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The Role of Chemotherapy at the End of Life: "When Is Enough, Enough?"

Sarah Elizabeth Harrington, MD

Thomas J. Smith, MD

THE PATIENT'S STORY

Mr L was a 56-year-old previously healthy businessman. He presented with progressive back pain in April 2005. Vertebral biopsy showed poorly differentiated non-small cell (squamous cell) lung cancer. His vertebral metastases and multiple asymptomatic brain metastases were treated with dexamethasone and radiation therapy.

After discussing prognosis and options with his oncologist, Dr O, he received chemotherapy with weekly gemcitabine and carboplatin. He tolerated treatment well, and for 4 months during this period his cancer did not grow. When the disease progressed, he switched to erlotinib orally. This prevented further cancer growth for almost 6 months, during which time he was asymptomatic, except for a mild rash and diarrhea. For a few months, he was able to travel and lead a normal life. However, in January 2006, Mr L's cancer again progressed. His chemotherapy was switched to pemetrexed but the tumor continued to grow.

Mr L developed diplopia in February 2006, and meningeal carcinomatosis was confirmed in March 2006 when magnetic resonance imaging of the brain showed enhancement of the fifth, seventh, and eighth cranial nerves. In the few days Mr L took to discuss his care with his medical student son, he progressed from manageable double vision to needing a wheelchair and becoming incontinent. An Ommaya reservoir was placed, and Dr O started the patient on twice weekly intrathecal methotrexate. He improved slightly, then remained stable for 2 months, enough to return to work part time and to travel a bit. Soon progression of the leptomeningeal disease resulted in additional cranial neuropathies. The intrathecal therapy was changed to liposomal cytarabine. Mr L continued to want active therapy; he attempted to enter a clinical trial for an investigational central nervous system chemotherapeutic treatment but was not accepted due to his general debility.

See also Patient Page.



CME available online at www.jamaarchivescme.com and questions on p 2695.

Patients face difficult decisions about chemotherapy near the end of life. Such treatment might prolong survival or reduce symptoms but cause adverse effects, prevent the patient from engaging in meaningful life review and preparing for death, and preclude entry into hospice. Palliative care and oncology clinicians should be logical partners in caring for patients with serious cancers for which symptom control, medically appropriate goal setting, and communication are paramount, but some studies have shown limited cooperation. We illustrate how clinicians involved in palliative care and oncology can more effectively work together with the story of Mr L, a previously healthy 56-year-old man, who wanted to survive his lung cancer at all costs. He lived 14 months with 3 types of chemotherapy, received chemotherapy just 6 days before his death, and resisted entering hospice until his prognosis and options were explicitly communicated. Approaches to communication about prognosis and treatment options and questions that patients may want to ask are discussed.

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Over the month prior to hospital admission, Mr L had a rapid decline with less appetite and reduced ability to walk. After several falls, he required a wheelchair for mobility. In July 2006, he was admitted to the hospital for aspiration pneumonia and hypoxemia. At the time of admission, Mr L was a "full code" and had appointed his wife as durable power of attorney for health care decisions. The patient and family had been considering hospice, as suggested by the oncologist, and had been visited at home by a hospice intake worker. However, the patient wanted to continue fighting the disease instead of entering hospice.

Author Affiliations: Department of Internal Medicine and the Thomas Palliative Care Program of the Massey Cancer Center of Virginia Commonwealth University, Richmond.

Corresponding Author: Thomas J. Smith, MD, Virginia Commonwealth University, Division of Hematology/Oncology and Palliative Care, MCV Box 980230, Richmond, VA 23298-0230 (tsmith@hsc.vcu.edu).

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On examination, Mr L was a chronically ill–appearing man whose breathing was aided by nasal oxygen and who sat on a bedside “neuro” chair. He had a fourth cranial nerve palsy and disconjugate gaze, facial droop, hoarse voice, absent gag reflex, and coarse breath sounds. Chest x-ray showed multiple pulmonary nodules and a new patchy left lower-lobe infiltrate.

The medical house staff called a palliative care specialist, Dr A, who noted that the patient was receiving a dose of intrathecal liposomal cytarabine during his initial visit. Dr A discussed the patient with Dr O, who now estimated that the patient had “only a month to live.” Dr A estimated a prognosis that could be as short as 2 weeks.

The palliative care team initially conferred with the patient’s son and sister, outlined the likely prognosis, advised them to proceed with hospice enrollment, and outlined the requirement for a do-not-attempt resuscitation and do not intubate order for this hospice. After this meeting, all acknowledged that this was the end of beneficial palliative chemotherapy, which his oncologist was now no longer recommending. The family accepted these plans. Dr A then met Mr L and his wife, who agreed to these recommendations, and he met with the executor of the patient’s estate whom he urged to immediately complete a durable power of attorney for legal and financial transactions. Later, Dr A met with Mrs L and 2 sons to answer their questions (eg, likely time course, signs of impending death, eating for pleasure rather than nutrition, how to inform relatives at a distance), then talked with the hospice nurse to begin hospice enrollment. Finally, at Mrs L’s request, Dr A spoke with the patient’s mother and brother in England, who were displeased with the plan for hospice enrollment.

Mr L was transferred to his home with hospice care, where he remained alert and interactive for several days. On the sixth day at home, Mr L died peacefully with his wife and his children at his side and with his favorite music playing, some 14 months after the initial diagnosis. His mother and brother flew in from abroad but arrived only after Mr L had died.

Mrs L, Dr A, and Dr O were interviewed by a Perspectives editor in August and September 2006, 2 months after Mr L’s death.

