



## Club soins palliatifs et d'accompagnement

Compléments à l'intervention de M. Lucas Morin (ONFV)

Mardi 10 décembre 2013

# « Chimiothérapie en fin de vie »

1) Etude de littérature : **Chimiothérapie dans les derniers mois de vie** (en % des patients ayant déjà reçu une chimiothérapie)

2) Craig C. Earle, Mary Beth Landrum, Jeffrey M. Souza, Bridget A. Neville, Jane C. Weeks, and John Z. Ayanian - **Aggressiveness of Cancer Care Near the End of Life: Is It a Quality-of-Care Issue?** - J Clin Oncol 26:3860-3866.

Le but de cet article est d'examiner la documentation et les analyses portant sur l'agressivité des soins proposés aux malades d'un cancer en fin de vie. Plus précisément, l'auteur discute des tendances et des facteurs responsables de la surutilisation des chimiothérapies et de la sous-utilisation des services de soins palliatifs juste avant le décès. Le fait que les traitements trop agressifs sont un problème de qualité de soins devrait constituer une question pour tous.

3) Sarah Elizabeth Harrington, MD and Thomas J. Smith, MD Department of Internal Medicine and the Thomas Palliative Care Program of the Massey Cancer Center of Virginia Commonwealth University, Richmond - **The Role of Chemotherapy at the End of Life: "When Is Enough, Enough?"** - JAMA. 2008 June 11; 299(22): 2667–2678. doi:10.1001/jama.299.22.2667.

La chimiothérapie à la fin de vie conduit les patients à des prises de décisions difficiles. Elle peut prolonger la survie ou réduire les symptômes mais entraîner des effets néfastes, empêcher le patient de faire le bilan de sa vie et de se préparer à la mort, empêcher son entrée en hospice. L'auteur développe une étude de cas (cancer du poumon) afin de montrer comment les cliniciens impliqués dans les soins palliatifs et en oncologie peuvent travailler plus efficacement.

4) S. Braga, Instituto Portugueês de Oncologia and Instituto Gulbenkian de Cieência (Gulbenkian Program for Advanced Medical Education), Lisboa, Portugal - Editorial - **Why do our patients get chemotherapy until the end of life?** - Annals of Oncology 22: 2345–2348, 2011 doi:10.1093/annonc/mdr416 Published online 13 September 2011

A partir d'un cas précis, l'auteur s'interroge : pourquoi ne sommes-nous pas capables d'arrêter une chimiothérapie quand elle est inutile, toxique et qu'elle nécessite une logistique complexe et coûteuse ?

## Chimiothérapie dans les derniers mois de vie (en % des patients ayant déjà reçu une chimiothérapie)

Etude	Localisation	Echantillon de l'étude	Année	3 derniers mois de vie	Dernier mois de vie	15 derniers jours de vie	Remarques
1 Keam B, Oh DY, Lee SH et al. Aggressiveness of cancer-care near the end-of-life in Korea. <i>Jpn J Clin Oncol</i> 2008; 38: 381–386	Lung, gastric, colorectal, biliary pancreatic and other malignancies,	298	2008	49%	18%	5,7%	
2 U. Näppa et al, Palliative chemotherapy during the last month of life; <i>Ann Oncol.</i> 2011 Nov;22(11):2375-80	Gastric, Lung, colorectal, ovarian, breast, other	374	2011	-	23%	-	(>75 years =13%)
3 Martoni AA, Tanneberger S, Mutri V. Cancer chemotherapy near the end of life: the time has come to set guidelines for its appropriate use. <i>Tumori.</i> 2007; 93(5):417–422	Lung, colorectal, breast	793	2007	-	23%	-	12.7% of all patients
4 Andreis F, Chemotherapy use at the end of life. A retrospective single centre experience analysis., <i>Tumori.</i> 2011 Jan-Feb;97(1):30-4.	Breast, Lung, colorectal, gastric, pancreatic	102	2011	50%	16%	6%	Un seul centre
5 Emanuel EJ, Young-Xu Y, Levinsky NG et al. Chemotherapy use among Medicare beneficiaries at the end of life. <i>Ann Intern Med</i> 2003; 138: 639–643.	All locations	?	2003	-	9% of >65 ans	-	
6 M. Frigeri et al , Chemotherapy in patients with advanced pancreatic cancer: too close to death?, <i>Support Care Cancer.</i> 2013 Jan;21(1):157-63	Pancreatic adenocarcinoma	231	2013	47%	24%	7%	
7 Braga S et al, The aggressiveness of cancer care in the last three months of life: a retrospective single centre analysis., <i>Psychooncology.</i> 2007 Sep;16(9):863-8.	Breast, Lung, ovarian, pancreatic, colorectal, other	319	2007	66%	37%	21%	Un seul centre

	Etude	Localisation	Echantillon de l'étude	Année	3 derniers mois de vie	Dernier mois de vie	15 derniers jours de vie	Remarques
8	Hashimoto K et al, Factors that affect the duration of the interval between the completion of palliative chemotherapy and death., <i>Oncologist</i> . 2009 Jul;14(7):752-9	Breast, ovarian	255	2009	47%	12,6%	3,1%	
9	Kristin M. Sheffield et al, End-of-life care in Medicare beneficiaries dying with pancreatic cancer., <i>Cancer</i> . 2011 Nov 1;117(21):5003-12.	Pancreatic malignancy	22 818	2011	-	16.4% (2004-2006)	-	8.1% (1992-1994)
10	O'Brien ME, Mortality within 30 days of chemotherapy: a clinical governance benchmarking issue for oncology patients. <i>Br J Cancer</i> . 2006 Dec 18;95(12):1632-6.	Breast, gastric, lung, other	161	2006	-	8%	-	
11	Earle CC, Neville BA, Landrum MB, Ayanian JZ, Block SD, Weeks JC. Trends in the aggressiveness of cancer care near the end of life. <i>J Clin Oncol</i> . 2004; 22(2):315–321.	Lung, breast, colorectal, gastric	28 777, aged ≥65	2004	-	-	18,5% des patients avec un cancer métastatique	5.7% ont commencé une nouvelle ligne au cours du dernier mois
12	Asola R, Huhtala H, Holli K. Intensity of diagnostic and treatment activities during the end of life of patients with advanced breast cancer. <i>Breast Cancer Res Treat</i> 2006; 100: 77–82	Breast	?	2006	-	19.7%	-	
13	Kao S, Shafiq J, Vardy J, Adams D., Use of chemotherapy at end of life in oncology patients. <i>Ann Oncol</i> . 2009 Sep;20(9):1555-9	Lung, colorectal, breast, pancreatic, prostate, other	747	2009	-	18%	4,2%	
14	Barbera L, Paszat L, Chartier C. Indicators of poor quality end-of-life cancer care in Ontario. <i>J Palliat Care</i> 2006; 22: 12–17	All locations	?	2006	-	16%	4,2%	
15	Earle CC, Landrum MB, Souza JM et al. Aggressiveness of cancer care near the end of life: is it a quality-of-care issue? <i>J Clin Oncol</i> 2008; 26: 2860–2866.	Colorectal, Lung, Breast, Prostate, Hematologic	215 484	2008	-	-	11.6%	

	<b>Etude</b>	<b>Localisation</b>	<b>Echantillon de l'étude</b>	<b>Année</b>	<b>3 derniers mois de vie</b>	<b>Dernier mois de vie</b>	<b>15 derniers jours de vie</b>	<b>Remarques</b>
16	Gonçalves J-F, Goyanes C, Use of chemotherapy at the end of life in a Portugues oncology center, <i>Support Care Cancer</i> , 2008, 16:321-327	All locations	1 064	2008	31%	13%	3%	Un seul centre
17	Hu W, Yasui Y, White J, Winget M., Aggressiveness of End-of-Life Care for Patients With Colorectal Cancer in Alberta, Canada: 2006-2009., <i>J Pain Symptom Manage.</i> 2013 Jul 16 [Epub]	Colorectal	2074		30,3% (6 derniers mois)	7.4%	3.7%	
18	Harrington SE et al, The Role of Chemotherapy at the End of Life, <i>JAMA.</i> 2008 June 11; 299(22): 2667–2678	-	-	2008	-	-	-	16%

## Aggressiveness of Cancer Care Near the End of Life: Is It a Quality-of-Care Issue?

Craig C. Earle, Mary Beth Landrum, Jeffrey M. Souza, Bridget A. Neville, Jane C. Weeks, and John Z. Ayanian

### ABSTRACT

The purpose of this article is to review the literature and update analyses pertaining to the aggressiveness of cancer care near the end of life. Specifically, we will discuss trends and factors responsible for chemotherapy overuse very near death and underutilization of hospice services. Whether the concept of overly aggressive treatment represents a quality-of-care issue that is acceptable to all involved stakeholders is an open question.

