phys*. 1997;37:745-751; full text.

This paper presents an analysis of tumor/patient characteristics and treatment variables in previous Radiation Therapy Oncology Group (RTOG) brain metastases studies, including 1,200 patients to evaluate the benefit of new interventions. Three patient classes with significantly different prognoses were identified: Class 1: patients with KPS ≥ 70 , <65 years of age with controlled primary and no extracranial metastases; Class 3: KPS <70 ; Class 2: all others.

- 27 Agboola O, Beniot B, Cross P, et al. Prognostic factors derived from recurrence partition analysis (RPA) of Radiation Therapy Oncology Group (RTOG) brain metastases trials applied to surgically resected and irradiated brain metastatic cases. *Int J Radiat Oncol Biol Phys.* 1998;42:155-159.

This retrospective review of 125 patients who underwent surgical resection and irradiation of tumors metastatic to brain was undertaken to identify prognostic factors for survival and determine whether the prognostic factors used in the recursive partition analysis (RPA) of brain metastases cases from Radiation Therapy Oncology Group (RTOG) studies are applicable to surgically resected and irradiated patients. The three classes of patients defined from RPA had median survivals of 14.8, 9.9, and 6.0 months, respectively ($p=0.0002$). Age of <65 years, KPS of $>$ or $= 70$, controlled primary disease, absence of extracranial metastases, and complete surgical resection of the brain lesion(s) were found to be independent prognostic factors for survival; the total dose of radiation was not.

- 28 Chernow B, Sahn SA. Carcinomatous involvement of the pleura. *Am J Med.* 1977;63:695-702. PMID: 930945

To better define the prevalence, presentation, primary sites, and survival of patients with carcinomatous involvement of the pleura, 96 cases of carcinoma of the pleura diagnosed by cytopathology or closed pleural biopsy were reviewed.

- 29 Burrows CM, Mathews WC, Colt HG. Predicting survival in patients with recurrent symptomatic malignant pleural effusions: An assessment of the prognostic values of physiologic, morphologic, and quality of life measures of extent of disease. *Chest.* 2000;117:73-78; full text.

To determine the prognostic value of pleural fluid pH, pleural fluid glucose, extent of pleural carcinomatosis (EPC) score, and Karnofsky Performance Scale (KPS) score in patients with recurrent symptomatic malignant pleural effusions, 85 consecutive patients with recurrent symptomatic malignant pleural effusions who were referred to the interventional pulmonary service for thoroscopic pleurodesis were evaluated. The KPS score was the only statistically significant predictor variable.

- 30 Werner-Wasik M, Scott C, Cox JD, et al. Recursive partitioning analysis of 1999 Radiation Therapy Oncology Group (RTOG) patients with locally-advanced non-small cell lung cancer (LA-NSCLC): Identification of five groups with different survival. *Int J Radiat Oncol Biol Phys*. 2000;48:1475-1482; full text.

This analysis of patients with locally-advanced nonsmall-cell lung cancer (LA-NSCLC) was undertaken to identify characteristics predictive of survival in a large cooperative group patient population, and to define subgroups of the population with differing outcomes. The authors concluded that cisplatinum-based CT improves survival over RT alone. The presence of a malignant pleural effusion is a major negative prognostic factor for survival.

- 31 Buckman R. *How to Break Bad News: A Guide for Health Care Professionals*. Baltimore, MD: The Johns Hopkins University Press; 1992:65-97.
- 32 Garg A, Buckman R, Kason Y. Teaching medical students how to break bad news. *CMAJ*. 1997 Apr 15;156(8):1159-64. PMID: 9141988; full text.
- 33 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 described.

- 34 Quill TE, Arnold RM, Platt F. "I wish things were different": Expressing wishes in response to loss, futility, and unrealistic hopes. *Ann Intern Med*. 2001;135:551-555; full text.
- 35 Clever SL, Tulsky JA. Dreaded conversations: Moving beyond discomfort in patient-physician communication. *J Gen Intern Med*. 2002;17:884-885.

The authors suggest ways to solve the problem of inconvenience faced by physicians while communicating with patients. Situations arising from the inconvenience; recognition of patient's feelings by physicians; response to colleagues in inconvenient situations; and creation of systems for health care at the institutional level are discussed.

- 36 Roter DL, Larson S, Fischer GS, Arnold RM, Tulsky JA. Experts practice what they preach: A descriptive study of best and normative practices in end-of-life decisions. *Arch Intern Med.* 2000;160:3477-3485; full text.

The article describes a nonexperimental, descriptive study of audiotaped discussions in outpatient primary care practices in the United States to explore best practices by describing what physicians who are considered expert in the area of end of-life bioethics or medical communication do when discussing advance directives with their patients. Expert physicians gave less information about treatment procedures and biomedical issues and asked fewer related questions but tended toward more psychosocial and lifestyle discussion and questions. Experts engaged in more partnership building with their patients.

Self-Assessment

Module 8: Clarifying Diagnosis and Prognosis

1. Mr. Gonzales is a 47-year-old man with colon cancer metastatic to liver. The most powerful predictor of life expectancy in this man is:
 - ☐ a). performance status
 - ☐ b). stage
 - ☐ c). grade
 - ☐ d). CEA level

2. For Mr. Gonzales, the severity and number of symptoms would have the following influence on his prognosis:
 - ☐ a). improve it
 - ☐ b). leave it unchanged
 - ☐ c). worsen it

3. Of the following common cancers treated with standard therapy, which is associated with a median survival of 9-14 months?
 - ☐ a). metastatic breast cancer
 - ☐ b). advanced liver cancer
 - ☐ c). advanced pancreas cancer
 - ☐ d). extensive small-cell lung cancer

4. As a general rule, when predicting prognosis for an individual patient, oncologists are usually:

- ☐ a). over optimistic
 - ☐ b). accurate
 - ☐ c). over pessimistic
-

Self-Assessment Answers

Question 1. The correct answer is: a)

Performance status is a measure to quantify the functional status of cancer patients, and with the Karnofsky performance scale (KPS), to measure medical care requirements. KPS, a reliable, valid, simple, and reproducible measure of patient function, is an independent predictor of survival. The predictability of KPS for survival is, however, valid only for patients with scores less than 50.

Question 2. The correct answer is: c)

Integrating the impact of various physical symptoms with performance status improves its predictive capability. A systematic review of prognostic factors in advanced cancer from 24 studies examined more than 100 variables and identified cognitive factors, weight loss, dysphagia, xerostomia, anorexia, and dyspnea as independent survival factors for patients with advanced cancer.

Question 3. The correct answer is: d)

The median survival for extensive small-cell lung cancer is 9-14 months; for metastatic breast cancer, it is 15-22 months; for advanced liver cancer, it is 3-10 months; for advanced pancreas cancer, it is 5-6 months.

Question 4. The correct answer is: a)

In 7 out of 8 studies, physicians overestimated survival in patients with advanced disease.