PERSPECTIVES

DR O (THE ONCOLOGIST): *We discussed with Mr L and his wife that this [leptomeningeal carcinomatosis] was a very ominous turn of events and that without intervention, his prognosis was clearly going to be weeks to a couple of months or so. His choices were to just focus on his comfort or to try to see if we could reverse that and . . . do additional systemic therapy. Without hesitation, Mr L did not want . . . hospice care or [to] just focus on palliative care. He absolutely wanted to try. . . .*

MRS L: *I think our doctor in this case was amazing. . . . He obviously knew what the outcome was going to be, but you always pray for the miracle. I think the miracle we got was an-*

other year of his life. . . . you know my husband was extremely determined to remain positive, and he never was going to give in [to the fact] that this could eventually kill him. . . . It didn’t really dawn on my husband that he was going to die until he was in the hospital with pneumonia, which was 2 weeks before he passed away. . . . I think my husband lived very well at the end and he died well.

DR A (THE PALLIATIVE CARE CONSULTANT): *I was called by the primary medicine team, who were taking care of him for an aspiration pneumonia. They wanted me to talk to the patient about future options and hospice, but he was still getting chemotherapy. Before I saw the patient, I called the oncologist. He said he would talk to the patient about his prognosis and about his chemotherapy. I went by later that day and the patient was seeing a speech therapist. Instead of talking to him first, I talked to his son, who was a medical student, and his sister, who was visiting from abroad, separately. They were shocked about the prognosis that I offered . . . of days to weeks. They were still expecting more chemotherapy. Here I was, walking into the room and basically saying, “Okay, folks, it’s time for hospice.”*

Seeking Balance: The Goals and Use of Chemotherapy Near the End of Life

The appropriate role of chemotherapy near the end of life is a complex issue.¹ As chemotherapy is increasingly available, and better tolerated, its use at life’s end involves sophisticated oncological assessment, a focus on the patient’s goals of care, and a balancing of perspectives of the patient and treating oncologist. Ultimately, it may involve judgments about the use or restraint of use of costly resources despite little chance of benefit.²

In some respects, Mr L’s care proceeded appropriately from a cancer diagnosis to hospice care. But were there missed opportunities to improve Mr L’s care? How can clinicians help patients and families determine when further chemotherapy is no longer beneficial and when they have had enough? Using the case of Mr L as an example, we discuss how clinicians can help patients identify the goals of therapy, the ways that oncology and palliative care clinicians can work together, and strategies to improve communication when chemotherapy is being considered at the end of life.

From the viewpoint of oncologist Dr O, Mr L presented with stage IV lung cancer, with brain and bone metastases. His cancer initially responded to brain and spinal radiation and first-line chemotherapy but then progressed. It stabilized for several months on a second-line agent, but a third-line agent did not halt its growth. He died of leptomeningeal metastases that progressed despite 2 types of intrathecal chemotherapy. He lived 14 months, fairly typical for non-small cell lung cancer, but spent only 6 days in home hospice before death. At the time of the first visit by Dr A, the palliative care physician, Mr L was still a full code and had not made any financial transition plans, although he did have a designated power of attorney for health care, which may

be more important,³ and Dr A believed that the family and patient were unprepared for the nearness of death. Dr A bore the brunt of some family anger when recommending hospice. He responded by stating that oncologists “need to be trained to involve palliative care folks earlier.” However, the oncologist had brought up hospice, and the patient initially declined it, only accepting palliative care involvement when death was imminent. The admitting house staff and palliative care consultant had a sense that this patient with brain metastases was not always making informed choices and had lost opportunities to do other important things with his remaining time while pursuing further chemotherapies and clinical trials. They had concerns about providing care (such as the final dose of intrathecal chemotherapy) that really could not help the patient.

Identifying the Appropriate Goals of Chemotherapy

Reasons for Late-Stage Chemotherapy. Patients may find it hard to get or accept truthful information about the benefits and harms of palliative chemotherapy. In the largest study of 95 consecutive patients receiving palliative chemotherapy, prognosis was discussed by only 39% of medical oncologists.⁴ In a longitudinal study of hospitalized patients for whom death was believed imminent, families reported that the attending physician never discussed the possibility of death 62% of the time and no one on the medical team discussed the possibility of death with cancer patients in 39% of cases.⁵ In other studies, at least one-third of patients and families reported they did not believe the information given them that treatment was not curative despite receiving such information.^{6,7} Another study showed that physicians may “collude” in this hopefulness by giving such a wide range of outcomes that people choose the most favorable.⁸

It is critical to understand that people looking death in the eye have a different perspective. Studies from the United States, England, Canada, Japan, Norway, and Italy consistently show that patients with cancer generally were willing to undergo aggressive treatment with major adverse effects for very small chance of benefit, different from what their well physicians or nurses would choose.⁹ Some patients with previously treated non-small cell lung cancer would accept chemotherapy for a survival benefit as short as 1 week, while others would not, even for a benefit of 2 years (the actual expected benefit was ~3 months).¹⁰ Highly educated and motivated patients enrolled in phase 1 studies at the National Cancer Institute said that they would be willing to take an experimental drug—with a 10% mortality rate—for an unknown small chance of benefit.¹¹ **BOX 1** lists some of the difficulties in giving and receiving information about prognosis in advanced cancer.