*J Clin Oncol* 26:3860-3866. © 2008 by American Society of Clinical Oncology

### INTRODUCTION

Despite advances in the early detection and treatment of cancer, a large proportion of patients still eventually die as a result of their disease.<sup>1</sup> Many of the issues these people face near the end of life are similar, regardless of their initial type of cancer. Therefore, the quality of medical care delivered to cancer patients near the end of life is of significant concern. Despite this, there has been relatively little work done to find ways to evaluate the quality of care that patients with incurable cancer receive.

The National Cancer Policy Board has defined poor-quality care as when “practices of known effectiveness are being underutilized, practices of known ineffectiveness are being overutilized, and when services of equivocal effectiveness are being utilized in accordance with provider rather than patient preferences.”<sup>2</sup> In an effort to address the gap in quality measurement for cancer patients near the end of life, we have previously used systematic literature review, focus groups with terminally ill cancer patients and bereaved family members, and an expert panel of physicians using a modified Delphi approach to identify and operationalize potential quality measures that could be evaluated with existing administrative data.<sup>3</sup> These exercises identified an overarching theme of overly aggressive cancer treatment as potentially representing poor-quality care, and produced a set of measures assessing three major areas: (1) the overuse of chemotherapy very near death; (2) possible misuse of treatment resulting in high rates of emergency room visits, hospitalization, or intensive care unit stays for terminal patients; and (3) underuse of hospice services as measured both by lack of referral or very late referral to hospice. We have applied these measures to co-

orts of patients with common aggressive solid tumors to define benchmarks empirically, evaluate the accuracy of the claims, assess reliability of the measures, and investigate geographic variation in practice.<sup>4</sup> From these analyses, we have previously reported secular trends of increasingly aggressive cancer care near the end of life during the mid-1990s.<sup>5</sup> In this article, we will review the literature on the aggressiveness of cancer treatment near the end of life and update analyses of practice patterns and methodologic development, focusing on the more methodologically sound measures of chemotherapy and hospice utilization near death.

### TRENDS AND PREDICTORS OF AGGRESSIVE CANCER CARE

Figure 1 and Table 1 show updated data on the trends and predictors of aggressive care near the end of life. This cohort consists of all 215,484 patients who died as a result of any malignancy, of any duration, between 1991 and 2000, who had been diagnosed while living in an area monitored by one of the Surveillance, Epidemiology, and End Results (SEER) registries, who were age 65 years and older at death, and enrolled in both parts of Medicare in the 3 months before death. We examined their Medicare claims to determine practice patterns following methods we have previously reported (Appendix Table A1, online only),<sup>4,5</sup> and supplemented sociodemographic information with geographic characteristics linked from the National Center for Health Workforce Information and Analysis’ Area Resource File and physician information from linking the American Medical Association Master File.

Figure 1 depicts trends over time in the aggressiveness of cancer care near the end of life. As we

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Submitted December 14, 2007; accepted May 20, 2008.

Supported by Grant No. CA 91753-02 from the National Cancer Institute.

Presented in part at 42nd Annual Meeting of the American Society of Clinical Oncology, June 2-6, 2006, Atlanta, GA.

Authors’ disclosures of potential conflicts of interest and author contributions are found at the end of this article.

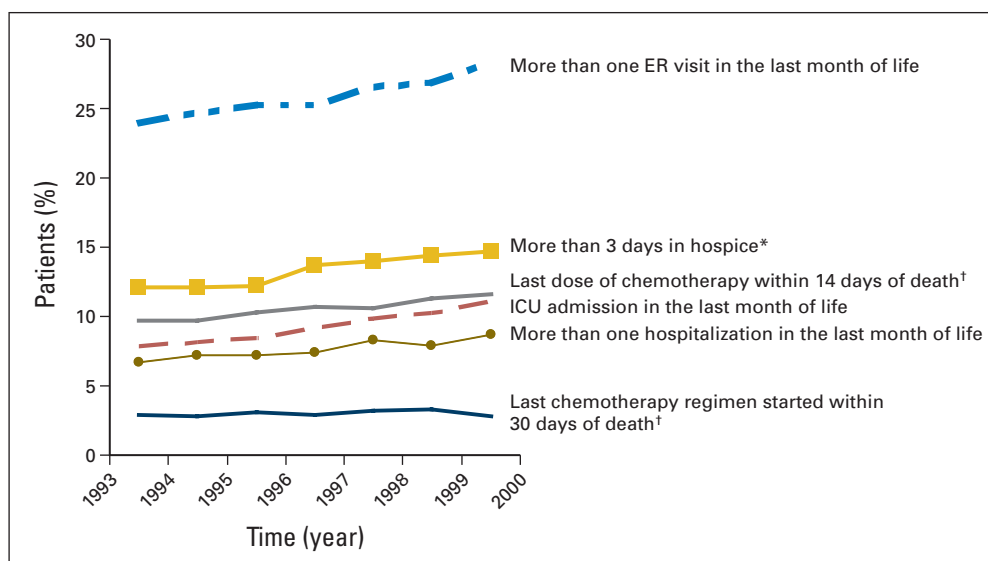
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0732-183X/08/2623-3860/\$20.00

DOI: 10.1200/JCO.2007.15.8253

### Consistency of End-of-Life Measures



**Fig 1.** Updated trends in the aggressiveness of cancer care near the end of life, all cancer types, all durations of disease among 215,484 Medicare enrollees in Surveillance, Epidemiology, and End Results (SEER) areas who died as a result of cancer. (\*) Among patients admitted to hospice. (†) Among patients who received chemotherapy. ER, emergency room; ICU, intensive care unit.

found in our previous analyses, most measures show an intensity of care that is continuing to increase. The proportion of patients still receiving chemotherapy within 14 days of death continues to rise monotonically, up from 9.7% in 1993 to 11.6% by 1999, although we could not detect an increase in proportion starting a new regimen

within the last month of life in this analysis. Although overall hospice utilization is increasing (Table 1), a large proportion of this increase represents patients admitted within 3 days of death, which accounted for 14.3% of all hospice admissions in 1999. We have also looked at several of these measures using the MarketScan MEDSTAT database

**Table 1.** Logistic Regression Analyses Predicting Aggressive Care

Factor	Chemotherapy Within 14 Days of Death		Lack of Hospice		Hospice Admission ≤ 3 Days Before Death*	
	Odds Ratio	95% CI	Odds Ratio	95% CI	Odds Ratio	95% CI
<b>Patient characteristic</b>						
Year of death	1.06	1.06 to 1.07	0.85	0.85 to 0.86	1.03	1.03 to 1.04
Age at death	0.94	0.94 to 0.94	1.01	1.00 to 1.01	0.99	0.99 to 0.99
Male	1.07	1.02 to 1.12	1.23	1.20 to 1.25	1.27	1.21 to 1.33
Black race	0.74	0.67 to 0.81	1.17	1.13 to 1.21	0.81	0.75 to 0.88
Other race	0.84	0.75 to 0.93	1.52	1.45 to 1.59	NS	
Single/widowed v married	0.77	0.74 to 0.81	1.16	1.14 to 1.19	0.95	0.91 to 0.99
Charlson score	0.92	0.90 to 0.95	1.09	1.07 to 1.10	1.05	1.02 to 1.07
SES decile	1.03	1.02 to 1.04	0.98	0.98 to 0.98	NS	
<b>Cancer characteristics</b>						
Disease site						
Colorectal	1.20	1.12 to 1.30	0.94	0.91 to 0.97	NS	
Breast	1.63	1.49 to 1.78	1.21	1.16 to 1.26	1.21	1.11 to 1.33
Lung	NS		NS		NS	
Prostate	NS		0.95	0.92 to 0.99	0.89	0.81 to 0.96
Hematologic	2.10	1.96 to 2.24	2.06	1.99 to 2.14	1.64	1.52 to 1.77
Nonmetastatic initial stage	0.82	0.79 to 0.86	1.06	1.04 to 1.08	0.89	0.86 to 0.94
Survival time (years)	0.98	0.97 to 0.99	0.99	0.98 to 0.99	0.98	0.97 to 0.99
<b>Provider characteristics</b>						
Teaching hospital	1.17	1.12 to 1.23	0.94	0.93 to 0.96	1.15	1.10 to 1.20
Oncologist	1.49	1.31 to 1.70	0.54	0.50 to 0.57	1.26	1.13 to 1.42
PCP	0.78	0.72 to 0.84	0.68	0.67 to 0.70	1.35	1.27 to 1.42
<b>Area characteristics</b>						
Availability of teaching hospitals	1.07	1.04 to 1.10	0.88	0.87 to 0.89	1.14	1.11 to 1.17
Hospice availability	0.94	0.92 to 0.97	0.97	0.96 to 0.98	0.84	0.82 to 0.86

NOTE. Among 215,484 Medicare enrollees in Surveillance, Epidemiology, and End Results areas who died as a result of cancer. Main effects only. Abbreviations: SES, each decile of increasing socioeconomic status; oncologist, ever saw oncologist in last month of life; PCP, ever saw a primary care physician in the last month of life.

\*Among patients who received hospice care (n = 82,579).

to evaluate a cohort of 18,812 younger, commercially-insured patients dying of cancer between 1991 and 2003. This analysis produced similar findings. Among those receiving chemotherapy in this MEDSTAT database, 17.1% were still being treated within 2 weeks of death and 9.7% had more than one hospitalization in the last month of life. Only 23.3% received any hospice care.

Table 1 shows logistic regression analyses predicting chemotherapy use within 14 days of death, hospice referral, and, among those referred to hospice, predictors of the likelihood that they would be admitted within 3 days of death. Measures focusing on emergency room visits, hospital admissions, and intensive care unit utilization were not included because we have found them to be strongly influenced by comorbidity and, therefore, appear less useful as measures of aggressive cancer care. This analysis confirms the secular trend that each successive year of death is independently associated with an increasing likelihood of patients experiencing late chemotherapy use and short hospice admissions. As with our previous findings, elderly, female, nonwhite, and unmarried patients were less likely to receive aggressive care. Not surprisingly, the hematologic malignancies were most strongly associated with aggressive care. Those who presented initially with early-stage cancer and later relapsed, and those with a longer duration of illness were less likely to be treated aggressively near the end of life. Patients cared for by an oncologist in the last month of life were more likely than those cared for by other types of physicians to be treated late with chemotherapy, and to be admitted to hospice; however, they were also more likely to initiate hospice within 3 days of death. Others have similarly found that patients cared for by oncologists were referred to hospice later than those cared for by other physicians.<sup>6</sup> As we found before, both receiving care in a teaching hospital and simply living in an area with more teaching hospitals appears to predispose to more aggressive care, while the local availability of hospice services leads to greater hospice utilization and a decrease in aggressive chemotherapy use. Teaching hospitals are associated with greater overall use of hospice, however.

**"CONTINUATION OF CHEMOTHERAPY VERY NEAR DEATH MAY INDICATE OVERUSE"**

Because of their rigorous methodologic development, the measures of cancer care intensity described above have been endorsed by the National Quality Forum (NQF) as surveillance measures for end-of-life care, and were recommended for further development to be used for quality-improvement purposes. The Agency for Healthcare Research and Quality (AHRQ) is currently funding contracts to validate these specific measures further. They have also undergone testing in other health care settings and in other countries.<sup>7,8</sup> One reason for this interest is that they have the relatively unique feature of assessing overuse. Oncologists have traditionally focused on underuse (surgery, adjuvant chemotherapy or radiation) as the source of most quality problems, with little attention to the possibility that overuse could result in poor quality care.

There is evidence that the use of chemotherapy near the end of life is not related to its likelihood of providing benefit.<sup>9</sup> Indeed, we found in our analyses that the mean duration of the last treatment regimen, which is sometimes used as a proxy for time to progression, was stable at 61 days during the last decade, whereas overall chemotherapy utilization was increasing. This suggests that there was no

increase in effectiveness of the chemotherapy being used, with patients mostly coming off treatment when restaged after approximately 2 months. So, why does overly aggressive care occur? In a survey of Medicare beneficiaries, observed geographic variation in end-of-life treatment could not be explained by patient preference,<sup>10</sup> suggesting that physician practice style is a major driver.<sup>11</sup> There are many rationales for recommending treatment with very limited potential benefits. For example, it can be seen as providing hope. Moreover, the discussion about changing the focus of treatment from fighting the cancer to providing symptomatic and supportive care is a difficult one that nobody relishes.<sup>12</sup> It is often easier to recommend another line of chemotherapy. The issue can be complicated by oncologists' anecdotal experiences of occasional patients who seemed to actually respond to late-line treatment, a concern that is becoming even more relevant now that relatively nontoxic targeted agents are altering the risk/benefit calculation. And lastly, there may be financial incentives. Jacobson et al<sup>13</sup> explored whether physicians who were relatively more generously reimbursed for chemotherapy made different decisions in situations with substantial clinical discretion about whether to give treatment and which drugs to use, namely the management of metastatic common solid tumors. They found that reimbursement did not affect the decision to give chemotherapy or not, but once that decision was made, oncologists tended to use drugs for which they were reimbursed the most. For example, a \$33 increase in reimbursement for carboplatin was associated with 17% higher utilization of that drug.

On the other hand, patients may request an aggressive treatment approach right to the end. They may not understand their true prognosis,<sup>14</sup> have unrealistic expectations about the benefits of chemotherapy,<sup>15</sup> want to be "a fighter," or feel that doing something (anything) is better than doing nothing.<sup>16,17</sup> Moreover, it has been shown many times that patients will accept much more toxicity for a smaller benefit than will providers.<sup>18</sup> This observation is commonly put forward to suggest that physicians cannot make these treatment decisions for patients. It begs the question, however, of why oncologists agree to provide treatments to patients that they would not take themselves.<sup>19</sup> By shepherding many patients through the journey towards death, oncologists have a broader perspective and experience than their patients can possibly have. Consequently, oncologists must be prepared to tell patients when they would be better off without the next line of possible chemotherapy.<sup>20</sup>

**"A HIGH PROPORTION OF PATIENTS NEVER REFERRED TO HOSPICE, OR REFERRED ONLY IN THE LAST FEW DAYS OF LIFE, MAY INDICATE POOR-QUALITY CARE"**

Hospice availability appears to independently affect physician practice, even the propensity to give chemotherapy. If high-quality palliative care is not available, oncologists apparently tend to continue giving chemotherapy longer than they otherwise would. Uneven access to hospice based on geography, rural settings, and patient socio-demographic factors have all been documented.<sup>21-24</sup> Studies have shown that patients in health maintenance organizations (HMOs) are more likely to receive hospice care, possibly reflecting more coordinated and appropriate treatment patterns.<sup>25</sup> However, it is also argued that this reflects a financial incentive to offload relatively expensive patients from the managed care organization's panel.<sup>22</sup> Even when hospice is available, however, barriers still exist. Some patients may

associate it with a stigma. Some are unable to get supportive medications such as growth factors or narcotic pumps because of policies necessitated by the hospice benefit, which pays hospices in the range of \$100 to \$150 (the exact amount varies by geography) per day to manage the patient's care, including all medications.<sup>26</sup> The increased overall use of hospice with concomitant increase in the proportion admitted within 3 days of death that we have observed raises the question of whether patients are simply being admitted to hospice to manage death, rather than obtaining the benefits of symptom management and palliative support that hospice can provide.<sup>27</sup>

## RECENT METHODOLOGIC DEVELOPMENT

### Stability Over Time

We and others have documented significant variation in practice patterns regarding these measures.<sup>4</sup> For example, the American Society of Clinical Oncology's (ASCO) Quality Oncology Practice Initiative (QOPI) reported at the ASCO Annual Meeting in 2006<sup>28</sup> that among 455 patients in 22 practices, use of chemotherapy within 14 days of death ranged from 0% to 33%. This was strongly correlated with either no hospice admission or admission only within less than a week before death. The proportion of patients enrolled in hospice before death ranged from 25% to 100%, with a mean of 62%. Wennberg et al<sup>29</sup> noted similar large variation in similar measures applied to the care at hospitals listed in the 2001 *US News & World Report* "best hospitals" list.

We further assessed the stability of these measures over time by examining the stability of relative aggressive care over time. If the relative aggressiveness of a provider or organization's practice appeared to change from year to year, then these measures might not be assessing a stable property of practice. To investigate this, we used hierarchical regression models to estimate regional variation in both levels and trends of each measure. We used as our geographic unit of analysis the Health Care Service Area (HCSA). HCSAs are groupings of Metropolitan Statistical Areas defined by the Centers for Medicare & Medicaid Services (CMS) based on observed patient flow patterns in Medicare for tertiary care.<sup>30</sup> As such, each HCSA can be considered to be a self-contained regional health system with a related group of providers. We ranked each region according to the model-estimated rate of each indicator and computed the correlation among relative ranks of each region during the 10-year study period. We observed significant variation both in levels of aggressive care and in trends in aggressiveness over time. As Table 2 indicates, the relative rankings of HCSAs from 1 year to the next were stable, with correlations of ranks ranging from 0.91 to 0.98 from 1991 to 1992, and still good to excellent

correlations of 0.66 to 0.84 over the 5-year span from 1991 to 1995. This stability of regional practice patterns provides supportive evidence of the reliability of these measures. However, we found only moderate correlations ranging from 0.40 to 0.61 during the entire decade, which is to be expected even with reliable measures because of differing strengths of trends in different regions eventually altering the relative rankings over time. For example, the poor correlation of hospice utilization over the 10-year period could reflect differential investment in hospice services in different regions. Figure 2 shows HCSAs in the regions monitored by the SEER program that consistently rank in the top and bottom 25 (of 77 HCSAs) of aggressiveness on each measure. One thing that is apparent is that these measures are evaluating different constructs: Counties that consistently have high rates of chemotherapy utilization within 14 days of death are not necessarily the same ones that have low hospice utilization or a high proportion of hospice admissions within 3 days of death.