Multiple studies document that palliative chemotherapy is increasingly given near death. More than 20% of patients receiving Medicare who had metastatic cancer started a new chemotherapy treatment regimen in the 2 weeks before

death.²⁹ In Italy, 23% of patients with incurable cancer received chemotherapy within 30 days of death.² In a US community practice, chemotherapy for patients with lung cancer was given within 30 days of death for 43% and 14 days for 20% of patients.³⁰ In 2008, a medical director of a large insurance company reported that 16% of its cancer patients receive chemotherapy within 14 days of death. Patients are unlikely to benefit from chemotherapy when they have already been failed by the standard regimens, have poor performance status, and otherwise have a poor prognosis. The largest study of matched patients who received hospice and no chemotherapy vs those who did not receive hospice care but had chemotherapy showed that survival was significantly longer for hospice patients with lung cancer and pancreatic cancer, marginally longer for colon cancer, but no different with breast or prostate cancer. The authors concluded that this was consistent with chemotherapy not prolonging and possibly shortening life for those eligible for hospice.³¹ Furthermore, chemotherapy produces adverse effects, precipitates hospitalization and emergency department visits, precludes entry into most hospices, and may require additional supportive care with erythropoietinlike drugs and colony-stimulating factors that are expensive and contribute little to the patient’s overall quality of life. For these reasons, the factors that go into patients’ decisions to undergo chemotherapy near the end of life bear examination.

Is Distinguishing Curative From Palliative Chemotherapy Important? Chemotherapy for metastatic solid tumors such as lung, breast, colon, or prostate cancer rarely if ever cures patients. The indication for such chemotherapy is to improve disease-free or overall survival, relieve symptoms, and improve quality of life. Palliative chemotherapy accounts for most of the work of everyday oncology given the rarity of curable disease. The American Society of Clinical Oncology could not decide on a minimal benefit for which chemotherapy was indicated, only that some benefit must be demonstrable.³² Consensus panels that include cancer advocates make little distinction between curative treatment and palliative treatment that could extend life,³³ since 6 months’ added survival could be as important as an increased rate of cure.

The increasing effectiveness and lessened toxicity of palliative chemotherapy is well supported by randomized trial data. First-line chemotherapy for patients with non-small cell lung cancer improves survival by 2 to 3 months, relieves symptoms, and improves quality of life compared with best supportive care.³⁴ Second-line treatment of patients with non-small cell lung cancer with docetaxel vs best supportive care is associated with significantly longer survival (7.0 vs 4.6 months, or 10 weeks, and a difference in 1-year survival, 29% vs 19%)³⁵; and improvements in pain and less deterioration in quality of life.³⁶ Even third-line treatment may improve survival or symptoms, especially with novel, relatively nontoxic oral agents such as erlotinib, which, in

Box 1. What Patients Know About Their Advanced Cancer and Its Prognosis**Patients Are Never Told or Are Not Told Well****Small Cell Lung Cancer**

Thirty-five patients reported learning more about their prognosis from other patients in the waiting room than from their health care professionals. Physicians did not always want to pronounce a "death sentence," and patients did not always want to hear it.¹²

High-Dose Chemotherapy (With Stem Cell Transplant)

Physicians prescribing high-dose chemotherapy overestimated survival, especially for patients with poor prognosis who might most need to balance toxicity with outcomes.¹³ The optimistic patients had no better survival than those who were more realistic.¹⁴

Terminally Ill With Cancer

Even if patients requested survival estimates, physicians said that they provided them only 37% of the time. Physicians reported that they would provide no estimate, conscious overestimates, or conscious underestimates 63% of the time.¹⁵

Solid Tumors

In Belgium, only 39% of oncologists reported ever reviewing prognosis with patients. Most of the interview was spent on active treatment, not alternatives.⁴

Nearly all patients could name their diagnosis, but only 23% knew their stage, which is critical to appropriate goal setting.¹⁶

Oncologists consistently overestimated prognosis by at least 30%.¹⁷ In our own study, physicians' estimate of survival could be divided by 3.5 for actual survival.¹⁸

Patients Don't Believe Information About Benefits and Risks of Treatment**Metastatic Lung Cancer**

One-third of patients thought they were receiving therapy with curative intent despite being told prognosis and goals of care.⁶

Head and Neck Cancer

Thirty-five percent of patients believed their palliative radiation was supposed to be curative.⁷

Phase 1: Overoptimistic

If told that a treatment helps 20% of people like them, patients reported a 44% chance of it helping them personally.¹⁹

Patients Change Their Mind About Communication**Metastatic Breast Cancer**

Between first and second lines of chemotherapy, 59% of 729 patients with advanced cancer changed their preference about involvement in decision making; 37% wanted a less active role, and 22% wanted a more active role.²⁰

Thirty-eight percent of women took an active role in decision making for first-line chemotherapy, and 43% for second-line chemotherapy. The reasons to take chemotherapy shifted from the possibility of controlling the tumor (50% for first chemotherapy, 38% for second) to providing hope (19% for first-line chemotherapy, 43% for second line); the proportion expecting to be cured fell from 10% to 0% with second-line chemotherapy.²¹

Patients Have Different Perspectives Than Their Well Health Care Professionals**Solid Tumors****England**

Patients would have toxic treatment for a 1% chance of cure, 10% chance of symptom relief, or chance to prolong life 12 months. Their physicians and nurses would require a 50% chance of cure, 75% chance of symptom relief, and 24 to 60 months added survival.²²

Patients accepted a lower chance of benefit from chemotherapy than their physicians or nurses, even when treatment involved great toxicity.²³

Canada

Fifty-seven percent of patients would choose chemotherapy for a survival benefit of 10% at 1 year. Some chose more toxic treatments even if they offered no survival advantage while others declined chemotherapy regardless of perceived advantage of treatment. It was difficult to predict what individual patients would choose.²⁴

Lung Cancer**Norway**

Patients younger than 40 years would accept the toxic treatment with only a small benefit: chance of cure (median, 7%), life prolongation (3 months), and symptom relief (8%).²⁵

Italy

Patients would be willing to undergo chemotherapy for small benefit, even if the physician presents the results pessimistically.²⁶