## VALIDITY

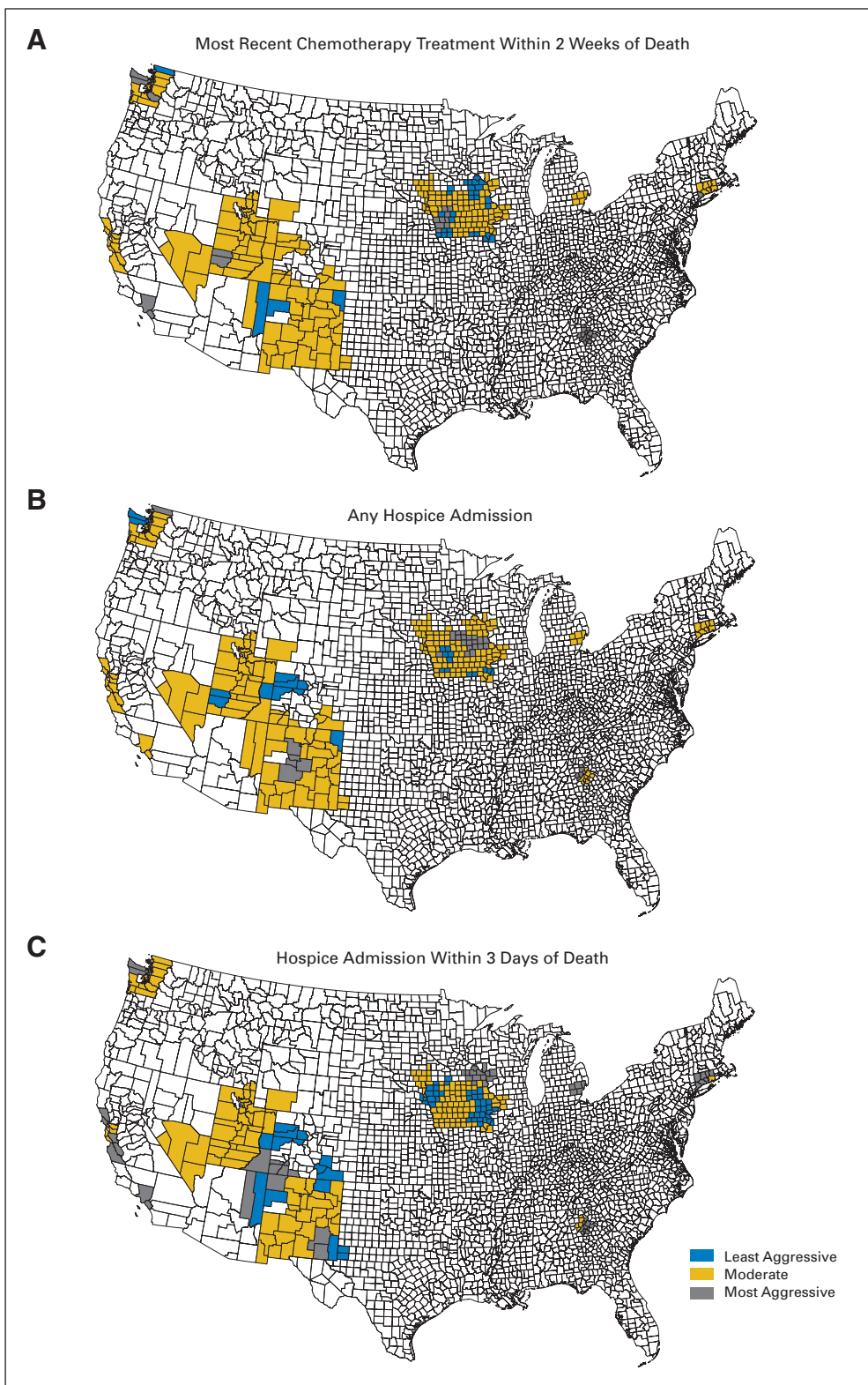
To explore the validity of the measures, we sought to relate each of our measures to the outcome of family members' satisfaction with quality of care near the end of life. We have examined data from a prospective cohort study looking at patient and family needs among women with hormone-refractory metastatic breast cancer treated at two Canadian regional cancer centers, and limited analysis to the patients who died during follow-up.<sup>31</sup> Family members were asked to complete the FAMCARE instrument<sup>32</sup> within 2 weeks of patient death. FAMCARE is a 20-question survey that asks about satisfaction with symptom control, psychosocial care, information provision, and availability of providers. Among 51 consecutive women who died and had a caregiver complete the FAMCARE instrument, there were trends toward less satisfaction with care when chemotherapy was continued within 14 days of death, death occurred in an acute care setting, or there was no or only a short ( $\leq 3$  day) hospice involvement. These did not reach statistical significance, however, perhaps because of the small sample size. Interestingly, variability in scores appeared to be mostly driven by the "information giving" and "physical care" subscales of the FAMCARE instrument, suggesting that inadequate communication and symptom management may be associated with aggressive anticancer treatment. A larger validation study is underway in the National Cancer Institute-funded Cancer Care Outcomes Research and Surveillance (CanCORS) consortium<sup>33</sup> comparing these measures with patient and family assessments of the overall quality of care patients with lung or colorectal cancer receive before death.

**Table 2.** Correlation in HCSA Ranks Over Time Among 215,484 Medicare Enrollees in SEER Areas Who Died As a Result of Cancer

Correlation in Ranks	New Chemotherapy in the Last Month of Life	Chemotherapy Dose During the Last 2 Weeks of Life	> 1 ER visit	> 1 Hospital Admission	ICU Admission	Hospice Admission	Hospice LOS < 3 Days
1991-1992	0.92	0.94	0.91	0.97	0.97	0.98	0.98
1991-1995	0.73	0.66	0.71	0.78	0.84	0.85	0.79
1991-2000	0.54	0.40	0.55	0.47	0.61	0.26	0.44

Abbreviations: HCSA, Health Care Service Area; SEER, Surveillance, Epidemiology, and End Results; ER, emergency room; ICU, intensive care unit; LOS, length of stay.





**Fig 2.** Maps showing distribution of aggressive chemotherapy use and hospice underutilization among 215,484 Medicare enrollees in Surveillance, Epidemiology, and End Results (SEER) Health Care Service Areas (HCSAs) who died as a result of cancer between 1991 and 2000. Gray HCSAs were ranked in the top 25 of 77 HCSAs monitored by SEER every year for 10 years, blue HCSAs were ranked in the bottom 25, and the rest are indicated by yellow. White HCSAs are those not monitored by the SEER program.

## DISCUSSION

Donabedian<sup>34</sup> articulated the rationale for quality measurement as “create an environment of watchful concern that motivates everyone

to perform better.” In this conceptual framework, health care providers are more careful if they know their clinical decisions are being monitored. By monitoring care and providing feedback on performance measures to providers with benchmarking to the performance

of their peers, most providers will examine their own practices for potential areas of improvement. In this way, monitoring performance can improve performance. We have systematically identified a series of candidate performance measures that can be applied to administrative data to profile cancer care near the end of life and have taken an empirical approach to assessing their properties. In the updated analyses presented here, we found predictable patterns over a broader array of clinical situations and consistent rankings of geographic service delivery areas over time. These results support the use of these performance measures for surveillance of end-of-life care.

There are some limitations to these measures, however. They have been mostly developed by assessing the care of elderly patients with fee-for-service insurance, and practice patterns may have been different for younger, commercially-insured patients. Because cancer is commonly a disease of the elderly, though, more than half of all cancer care in the United States is covered by Medicare. The SEER-Medicare database also represents only specific geographic locations and misses the 10% to 15% of patients enrolled in Medicare HMOs. Measures that start with death and look backward are inherently artificial because decisions are made in real time, prospectively, not in hindsight.<sup>35</sup> It is difficult to prospectively identify the preterminal phase analytically, however, and currently available methods may produce a biased subpopulation.<sup>36</sup> Physicians tend to overestimate survival and consequently may not realize that the end of life is approaching for their patients, although their predictions are highly correlated with actual survival.<sup>37</sup> Several clinical scales exist, all with limitations, that provide marginal improvements over clinician estimates of survival,<sup>38</sup> but there are no clear “stopping rules” for anticancer treatment.<sup>39</sup> Refinement of these prognostic tools is an important area for future research.

Finally, further work is needed to establish the contribution of patient preferences to the aggressiveness of end-of-life care, and to

estimate the effect of aggressive care on outcomes such as overall survival, patient and family satisfaction with care and perceptions of quality, and cost. We have argued that patterns of injudicious use of anticancer treatment near the end of life may be a marker for lack of difficult end-of-life discussions with patients, poor prognostic ability, or a paucity of available palliative resources. It may also be patient driven, though, because patients and their families generally have not experienced the entire course of cancer through death and consequently may desire inappropriately aggressive care. It may not be possible to both achieve patient satisfaction and avoid futile care, but it is the physicians’ responsibility to counsel patients and their families and advise them when it is time to stop anticancer treatments and focus on the need for effective palliative care as patients approach the end of life.

#### AUTHORS’ DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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#### REFERENCES

- Rowland J, Mariotto A, Aziz N, et al: Cancer survivorship: United States, 1971-2001. *MMWR* 53: 526-529, 2004
- National Cancer Policy Board: Ensuring Quality Cancer Care. Washington, DC, National Academy Press, 1999
- Earle CC, Park ER, Lai B, et al: Identifying potential indicators of the quality of end-of-life cancer care from administrative data. *J Clin Oncol* 21:1133-1138, 2003
- Earle CC, Neville BA, Landrum MB, et al: Evaluating claims-based indicators of the intensity of end-of-life cancer care. *Int J Qual Health Care* 17: 505-509, 2005
- Earle CC, Neville BA, Landrum ME, et al: Trends in the aggressiveness of cancer care near the end of life. *J Clin Oncol* 22:315-321, 2004
- Lamont EB, Christakis NA: Physician factors in the timing of cancer patient referral to hospice palliative care. *Cancer* 94:2733-2737, 2002
- Grunfeld E, Lethbridge L, Dewar R, et al: Towards using administrative databases to measure population-based indicators of quality of end-of-life care: Testing the methodology. *Palliat Med* 20:769-777, 2006
- Murillo JR Jr, Koeller J: Chemotherapy given near the end of life by community oncologists for advanced non-small cell lung cancer. *Oncologist* 11:1095-1099, 2006
- Emanuel EJ, Young-Xu Y, Levinsky NG, et al: Chemotherapy use among Medicare beneficiaries at the end of life. *Ann Intern Med* 138:639-643, 2003
- Voogt E, van der HA, Rietjens JA, et al: Attitudes of patients with incurable cancer toward medical treatment in the last phase of life. *J Clin Oncol* 23:2012-2019, 2005
- Barnato AE, Herndon MB, Anthony DL, et al: Are regional variations in end-of-life care intensity explained by patient preferences? A study of the US Medicare population. *Med Care* 45:386-393, 2007
- von Gunten CF: Discussing hospice care. *J Clin Oncol* 21:31s-36s, 2003
- Jacobson M, O’Malley AJ, Earle CC, et al: Does reimbursement influence chemotherapy treatment for cancer patients? *Health Aff (Millwood)* 25:437-443, 2006
- Mack JW, Cook EF, Wolfe J, et al: Understanding of prognosis among parents of children with cancer: Parental optimism and the parent-physician interaction. *J Clin Oncol* 25:1357-1362, 2007
- Lee SJ, Fairclough D, Antin JH, et al: Discrepancies between patient and physician estimates for the success of stem cell transplantation. *JAMA* 285:1034-1038, 2001
- Weissman DE, O’Donnell J, Brady A: A cry from the fringe. *J Clin Oncol* 11:1006, 1993
- Weeks JC, Cook EF, O’Day SJ, et al: Relationship between cancer patients’ predictions of prognosis and their treatment preferences. *JAMA* 279: 1709-1714, 1998
- Matsuyama R, Reddy S, Smith TJ: Why do patients choose chemotherapy near the end of life? A review of the perspective of those facing death from cancer. *J Clin Oncol* 24:3490-3496, 2006
- Slevin ML, Stubbs L, Plant HJ, et al: Attitudes to chemotherapy: Comparing views of patients with cancer with those of doctors, nurses, and general public. *BMJ* 300:1458-1460, 1990
- Mack JW, Wolfe J, Cook EF, et al: Hope and prognostic disclosure. *J Clin Oncol* 25:5636-5642, 2007
- Virnig BA, Kind S, McBean M, et al: Geographic variation in hospice use prior to death. *J Am Geriatr Soc* 48:1117-1125, 2000
- McCarthy EP, Burns RB, Ngo-Metzger Q, et al: Hospice use among Medicare managed care and fee-for-service patients dying with cancer. *JAMA* 289:2238-2245, 2003
- Keating NL, Herrinton LJ, Zaslavsky AM, et al: Variations in hospice use among cancer patients. *J Natl Cancer Inst* 98:1053-1059, 2006
- Virnig BA, Ma H, Hartman LK, et al: Access to home-based hospice care for rural populations: Identification of areas lacking service. *J Palliat Med* 9:1292-1299, 2006
- Virnig BA, Fisher ES, McBean MA, et al: Hospice use in Medicare managed care and fee-for-service systems. *Am J Manag Care* 7:777-786, 2001

- 26.** Daugherty CK: Examining ethical dilemmas as obstacles to hospice and palliative care for advanced cancer patients. *Cancer Invest* 22:123-131, 2004
- 27.** Christakis NA, Escarce JJ: Survival of Medicare patients after enrollment in hospice programs. *N Engl J Med* 335:172-178, 1996
- 28.** Neuss MN, Jacobson JO, Earle C, et al: Evaluating end of life care: The Quality Oncology Practice Initiative (QOPI) experience. *J Clin Oncol* 20:486s, 2006 (suppl; abstr 8573)
- 29.** Wennberg JE, Fisher ES, Stukel TA, et al: Use of hospitals, physician visits, and hospice care during last six months of life among cohorts loyal to highly respected hospitals in the United States. *BMJ* 328:607, 2004
- 30.** Makuc DM, Haglund B, Ingram DD, et al: Vital and Health Statistics: Health Service Areas for the United States—Series 2: Data Evaluation and Methods Research 112. DHHS Publication No. (PHS) 92-1386, 1991
- 31.** Grunfeld E, Coyle D, Whelan T, et al: Family caregiver burden: Results of a longitudinal study of breast cancer patients. *CMAJ* 170:1795-1801, 2004
- 32.** Kristjanson L: Validity and reliability testing of the FAMCARE scale: Measuring family satisfaction with advanced cancer care. *Soc Sci Med* 36:693-701, 1993
- 33.** Ayanian JZ, Chrischilles EA, Fletcher RH, et al: Understanding cancer treatment and outcomes: The Cancer Care Outcomes Research and Surveillance Consortium. *J Clin Oncol* 22:2992-2996, 2004
- 34.** Donabedian A: The quality of care: How can it be assessed? *JAMA* 260:1743-1748, 1988
- 35.** Bach PB, Schrag D, Begg CB: Resurrecting treatment histories of dead patients: A study design that should be laid to rest. *JAMA* 292:2765-2770, 2004
- 36.** Earle CC, Ayanian JZ: Looking back from death: The value of retrospective studies of end-of-life care. *J Clin Oncol* 24:838-840, 2006
- 37.** Glare P, Virik K, Jones M, et al: A systematic review of physicians' survival predictions in terminally ill cancer patients. *BMJ* 327:195-198, 2003
- 38.** Stone PC, Lund S: Predicting prognosis in patients with advanced cancer. *Ann Oncol* 18:971-976, 2007
- 39.** Benner SE, Fetting JH, Brenner MH: A stopping rule for standard chemotherapy for metastatic breast cancer: Lessons from a survey of Maryland medical oncologists. *Cancer Invest* 12:451-455, 1994

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### Appendix

The Appendix is included in the full-text version of this article, available online at [www.jco.org](http://www.jco.org). It is not included in the PDF version (via Adobe® Reader®).



Published in final edited form as:

*JAMA*. 2008 June 11; 299(22): 2667–2678. doi:10.1001/jama.299.22.2667.

## The Role of Chemotherapy at the End of Life:

“When Is Enough, Enough?”

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### Abstract

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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### 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

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**Financial Disclosures:** None reported.

**Other Sources:** For a list of relevant Web sites, see the article on the *JAMA* Web site at <http://www.jama.com>.

**Additional Contributions:** We would like to thank Karen Scott, BA, for administrative assistance, the Center to Advance Palliative Care, <http://www.capc.org>.

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.

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.

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 another 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.<sup>1</sup> 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.<sup>2</sup>

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,<sup>3</sup> 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.<sup>4</sup> 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.<sup>5</sup> 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.<sup>6,7</sup> Another study showed that physicians may “collude” in this hopefulness by giving such a wide range of outcomes that people choose the most favorable.<sup>8</sup>

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.<sup>9</sup> 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).<sup>10</sup> 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.<sup>11</sup> Box 1 lists some of the difficulties in giving and receiving information about prognosis in advanced cancer.

#### 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.<sup>12</sup>

##### 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.<sup>13</sup> The optimistic patients had no better survival than those who were more realistic.<sup>14</sup>

##### 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 over-estimates, or conscious underestimates 63% of the time.<sup>15</sup>

##### 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.<sup>4</sup>

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

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

### **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.<sup>6</sup>

#### **Head and Neck Cancer**

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

#### **Phase 1: Overoptimistic**

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

### **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.<sup>20</sup>

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.<sup>21</sup>

### **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.<sup>22</sup>

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

**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.<sup>24</sup>

#### **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%).<sup>25</sup>

**Italy:** Patients would be willing to undergo chemotherapy for small benefit, even if the physician presents the results pessimistically.<sup>26</sup>



**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.<sup>4</sup>

**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.<sup>27</sup>

#### **Palliative Chemotherapy, Belgium**

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

#### **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.<sup>11</sup> "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."