United States

Patients who had undergone chemotherapy for lung cancer would take it again if it added survival of 4.5 months with mild toxicity or 9 months with severe toxicity. When given the choice between supportive care and chemotherapy, 22% chose chemotherapy for a survival benefit of 3 months, which was the actual expected benefit. Sixty-eight percent would choose chemotherapy if it substantially reduced symptoms without prolonging life. Only a quarter remembered hearing any options about treatment that did not involve chemotherapy, such as palliative care.⁴

Japan

If their lives would be prolonged by 3 months, 19% would choose to receive intensive treatment, and 21% would choose less intensive treatment. With a 70% chance of symptom relief, 73% of patients were willing to choose intensive chemotherapy.²⁷

Palliative Chemotherapy, Belgium

Patients' choice for chemotherapy or palliative care was most strongly predicted by their preconsultation treatment preference.²⁸

Phase 1 Participants

Of 163 patients participating in a phase 1 study, for which by definition, the goal is to assess toxicity, only 7% considered no treatment at all; 81% were aware of hospice, but only 6% had seriously considered hospice for themselves.¹¹ "More than 90% of patients said they would still participate in the study even if the experimental drug caused serious adverse effects, including a 10% chance of dying."

1 study, improved survival compared with best supportive care from 4.7 to 6.7 months with improved results for pain, dyspnea, and physical functioning.³⁷ Palliative chemotherapy has also increased survival and quality of life in metastatic colorectal³⁸ and prostate cancer³⁹ (TABLE 1). Mr L benefited from receiving 3 separate types of palliative non-small cell lung cancer chemotherapy: gemcitabine and carboplatin, oral erlotinib, and pemetrexed. Although he never had dramatic responses to treatment, his disease stabilized for months while he received the first 2 treatments, and his central nervous system disease was stable for weeks because of intrathecal methotrexate.

How Can Clinicians Help Patients With Decision Making? Mr L's palliative care specialist noted that because patients are vulnerable to fastening on slim hopes, oncologists must improve their skills in helping patients think clearly about the appropriateness of chemotherapy.^{44,45} To help their patients make wise decisions, oncologists can start with a prompt list of questions, proven to enhance communication⁴⁶⁻⁴⁸ and similar to one in use in several oncology practices,^{49,50} including ours (BOX 2). This can be provided to the patient in the waiting room for discussion with his or her physician.

Another important communication is a straightforward discussion of the quality and quantity of life with or without chemotherapy. In most cases, there will not be a randomized trial of best supportive care vs best supportive care plus chemotherapy, but at least the important discussion points can be raised. There must be some definable benefit before chemotherapy can be recommended. TABLE 2 provides some examples of helpful communication strategies.

Studies consistently document that patients want and use such information. Of 126 terminally ill patients, 98% said they wanted their oncologists to be realistic⁵¹ and patients want oncologists to be truthful and compassionate and to continue caring for them during their illness.⁵² A comprehensive review found that randomized trials of decision aids in oncology yielded increased patient knowledge and more involvement in decision making,⁵³ and a decision aid for adjuvant therapy of breast cancer (<http://www.adjuvantonline.org>) improved medical decision making and helped low-risk patients avoid unnecessary chemotherapy.^{54,55} A preliminary study showed that directly giving patients information about prognosis and treatment to share with their oncologist is desired and helpful.⁵⁶ We use decision aids in our own practice that address prognosis with and without chemotherapy in a question-and-answer format, using simple terms (ie, "10 in 100 people" instead of "10%") and figures.

What Should the Clinician Do When the Patient Wants to Continue Chemotherapy at the Very End of Life? DR O: *I couldn't get him to stop thinking that he needed one more treatment. One more treatment was what he needed to spring him loose.*

In the difficult situation faced by Dr O and Mr L, when the oncologist thinks further chemotherapy is not indi-

cated, a number of strategies may be tried: holding family conferences to identify the decision makers in the family and getting the same information to all involved; informing people of and giving them access to the actual medical research studies and results; or writing the options down in concrete terms.⁵⁷ Much of the time, patients and families may simply need more time to adjust to a difficult situation. Sometimes, they just have a different perspective that must be valued as much as the health care professional's.

TRANSITIONING TO PALLIATIVE OR HOSPICE CARE

When Should Patients Stop Chemotherapy and Transition to Palliative or Hospice Care?

MRS L: *I think that he felt he was in control until the last 2 weeks of his life, and that was important. The kids were very involved. We had a lot of closure.*

DR O: *[Within weeks of his death,] Mr L was still in a "I've got to do something" mode, but I was telling him . . . "We've got to get hospice going so that you can relax and everyone [in your family] can get what they need and they can move on." He was not having any of it, though.*

Table 1. Palliative Chemotherapy for Metastatic Disease for 4 Common Solid Tumors

Cancer Treatment	Comment
Non-small cell lung cancer First-line chemotherapy with modern regimens	Improves survival by ≥ 3 mo with acceptable toxicity, better symptom control, manageable toxicity ³⁴
Second-line (docetaxol)	Improves survival by about 2 mo vs best supportive care, with better symptom control while taking treatment ^{35,36}
Second- or third-line (erlotinib)	Improves survival by about 2 mo vs placebo, with acceptable toxicity ³⁷
Third- or fourth-line	Response rate only 2% and 0% when patients have previously received docetaxol and platinum ⁴⁰
Breast cancer First-, second-, and third-line chemotherapy	Average survival has improved over the past decades with lessened adverse effects from chemotherapy, but there are no randomized clinical trials of treatment vs best supportive care ⁴¹
Colon cancer First-, second-, and third-line chemotherapy	Average survival from diagnosis of metastatic disease has improved from 9 to 22 mo with the new drugs available, eg, oxaliplatin, irinotecan, cetuximab, bevacizumab ³⁸
Prostate cancer First-line chemotherapy	Docetaxol every 3 wk improves survival by 2.4 mo, with no adverse effect on quality of life. ⁴² Second-line chemotherapy can palliate symptoms and decrease prostate-specific antigen level but does not improve survival ⁴³

Box 2. Helpful Questions to Consider Asking About Palliative Chemotherapy

Treatment

- What is my chance of cure?
- What is the chance that this chemotherapy will make my cancer shrink? Stay stable? Grow?
- If I cannot be cured, will I live longer with chemotherapy? How much longer?
- What are the main side effects of the chemotherapy?
- Will I feel better or worse?
- Are there other options, such as hospice or palliative care?
- How do other people make these decisions?
- Are there clinical trials available?
 - What are the benefits?
 - Am I eligible?
 - What is needed to enroll?