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.<sup>29</sup> In Italy, 23% of patients with incurable cancer received chemotherapy within 30 days of death.<sup>2</sup> 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.<sup>30</sup> 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.<sup>31</sup> 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.<sup>32</sup> Consensus panels that include cancer advocates make little distinction between curative treatment and

palliative treatment that could extend life,<sup>33</sup> 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.<sup>34</sup> 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%)<sup>35</sup>; and improvements in pain and less deterioration in quality of life.<sup>36</sup> Even third-line treatment may improve survival or symptoms, especially with novel, relatively nontoxic oral agents such as erlotinib, which, in 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.<sup>37</sup> Palliative chemotherapy has also increased survival and quality of life in metastatic colorectal<sup>38</sup> and prostate cancer<sup>39</sup> (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.<sup>44,45</sup> To help their patients make wise decisions, oncologists can start with a prompt list of questions, proven to enhance communication<sup>46–48</sup> and similar to one in use in several oncology practices,<sup>49,50</sup> including ours (Box 2). This can be provided to the patient in the waiting room for discussion with his or her physician.

## 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?

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 realistic<sup>51</sup> and patients want oncologists to be truthful and compassionate and to continue caring for them during their illness.<sup>52</sup> A comprehensive review found that randomized trials of decision aids in oncology yielded increased patient knowledge and more involvement in decision making,<sup>53</sup> 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.<sup>54,55</sup> A preliminary study showed that directly giving patients information about prognosis and treatment to share with their oncologist is desired and helpful.<sup>56</sup> 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.***

*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 indicated, 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.<sup>57</sup> 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.*

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 available 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.<sup>58</sup> 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](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.<sup>59</sup>

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.<sup>60</sup> Families' perception of late referral is associated with lower satisfaction with hospice care overall.<sup>61</sup> 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.<sup>62</sup> 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.<sup>63</sup> 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 al<sup>62</sup> 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.<sup>64</sup> 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.<sup>65</sup> (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 al<sup>66</sup> 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%.<sup>67</sup>

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 efforts, patients and families may continue to want chemotherapy.<sup>44</sup> 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.<sup>68</sup>

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.<sup>69</sup> 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.<sup>70</sup>

### **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.<sup>7</sup> Clinicians should generally respond with patience, emphasizing support (non-abandonment) and assurance of aggressive symptom management<sup>71</sup> (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.<sup>72</sup> 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.<sup>73</sup> 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.<sup>74</sup> 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.<sup>75</sup>

### **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.<sup>76,77</sup> As the Education Physicians End of Life Care for Oncologists (EPEC-O) curriculum<sup>78</sup> 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 pediatric oncology, full prognostic disclosure supported hope, even when the prognosis was poor.<sup>79</sup>

### **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.<sup>81</sup> The one randomized trial of concurrent hospice care plus usual oncology care vs usual oncology care alone has been published only in abstract form.<sup>80</sup> 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 colleagues<sup>84</sup> 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.<sup>1</sup> 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.<sup>85</sup> 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.<sup>45</sup> Some have changed to palliative care programs under home health care services, integrating palliative chemotherapy and radiation and related treatments (paid for by the patient's insurance or Medicare drug benefit) with elements of traditional hospice care. Passik and colleagues<sup>86</sup> 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.<sup>85</sup> 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.<sup>19</sup> 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.<sup>87</sup> 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.<sup>88</sup> Some drugs (oxaliplatin for metastatic colon cancer<sup>89</sup> and docetaxol for metastatic prostate cancer<sup>42</sup>) have acceptable cost-effectiveness ratios in which 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.<sup>90</sup> 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.<sup>91</sup> 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.<sup>92</sup> Although hospice care and in-patient palliative care<sup>93</sup> may save money during the last month of life, total disease costs are unchanged or increased,<sup>94</sup> 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.<sup>69</sup>

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,"<sup>95</sup> 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.<sup>96</sup>

## CONCLUSION

Given understandable patient, family, clinician, and societal goals and concerns, how can all individuals be educated 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,<sup>12</sup> 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.<sup>9</sup>



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.<sup>68</sup> 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.

## Acknowledgments

**Funding/Support:** The Perspectives on Care at the Close of Life series is made possible by funding from the California Archstone Foundation. The authors are also supported in part by grant funding from the Justice, Equality, Human Dignity, and Tolerance (JEHT) Foundation, New York; by grants 1G08LM009525-01 of the National Library of Medicine, National Institutes of Health, and R01CA116227-01 of the National Cancer Institute (NCI) to study outcomes of hospitalized cancer patients (Dr Meier, PI); and by the Palliative Care Leadership Program (<http://www.capec.org/palliative-care-leadership-initiative>).

**Role of the Sponsors:** None of the funding agencies had a role in the preparation, review, or approval of the manuscript.

## References

1. Temel JS, Jackson VA, Billings JA, et al. Phase II study: integrated palliative care in newly diagnosed advanced non-small-cell lung cancer patients. *J Clin Oncol*. 2007; 25(17):2377–2382. [PubMed: 17557950]
2. Martoni AA, Tanneberger S, Mutri V. Cancer chemotherapy near the end of life: the time has come to set guidelines for its appropriate use. *Tumori*. 2007; 93(5):417–422. [PubMed: 18038871]
3. Teno JM. Advance directives: time to move on. *Ann Intern Med*. 2004; 141(2):159–160. [PubMed: 15262674]
4. Koedoot CG, Oort FJ, de Haan RJ, Bakker PJ, de Graeff A, de Haes JC. The content and amount of information given by medical oncologists when telling patients with advanced cancer what their treatment options are: palliative chemotherapy and watchful-waiting. *Eur J Cancer*. 2004; 40(2): 225–235. [PubMed: 14728937]
5. Sullivan AM, Lakoma MD, Matsuyama RK, Rosenblatt L, Arnold RM, Block SD. Diagnosing and discussing imminent death in the hospital: a secondary analysis of physician interviews. *J Palliat Med*. 2007; 10(4):882–893. [PubMed: 17803409]
6. Mackillop WJ, Stewart WE, Ginsburg AD, Stewart SS. Cancer patients' perceptions of their disease and its treatment. *Br J Cancer*. 1988; 58(3):355–358. [PubMed: 2460120]
7. Chow E, Andersson L, Wong R, et al. Patients with advanced cancer: a survey of the understanding of their illness and expectations from palliative radiotherapy for symptomatic metastases. *Clin Oncol (R Coll Radiol)*. 2001; 13(3):204–208. [PubMed: 11527297]
8. Helft PR. Necessary collusion: prognostic communication with advanced cancer patients. *J Clin Oncol*. 2005; 23(13):3146–3150. [PubMed: 15860876]
9. Matsuyama R, Reddy S, Smith TJ. Why do patients choose chemotherapy near the end of life? a review of the perspective of those facing death from cancer. *J Clin Oncol*. 2006; 24(21):3490–3496. [PubMed: 16849766]
10. Silvestri G, Pritchard R, Welch HG. Preferences for chemotherapy in patients with advanced non-small cell lung cancer: descriptive study based on scripted interviews. *BMJ*. 1998; 317(7161):771–775. [PubMed: 9740561]

11. Agrawal M, Grady C, Fairclough DL, Meropol NJ, Maynard K, Emanuel EJ. Patients' decision-making process regarding participation in phase I oncology research. *J Clin Oncol.* 2006; 24(27): 4479–4484. [PubMed: 16983117]
12. The AM, Hak T, Koeter G, van der Wal G. Collusion in doctor-patient communication about imminent death: an ethnographic study. *West J Med.* 2001; 174(4):247–253. [PubMed: 11290678]
13. Lee SJ, Fairclough D, Antin JH, Weeks JC. Discrepancies between patient and physician estimates for the success of stem cell transplantation. *JAMA.* 2001; 285(8):1034–1038. [PubMed: 11209174]
14. Lee SJ, Loberiza FR, Rizzo JD, Soiffer RJ, Antin JH, Weeks JC. Optimistic expectations and survival after hematopoietic stem cell transplantation. *Biol Blood Marrow Transplant.* 2003; 9(6): 389–396. [PubMed: 12813447]
15. Lamont EB, Christakis NA. Prognostic disclosure to patients with cancer near the end of life. *Ann Intern Med.* 2001; 134(12):1096–1105. [PubMed: 11412049]
16. Santoso JT, Engle DB, Schaffer L, Wan JY. Cancer diagnosis and treatment: communication accuracy between patients and their physicians. *Cancer J.* 2006; 12(1):73–76. [PubMed: 16613666]
17. Glare P, Virik K, Jones M, et al. A systematic review of physicians' survival predictions in terminally ill cancer patients. *BMJ.* 2003; 327(7408):195–198. [PubMed: 12881260]
18. Smith TJ, Staats PS, Deer T, et al. Randomized clinical trial of an implantable drug delivery system compared with comprehensive medical management for refractory cancer pain: impact on pain, drug-related toxicity, and survival. *J Clin Oncol.* 2002; 20(19):4040–4049. [PubMed: 12351602]
19. Meropol NJ, Weinfurt KP, Burnett CB, et al. Perceptions of patients and physicians regarding phase I cancer clinical trials: implications for physician-patient communication. *J Clin Oncol.* 2003; 21(13):2589–2596. [PubMed: 12829680]
20. Mallinger JB, Shields CG, Griggs JJ, et al. Stability of decisional role preference over the course of cancer therapy. *Psychooncology.* 2006; 15(4):297–305. [PubMed: 16041829]
21. Grunfeld EA, Maher EJ, Browne S, et al. Advanced breast cancer patients' perceptions of decision making for palliative chemotherapy. *J Clin Oncol.* 2006; 24(7):1090–1098. [PubMed: 16505428]
22. Slevin ML, Stubbs L, Plant HJ, et al. Attitudes to chemotherapy: comparing views of patients with cancer with those of doctors, nurses, and general public. *BMJ.* 1990; 300(6737):1458–1460. [PubMed: 2379006]
23. Balmer CE, Thomas P, Osborne RJ. Who wants second-line, palliative chemotherapy? *Psychooncology.* 2001; 10(5):410–418. [PubMed: 11536419]
24. Brundage MD, Feldman-Stewart D, Cosby R, et al. Cancer patients' attitudes toward treatment options for advanced non-small cell lung cancer: implications for patient education and decision support. *Patient Educ Couns.* 2001; 45(2):149–157. [PubMed: 11687329]
25. Bremnes RM, Andersen K, Wist EA. Cancer patients, doctors and nurses vary in their willingness to undertake cancer chemotherapy. *Eur J Cancer.* 1995; 31A(12):1955–1959. [PubMed: 8562147]
26. Tamburini M, Buccheri G, Brunelli C, Ferrigno D. The difficult choice of chemotherapy in patients with unresectable non-small-cell lung cancer. *Support Care Cancer.* 2000; 8(3):223–228. [PubMed: 10789964]
27. Hirose T, Horichi N, Ohmori T, et al. Patients preferences in chemotherapy for advanced non-small-cell lung cancer. *Intern Med.* 2005; 44(2):107–113. [PubMed: 15750269]
28. Koedoot CG, de Haan RJ, Stiggelbout AM, et al. Palliative chemotherapy or best supportive care? a prospective study explaining patients' treatment preference and choice. *Br J Cancer.* 2003; 89(12):2219–2226. [PubMed: 14676798]
29. Earle CC, Neville BA, Landrum MB, Ayanian JZ, Block SD, Weeks JC. Trends in the aggressiveness of cancer care near the end of life. *J Clin Oncol.* 2004; 22(2):315–321. [PubMed: 14722041]
30. Murillo JR Jr, Koeller J. Chemotherapy given near the end of life by community oncologists for advanced non-small cell lung cancer. *Oncologist.* 2006; 11(10):1095–1099. [PubMed: 17110629]

31. Connor SR, Pyenson B, Fitch K, Spence C, Iwasaki K. Comparing hospice and nonhospice patient survival among patients who die within a three-year window. *J Pain Symptom Manage.* 2007; 33(3):238–246. [PubMed: 17349493]
32. American Society of Clinical Oncology Outcomes Working Group. Outcomes of cancer treatment for technology assessment and cancer treatment guidelines. *J Clin Oncol.* 1996; 14(2):671–679. [PubMed: 8636786]
33. Smith TJ, Khatcheressian J, Lyman GH, et al. 2006 Update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. *J Clin Oncol.* 2006; 24(19):3187–3205. [PubMed: 16682719]
34. Pfister DG, Johnson DH, Azzoli CG, et al. American Society of Clinical Oncology treatment of unresectable non-small-cell lung cancer guideline: Update 2003. *J Clin Oncol.* 2004; 22(2):330–353. [PubMed: 14691125]
35. Shepherd FA, Dancey J, Ramlau R, et al. Prospective randomized trial of docetaxel versus best supportive care in patients with non-small-cell lung cancer previously treated with platinum-based chemotherapy. *J Clin Oncol.* 2000; 18 (10):2095–2103. [PubMed: 10811675]
36. Dancey J, Shepherd FA, Gralla RJ, Kim YS. Quality of life assessment of second-line docetaxel versus best supportive care in patients with non-small-cell lung cancer previously treated with platinum-based chemotherapy: results of a prospective, randomized phase III trial. *Lung Cancer.* 2004; 43(2):183–194. [PubMed: 14739039]
37. Shepherd FA, Rodrigues Pereira J, Ciuleanu T, et al. Erlotinib in previously treated non-small-cell lung cancer. *N Engl J Med.* 2005; 353(2):123–132. [PubMed: 16014882]
38. Goldberg RM, Rothenberg ML, Van Cutsem E, et al. The continuum of care: a paradigm for the management of metastatic colorectal cancer. *Oncologist.* 2007; 12(1):38–50. [PubMed: 17227899]
39. Tannock IF, de Wit R, Berry WR, et al. Docetaxel plus prednisone or mitox-antrone plus prednisone for advanced prostate cancer. *N Engl J Med.* 2004; 351(15):1502–1512. [PubMed: 15470213]
40. Massarelli E, Andre F, Liu DD, et al. A retrospective analysis of the outcome of patients who have received two prior chemotherapy regimens including platinum and docetaxel for recurrent non-small-cell lung cancer. *Lung Cancer.* 2003; 39(1):55–61. [PubMed: 12499095]
41. Hayes, DF. An overview of treatment for locally advanced recurrent, and metastatic breast cancer. In: Rose, BF., editor. *UpToDate.* Waltham, MA: UpToDate; 2008.
42. Collins R, Fenwick E, Trowman R, et al. A systematic review and economic model of the clinical effectiveness and cost-effectiveness of docetaxel in combination with prednisone or prednisolone for the treatment of hormone-refractory metastatic prostate cancer. *Health Technol Assess.* 2007; 11(2):iii–iv. xv–xviii, 1–179.
43. El Demery M, Pouessel D, Avances C, et al. What is the objective of second-line chemotherapy after failure of first-line chemotherapy in hormone-resistant metastatic prostate? *Prog Urol.* 2006; 16(3):320–323. [PubMed: 16821344]
44. Casarett DJ, Quill TE. “I’m not ready for hospice”: strategies for timely and effective hospice discussions. *Ann Intern Med.* 2007; 146(6):443–449. [PubMed: 17371889]
45. Wright AA, Katz IT. Letting go of the rope—aggressive treatment, hospice care, and open access. *N Engl J Med.* 2007; 357(4):324–327. [PubMed: 17652646]
46. Bruera E, Sweeney C, Willey J, et al. Breast cancer patient perception of the helpfulness of a prompt sheet versus a general information sheet during outpatient consultation: a randomized, controlled trial. *J Pain Symptom Manage.* 2003; 25(5):412–419. [PubMed: 12727038]
47. Brown RF, Butow PN, Dunn SM, Tattersall MH. Promoting patient participation and shortening cancer consultations: a randomised trial. *Br J Cancer.* 2001; 85(9):1273–1279. [PubMed: 11720460]
48. Glynne-Jones R, Ostler P, Lumley-Graybow S, et al. Can I look at my list? an evaluation of a ‘prompt sheet’ within an oncology outpatient clinic. *Clin Oncol (R Coll Radiol).* 2006; 18(5): 395–400. [PubMed: 16817331]
49. Smith TJ. The art of oncology: when the tumor is not the target. tell it like it is. *J Clin Oncol.* 2000; 18(19):3441–3445. [PubMed: 11013287]
50. Eisenberg PD. Caring for patients at the end of life. *Ann Intern Med.* 2002; 136(6) 1 paragraph.