Prognosis

- What are the likely things that will happen to me?
- How long will I live? (Ask for a range, and the most likely scenario for the period ahead, and when death might be expected.)
- Are there other things I should be doing?
 - Will?
 - Advance directives?
 - Durable power of attorney for health care who can speak for me, if I am unable?
 - Financial or family legal issues?
 - Durable power of attorney for financial affairs?
 - Trust?
 - Family issues
 - Will you help me talk with my children?
 - Spiritual and psychological issues
 - Who is available to help me cope with this situation?
 - Legacy and life review
 - What do I want to pass on to my family to tell them about my life?
 - Other concerns?

DR A: I was going in there to talk hospice, prognosis less than 6 months, and he was still full code. He had to be made no code. He was still expecting chemotherapy, [and] at least some of the members in his family were, and he was getting chemotherapy. When I went in on Saturday morning, it was a totally changed picture. The patient and his wife were now demanding to go home on hospice.

Making the transition to palliative care or hospice is difficult for both patients and oncologists. There are usually some treatment options, even for relapsed disease. The avail-

able lung cancer treatment data suggest that each 3.3% of response rate leads to better survival of 1 week and increases survival at 1 year by 1.6%, which might be important to some patients.⁵⁸ The National Comprehensive Cancer Center Network guidelines recommend that after 2 chemotherapy regimens have failed to benefit the patient or if the patient's performance status declines to 3 or more, such that chemotherapy will not be tolerated, a switch to palliative or hospice care be made (http://www.nccn.org/professionals/physician_gls/default.asp). The American Society of Clinical Oncology and other major professional societies have long recommended hospice as the best available care for dying patients.⁵⁹

In our experience, many families and patients who choose, like Mr. L, to enroll in hospice wish they had done so sooner. The median length of stay on hospice has declined from 29 days in 1995 to 26 days in 2005, with one-third enrolling in the last week of life and 10% on the last day of life (<http://www.nphco.org>). Hospice care may help the family as well as the patient. One study showed that hospice care was associated with a 0.5% lower absolute risk of death for the Medicare-age surviving spouse.⁶⁰ Families' perception of late referral is associated with lower satisfaction with hospice care overall.⁶¹ In the most recent and largest study, among those with hospice stays of less than 30 days, 16% of families said they were referred too late.⁶² Of note, the perception of being referred too late, but not the actual length of stay, was associated with more unmet needs, lower satisfaction, and more concerns. One study found that patients would have liked palliative care consultation earlier in their course.⁶³ It is unknown whether this view of "too-late" referrals to palliative care and hospice will change with the new relatively nontoxic chemotherapy treatments.

Improving Communication About Hospice and End of Life

MRS L: *He wanted to keep fighting. There was also a lot of animosity [from the overseas family members] toward Dr A, who is the most honest and incredible person on the planet. They felt that he had talked my husband into stopping treatment, and that was not the case at all. Dr A never really had anything to do with that. It was strictly between my husband and his oncologist.*

Dr O suggested hospice enrollment to Mr L and he was even visited by a hospice intake worker, but he chose not to enroll until it was explicitly clarified that there were no further chemotherapy options. This is not unusual: Teno et al⁶² estimated that 23% to 61% of short-stay hospice patients could not have been referred earlier due to late diagnosis or patient refusal.

In our opinion, oncologists should note the availability of hospice from the beginning, as part of routine good care of the seriously ill patient. After all, in 2005 hospices enrolled more than 1.2 million patients, representing one-third of all deaths in the United States, with nearly half of

the patients having cancer. Unfortunately, families often receive little information from physicians about hospice.⁶⁴ In one study, physicians initiated the discussion about hospice about half the time, while patients or families initiated one-third of the discussions. Patients and families identified as important in deciding about hospice the frequency of visits, payment, and the practical help it provides.⁶⁵ (A list of the resources that hospices can provide to patients is found in the online resources [<http://www.getpalliativecare.org>].) Barriers include physicians' lack of knowledge of hospice philosophy, services, and patient eligibility requirements. Brickner et al⁶⁶ found that 84% of physicians surveyed were unable to identify appropriate hospice diagnoses and that only 12% were aware of the National Hospice Organization Medical Guidelines for Determining Prognosis in Selected Non-Cancer Diagnoses. In a randomized trial of nursing home residents, a structured interview on admission—in essence bypassing physician reluctance and making the hospice benefit known to families and patients—increased appropriate hospice enrollment from 1% to 20%.⁶⁷

In our opinion, patients and families should receive all of the necessary information about hospice and palliative care in order to permit the most informed decision about how to spend their last few weeks or months. We also recognize that even after the most earnest communication ef-

forts, patients and families may continue to want chemotherapy.⁴⁴ Communication about prognosis, what to expect with disease progression, and advanced directive and financial planning can all be done independently of a hospice decision and should remain a high priority for patients with advanced disease.

WHY DON'T PATIENTS AND ONCOLOGISTS DISCUSS PROGNOSIS?

DR O: *I thought that it would help everybody for Mr L to hear that he couldn't get into a clinical trial because physically he wasn't up to the standards of the trial. That, I thought, would have allowed Mr L to accept palliative care sooner than he did.*

MRS L: *I never thought "too much" was too much. You always hope that he can come out of this by some miracle. The "too much" was when he became ill in the hospital.*

When the prognosis is predictable, as with Mr L, why do most oncologists not directly address it? One paradoxical explanation is that patients do not want to discuss such terrible issues with their oncologist. Of 101 inpatients with cancer admitted without advanced directives, only 23 wished to discuss the issue with their oncologists; however, 56% of those without advanced directives (44 of 78) supported discussing it with the admitting physician and not the oncologist.⁶⁸

Table 2. Things to Do or Say (and Not to Do or Say) About Chemotherapy for Advanced Cancer

Do	Don't	Comment
Diagnosis		
Ask patients how much they want to know.	Don't assume that people will or won't want to know their diagnosis.	Although cultures vary, most patients want to know their prognosis and options. They may underestimate their odds, too, and forgo useful chemotherapy.
Define "response" and "cure."		Patients can mistake a 20% chance of response with a 20% chance of cure.
Write down a list of benefits of and adverse effects from chemotherapy.	Don't assume that patients will know their odds of being helped.	There must be some definable benefit before chemotherapy is justified.
Ask patients their goals.		Two months may be critical to some people, unimportant to others.
Begin a discussion about what to do if or when the cancer is resistant to chemotherapy.		This is a good place to say, "We hope to control the disease, but at some point it may grow so that it will end your life. We need to prepare for that, too."
Treatment		
Say, "The cancer is shrinking, but is still there."	Don't say, "The cancer is responding." If you say this, estimate that it will likely last for however many months.	Important to emphasize what is likely to happen, so that people can make plans.
Be hopeful if there is reason to hope about the cancer.		Most people can be hopeful about something, even if their cancer is growing.
Begin a discussion about do-not-attempt-resuscitation orders.		This is a good place to say, "The cancer is growing, and may end your life. There are some important issues to discuss. Tell me how much you want to know."
End of Life or Cancer Progression		
Bring up hospice when there are still some oncology options, not at the end of life.	Don't ask hospice to just manage the acute deaths at home.	Make hospice an option that is part of usual medical care for someone with cancer.
Ask for your own hospice length of stay and the number of your patients who die within 7 days of enrollment.		Make this a performance improvement goal for the practice to meet or exceed the national length of stay in hospice.
Tell people you will not abandon them if they enroll in hospice.		Some physicians make appointments for every 2 weeks even for hospice patients. If they are too sick to attend, it is a good reminder to check in by telephone or visit.

Another explanation is that such discussions are simply too difficult and painful. Even clinicians who are well trained and skilled at giving bad news can find it burdensome and emotionally difficult. Prior surveys documented “serious shortcomings in the training and current practices of oncologists” of palliative care and that only 25% of oncologists found end-of-life care highly satisfying.⁶⁹ Given the incurability of some cancers, such as with Mr L, there is a need for these conversations and consideration of hospice care. At the very least, finding out how much a patient wants to know and then providing that information should be addressed by all clinicians.⁷⁰

Shifting Goals of Care to Palliation: Why Is It So Difficult for Physicians?

Clinicians often struggle with initiating discussions about shifting treatment goals and in particular transitioning to palliative care. Patients may respond with denial, anger, or sadness. These are all normal responses to the associated loss of control, a fear of the immediate future, or an underlying fear of death. For the most part, patients and families will have their own unique timetable and method for processing this information.⁷ Clinicians should generally respond with patience, emphasizing support (non-abandonment) and assurance of aggressive symptom management⁷¹ (Table 2).

Not surprisingly, physicians may respond to their patients, particularly those with whom they share a long-term relationship, with powerful emotions of their own.⁷² These can include a personal and professional sense of failure and frustration, guilt, powerlessness against the illness, grief, a need to rescue the patient, or a desire to separate from and avoid patients to escape these feelings.⁷³ Clinicians’ feelings of medical ineffectiveness can lead to failure to identify patient-specific and family-specific values influencing decisions, which may lead to a lack of clarity about care goals. Avoidance of the discussion altogether can lead to mistrust of the health care system and medical profession, inappropriate use of life-sustaining medical technologies, increased medical complications, and long hospital stays.⁷⁴ Recognizing, accepting, and reflecting on the normalcy of such feelings allows the professional to make a conscious choice about how to proceed in the relationship with the patient. Finding a trusted colleague in whom to confide can be part of a plan to prevent isolation, improve objectivity, and avoid burnout.⁷⁵

Doesn't Honesty Take Away Hope?

No data are available that show hope can be taken from patients, as was once thought, or that patients are harmed by carefully provided information.^{76,77} As the Education Physicians End of Life Care for Oncologists (EPEC-O) curriculum⁷⁸ states, “Information carefully shared is a gift to the patient and the family who want it and minimizes the risk that patients will distrust the cancer care team.” In pedi-

atric oncology, full prognostic disclosure supported hope, even when the prognosis was poor.⁷⁹

Ways That Oncologists and Palliative Care Specialists Can Work Together

DR A: I think oncologists, in general, need to get more comfortable with palliative care. It's not an “either, or” situation, it's a “both, and.” I think physicians, in general, including people like this excellent oncologist, need to be bolder at offering more real prognoses.

Evidence, albeit far from conclusive, suggests that “concurrent” palliative or hospice care alongside routine oncology care improves health outcomes (TABLE 3). Project Safe Conduct was started to integrate hospice care into lung cancer care at the Ireland Cancer Center. Before the study, 13% of patients with advanced lung cancer were referred to hospice; afterward, 80% of such patients enrolled in hospices and the average length of stay in hospice increased from 10 days to 44 days.⁸¹ The one randomized trial of concurrent hospice care plus usual oncology care vs usual oncology care alone has been published only in abstract form.⁸⁰ The group with concurrent care lived slightly longer (not statistically significant), had quality of life preserved longer, used less chemotherapy, and transitioned to hospice enrollment sooner. The clinical care differences were modestly in favor of the concurrent-care approach, but the hospice cost was substantial and much higher than the cost of hospitalizations avoided (oral communication, John Finn, MD, Ascension Health Systems, Detroit, Michigan, October 2004). Meyers and colleagues⁸⁴ enrolled patients in a phase 1 and 2 cancer treatment study and into a simultaneous care program that emphasized symptom management and transition to hospice. The uptake of the program was excellent. Patients received as many cycles of chemotherapy as without simultaneous care and were referred to hospice more frequently and earlier. A study at the Dana Farber Cancer Institute showed that cancer patients will use a free palliative care service alongside their usual oncology care, but health outcomes are not yet available.¹ The one large randomized controlled trial of usual care plus palliative care consultation, in which 27% to 34% of patients had cancer, showed no difference in symptoms or survival but did show a \$4855-per-patient cost savings.⁸⁵ Proof of symptom control or survival improvement at a cost society can afford will require rigorous testing, preferably in randomized clinical trials.

One of the largest barriers to hospice in the United States is the way it is defined in the Medicare Hospice Benefit. Patients must have a life expectancy of 6 months or less and must forego curative treatment. Funding for chemotherapy and radiation is limited; thus, being enrolled in hospice can significantly limit very useful palliative treatment. Several hospice programs have begun to respond to these eligibility barriers and are providing a broader range of services.⁴⁵ Some have changed to palliative care programs under home health care services, integrating palliative che-

motherapy and radiation and related treatments (paid for by the patient's insurance or Medicare drug benefit) with elements of traditional hospice care. Passik and colleagues⁸⁶ at Hospice of the Bluegrass showed that patients who transition from acute care to palliative care then to the hospice benefit, compared with those who transition directly from acute care to the hospice benefit, may prove to be both financial and care burdens to the hospice. As noted above, a randomized trial showed palliative care consultation alongside usual medical care saved the insurer \$4855 per patient with no decrement in survival or symptoms.⁸⁵ Several larger insurance-sponsored trials are ongoing.

INTEGRATING OTHER CANCER CARE ISSUES INTO DECISION MAKING AT THE END OF LIFE

Experimental Chemotherapy

DR O: *We were continuing the current course of treatment because he wanted it, but it was quite appropriate to initiate palliative care. Then Mr L and his wife embarked on this idea that he needed to get into a clinical trial. . . . Dr A was able to help the family put aside their differences in order to allow Mr L to enter into palliative care and go home and stay home.*

Patients on clinical trials have as good an understanding of the risks and benefits as we can give them—after all, they

have read and signed informed consent documents—but this understanding is far from perfect. Despite written information, many will still overestimate their own particular chance of success.¹⁹ Mrs L expressed, as do many patients and families, that they hoped Mr L would survive long enough to receive a new treatment, or even a cure. And as we noted above, informed phase 1 patients are willing to undergo new treatments with a 10% mortality risk for an unknown but low chance of benefit.

Reimbursement and Economic Issues: Why Oncology is Different

Most palliative care is relatively inexpensive. However, palliative chemotherapy regimens have a huge price tag, at a cost of up to \$100 000 a year per patient, and even insured patients can be burdened by a 20% co-payment requirement. The cost of palliative chemotherapy for colorectal cancer could easily be \$50 000 a year, not counting supportive care drugs or imaging.⁸⁷ Patients with cancer account for about 40% of all Medicare drug costs, totaling an estimated \$5.3 billion in 2006, with \$1.5 billion for erythropoietin-like drugs alone.⁸⁸ Some drugs (oxaliplatin for metastatic colon cancer⁸⁹ and docetaxol for metastatic prostate cancer⁴²) have acceptable cost-effectiveness ratios in which

Table 3. Studies of Concurrent Palliative Care With Oncology Care

Source	Results	Comments
Finn et al, ⁸⁰ 2002	Randomized oncology patients to standard care with or without hospice or palliative care consultation. Intervention group had longer preserved quality of life, fewer symptoms, and (nonsignificantly) better survival. No difference in symptom control but quality of life declined less in the intervention group. Intervention cost >\$1.5 million, or >\$17 800 per patient, but was associated with cost savings >\$2500 per person by avoided hospitalizations. Final results are in process. (John Finn, MD, personal communication, January 2004).	Only shows some improvement in symptoms but no difference in survival at increased cost due to the high cost of interdisciplinary hospice services when used for palliative care (unpublished).
Pitorak et al, ⁸¹ 2003	Project Safe Conduct gave modified hospice consultations for all patients with lung cancer starting treatment. After the program, 75% died in hospice care vs 13% before, with a median length of stay in hospice of 36 d after vs 10 d before. Program expanded to include advanced cancers, specifically lung, gastrointestinal, and head and neck cancers.	Project Safe Conduct has been sustained, is highly successful, and well received with demand for more teams at the Ireland Cancer Center. (Elizabeth Pitorak, RN, PhD, written communication, February 2, 2004).
Bakitas et al, ⁸² 2002	Project ENABLE, a joint hospice–cancer center program. The program was well received at 2 of 3 sites, and the palliative care team experts were often called to help deliver bad news. No outcome data are available.	Demonstration project that showed the approach was feasible.
Elsayem et al, ⁸³ 2004	For patients at a comprehensive cancer center referred to palliative care, severe distress on admission and severe symptoms of distress significantly improved after palliative care consultation. Mean daily charges in the patient care information system were 38% lower than the mean daily charges for the rest of the hospital.	First published demonstration of better symptom control and lower costs for patients at a tertiary comprehensive cancer center; not really concurrent care.
Meyers et al, ⁸⁴ 2004	44 Patients in phase 3 trials “simultaneously enrolled into a defined home care program focused on supportive care needs of the patient and family, as well as assessment of the toxicities of investigational therapy” vs 20 usual-care patients. Quality of life improved but not significantly; 35 of 44 receiving supported care were referred to hospice vs 8 of 15 receiving usual care ($P = .03$) with longer mean but not median stay. Use of 2.5 cycles of chemotherapy did not differ and was well accepted.	Supportive care may enhance coordination of care and facilitate patients' explicit transition from curative intent to palliative intent; a comparative randomized trial evaluating supportive care has yet to be completed.
Temel et al, ¹ 2007	51 of 53 Patients with lung cancer enrolled in a study during which they were seen concurrently by oncology and a palliative care team, which visited most several times and all who survived 6 mo, continued team visits in addition to oncologist visits. Only 2 (of 53 patients) refused to meet with the team. No outcome data.	Concurrent care is feasible, but whether it improves health outcomes (effectiveness) and cost-effectiveness vs usual care should be evaluated in a randomized trial.

treated patients gain several weeks or months of life, at a cost less than \$100 000 per additional year of life saved, but for Medicare, these are new costs to pay. For Mr L, his last dose of intrathecal cytarabine given 6 days before his death would cost \$3400 at our institution.

The manner in which oncologists are reimbursed may play a role in chemotherapy use. Over the past 10 years, oncologists have become some of the highest paid medical specialists.⁹⁰ Some of oncologists' practice income comes from administering and selling chemotherapeutic agents and supportive care drugs (eg, bisphosphonates, erythropoietin-like drugs and colony stimulating factors). As is the case in other medical specialties, oncologists are reimbursed more for their specialized treatment of chemotherapy than for lengthy discussions about prognosis and palliative care options.⁹¹ This potential for conflict of interest has been the subject of controversy. The only published study was conducted before Medicare chemotherapy reimbursement was reduced in 2003 and found that reimbursement did not affect the decision to give palliative chemotherapy but that oncologists tended to choose chemotherapy that gave the highest profit to the practice.⁹² Although hospice care and inpatient palliative care⁹³ may save money during the last month of life, total disease costs are unchanged or increased,⁹⁴ so hospices cannot save enough money to allow more chemotherapy. It is critical to improve reimbursement incentives. For example, in 1 study, more than 25% of oncologists reported insufficient reimbursement for time spent in discussion with patients and families as "the most troublesome" reimbursement barrier to providing better end-of-life-care.⁶⁹

If societal resources become limited, and maximizing health benefit becomes more difficult, there are only a few ways to reduce the cost of oncology care:

- Reduce the services provided (eg, "stopping rules,"⁹⁵ in which no more than 3 lines of chemotherapy would be given for refractory metastatic breast cancer or no erythropoietinlike drug treatment for anemia would be given unless the hemoglobin is <10 g/dL):
 - Reduce requested services by increasing patient co-payments.
 - Reduce the amount that Medicare or insurers pay for chemotherapy and supportive care drugs, health care professional services, or hospitalizations.
 - Prevent or delay new drugs from entering the market, or delay reimbursement for them.
 - Reduce the payment to oncologists for administering chemotherapy and supportive care drugs, perhaps influencing the type of chemotherapy administered.

Ultimately, unless resources are unlimited, patients and families (or society at large) may be asked to balance individual patient needs against those of society.⁹⁶

CONCLUSION

Given understandable patient, family, clinician, and societal goals and concerns, how can all individuals be edu-

cated and informed as to the appropriate use of chemotherapy and the value of palliative care and hospice? First, as suggested by hospice experts and oncologists,¹² someone other than the oncologist might give information about the hospice option and provide specific prognosis and palliative treatment information. Second, palliative care specialists should be aware of the difficult decision making that cancer patients face near death, and how different their perspective is about benefit and toxicity.⁹ Decision aids may be used. Finally, regarding palliative care options, completion of studies integrating hospice and palliative care into usual oncology care will permit evidence-based decision making.

The conundrum for today's oncologist is that moving on to third- or fourth-line chemotherapy may be easier than discussing hospice care, the patient and family may be less upset, and they may prefer to not discuss the issue with the oncologist.⁶⁸ Adverse effects of chemotherapy may be minimal, discussions take more time, and chemotherapy intervention is better compensated than are discussions. However, without a clear goals-of-care discussion, patients like Mr L and their families may be unprepared for what the final few months, weeks, or even days may bring. Through honest and respectful communication about the last stages of cancer, physicians can give patients a genuine choice about how to spend their last phase of life.

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Web Sites for End-of-Life Care Resources

AMERICAN CANCER SOCIETY

<http://www.cancer.org>

The American Cancer Society offers a complete listing of cancer services.

AMERICAN SOCIETY OF CLINICAL ONCOLOGY

<http://www.cancer.net>

Patient Information Web site has

disease and symptom management information.

CENTER TO ADVANCE PALLIATIVE CARE

<http://www.getpalliativecare.org>

This Web site is geared toward patients, and tells them where to find palliative care.

NATIONAL CANCER INSTITUTE

<http://www.cancer.gov>

The National Cancer Institute has a complete listing of cancer treatment for the public and health care professionals. It also lists ongoing clinical trials. The Web site address for “Coping With Cancer” is <http://www.cancer.gov/cancertopics/coping>.