51. Hagerty RG, Butow PN, Ellis PM, et al. Communicating with realism and hope: incurable cancer patients' views on the disclosure of prognosis [published correction appears in *J Clin Oncol*. 2005;23(15):3652]. *J Clin Oncol*. 2005; 23(6):1278–1288. [PubMed: 15718326]
52. Kirk P, Kirk I, Kristjanson LJ. What do patients receiving palliative care for cancer and their families want to be told? a Canadian and Australian qualitative study. *BMJ*. 2004; 328(7452): 1343. [PubMed: 15151964]
53. Whelan, TM.; O'Brien, MA.; Villasis-Keever, M., et al. Impact of Cancer-Related Decision Aids. Rockville, MD: Agency for Healthcare Research and Quality; July. 2002 Evidence Report/ Technology Assessment 46. AHRQ publication no 01-E004
54. Peele PB, Siminoff LA, Xu Y, Ravdin PM. Decreased use of adjuvant breast cancer therapy in a randomized controlled trial of a decision aid with individualized risk information. *Med Decis Making*. 2005; 25(3):301–307. [PubMed: 15951457]
55. Siminoff LA, Gordon NH, Silverman P, Budd T, Ravdin PM. A decision aid to assist in adjuvant therapy choices for breast cancer. *Psychooncology*. 2006; 15(11):1001–1013. [PubMed: 16511899]
56. Leighl NB, Shepherd H, Butow P, et al. When the goal is not cure: a randomized trial of a patient decision aid in advanced colorectal cancer. *J Clin Oncol*. 2007; 25(suppl 18):6509.
57. Neff P, Lyckholm L, Smith T. Truth or consequences: what to do when the patient doesn't want to know. *J Clin Oncol*. 2002; 20(13):3035–3037. [PubMed: 12089236]
58. Shanafelt TD, Loprinzi C, Marks R, Novotny P, Sloan J. Are chemotherapy response rates related to treatment-induced survival prolongations in patients with advanced cancer? *J Clin Oncol*. 2004; 22(10):1966–1974. [PubMed: 15111619]
59. Smith TJ, Schnipper LJ. The American Society of Clinical Oncology program to improve end-of-life care. *J Palliat Med*. 1998; 1(3):221–230. [PubMed: 15859832]
60. Christakis NA, Iwashyna TJ. The health impact of health care on families: a matched cohort study of hospice use by decedents and mortality outcomes in surviving, widowed spouses. *Soc Sci Med*. 2003; 57(3):465–475. [PubMed: 12791489]
61. Schockett ER, Teno JM, Miller SC, Stuart B. Late referral to hospice and bereaved family member perception of quality of end-of-life care. *J Pain Symptom Manage*. 2005; 30(5):400–407. [PubMed: 16310614]
62. Teno JM, Shu JE, Casarett D, Spence C, Rhodes R, Connor S. Timing of referral to hospice and quality of care: length of stay and bereaved family members' perceptions of the timing of hospice referral. *J Pain Symptom Manage*. 2007; 34(2):120–125. [PubMed: 17583469]
63. Rabow MW, Schanche K, Petersen J, Dibble SL, McPhee SJ. Patient perceptions of an outpatient palliative care intervention: "It had been on my mind before, but I did not know how to start talking about death ...". *J Pain Symptom Manage*. 2003; 26(5):1010–1015. [PubMed: 14585552]
64. Casarett D, Crowley R, Stevenson C, Xie S, Teno J. Making difficult decisions about hospice enrollment: what do patients and families want to know? *J Am Geriatr Soc*. 2005; 53(2):249–254. [PubMed: 15673348]
65. Casarett DJ, Crowley RL, Hirschman KB. How should clinicians describe hospice to patients and families? *J Am Geriatr Soc*. 2004; 52(11):1923–1928. [PubMed: 15507073]
66. Brickner L, Scannell K, Marquet S, Ackerson L. Barriers to hospice care and referrals: survey of physicians' knowledge, attitudes, and perceptions in a health maintenance organization. *J Palliat Med*. 2004; 7(3):411–418. [PubMed: 15265350]
67. Casarett D, Karlawish J, Morales K, Crowley R, Mirsch T, Asch DA. Improving the use of hospice services in nursing homes: a randomized controlled trial. *JAMA*. 2005; 294(2):211–217. [PubMed: 16014595]
68. Lamont EB, Siegler M. Paradoxes in cancer patients' advance care planning. *J Palliat Med*. 2000; 3(1):27–35. [PubMed: 15859719]
69. Foley, K.; Gellband, H., editors. *Improving Palliative Care for Cancer*. Washington, DC: National Academy Press; 2001.
70. Back A. Patient-physician communication in oncology: what does the evidence show? *Oncology (Williston Park)*. 2006; 20(1):67–74. [PubMed: 16572594]

71. Rabinowitz T, Peirson R. “Nothing is wrong, doctor”: understanding and managing denial in patients with cancer. *Cancer Invest.* 2006; 24(1):68–76. [PubMed: 16466995]
72. Quill TE, Williamson PR. Healthy approaches to physician stress. *Arch Intern Med.* 1990; 150(9): 1857–1861. [PubMed: 2393317]
73. Meier DE, Back AL, Morrison RS. The inner life of physicians and care of the seriously ill. *JAMA.* 2001; 286(23):3007–3014. [PubMed: 11743845]
74. Smith RC, Zimny GH. Physicians’ emotional reactions to patients. *Psychosomatics.* 1988; 29(4): 392–397. [PubMed: 3227094]
75. Creagan ET. Burnout and balance: how to go the distance in the 21st century. *Cancer Control.* 2004; 11(4):266–268. [PubMed: 15284719]
76. Tobias JS, Souhami RL. Fully informed consent can be needlessly cruel. *BMJ.* 1993; 307(6913): 1199–1201. [PubMed: 8135933]
77. Fallowfield L. Participation of patients in decisions about treatment for cancer. *BMJ.* 2001; 323(7322):1144. [PubMed: 11711388]
78. Emanuel, LL.; Ferris, FD.; von Gunten, CF.; Von Roenn, J. Education in Palliative and End of Life Care for Oncology [CD-ROM]. Chicago, IL: EPEC-O; 2007. NIH publication 07–6114
79. Mack JW, Wolfe J, Cook EF, Grier HE, Cleary PD, Weeks JC. Hope and prognostic disclosure. *J Clin Oncol.* 2007; 25(35):5636–5642. [PubMed: 18065734]
80. Finn J, Pienta K, Parzuchowski J. Palliative care project: bridging cancer treatment and hospice care. *Proc Am Soc Clin Oncol.* 2002; 21:1452.
81. Pitorak, EF.; Armour, M.; Sivec, HD. Project Safe Conduct integrates palliative goals into comprehensive cancer care: an interview with Elizabeth Ford Pitorak and Meri Armour. 2002. <http://www2.edc.org/lastacts/archives/archivesjuly02/featureinn.asp>
82. Bakitas M, Stevens M, Ahles T, et al. Project ENABLE: a palliative care demonstration project for advanced cancer patients in three settings. *J Palliat Med.* 2004; 7(2):363–372. [PubMed: 15130218]
83. Elsayem A, Swint K, Fisch MJ, et al. Palliative care inpatient service in a comprehensive cancer center: clinical and financial outcomes. *J Clin Oncol.* 2004; 22(10):2008–2014. [PubMed: 15143094]
84. Meyers FJ, Linder J, Beckett L, Christensen S, Blais J, Gandara DR. Simultaneous care: a model approach to the perceived conflict between investigational therapy and palliative care. *J Pain Symptom Manage.* 2004; 28(6):548–556. [PubMed: 15589080]
85. Gade G, Venohr I, Conner D, et al. Impact of an inpatient palliative care team: a randomized control trial. *J Palliat Med.* 2008; 11(2):180–190. [PubMed: 18333732]
86. Passik SD, Ruggles C, Brown G, et al. Is there a model for demonstrating a beneficial financial impact of initiating a palliative care program by an existing hospice program? *Palliat Support Care.* 2004; 2(4):419–423. [PubMed: 16594406]
87. Schrag D. The price tag on progress—chemotherapy for colorectal cancer. *N Engl J Med.* 2004; 351(4):317–319. [PubMed: 15269308]
88. Meropol NJ, Schulman KA. Cost of cancer care: issues and implications. *J Clin Oncol.* 2007; 25(2):180–186. [PubMed: 17210937]
89. Hillner BE, Schrag D, Sargent DJ, Fuchs CS, Goldberg RM. Cost-effectiveness projections of oxaliplatin and infusional fluorouracil versus irinotecan and bolus fluorouracil in first-line therapy for metastatic colorectal carcinoma. *Cancer.* 2005; 104(9):1871–1884. [PubMed: 16177989]
90. Bodenheimer T, Berenson RA, Rudolf P. The primary care-specialty income gap: why it matters. *Ann Intern Med.* 2007; 146(4):301–306. [PubMed: 17310054]
91. Smith TJ, Girtman J, Riggins J. Why academic divisions of hematology/oncology are in trouble and some suggestions for resolution. *J Clin Oncol.* 2001; 19(1):260–264. [PubMed: 11134221]
92. Jacobson M, O’Malley AJ, Earle CC, Pakes J, Gaccione P, Newhouse JP. Does reimbursement influence chemotherapy treatment for cancer patients? *Health Aff (Millwood).* 2006; 25(2):437–443. [PubMed: 16522584]

93. Smith TJ, Coyne P, Cassel B, Penberthy L, Hopson A, Hager MA. A high-volume specialist palliative care unit and team may reduce in-hospital end-of-life care costs. *J Palliat Med.* 2003; 6(5):699–705. [PubMed: 14622449]
94. Campbell DE, Lynn J, Louis TA, Shugarman LR. Medicare program expenditures associated with hospice use. *Ann Intern Med.* 2004; 140(4):269–277. [PubMed: 14970150]
95. Benner SE, Fetting JH, Brenner MH. A stopping rule for standard chemotherapy for metastatic breast cancer: lessons from a survey of Maryland medical oncologists. *Cancer Invest.* 1994; 12(5): 451–455. [PubMed: 7922700]
96. Smith TJ, Bodurtha JN. Ethical considerations in oncology: balancing the interests of patients, oncologists, and society. *J Clin Oncol.* 1995; 13(9):2464–2470. [PubMed: 7666106]

**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 $\geq 3$ mo with acceptable toxicity, better symptom control, manageable toxicity <sup>34</sup>
Second-line (docetaxol)	Improves survival by about 2 mo vs best supportive care, with better symptom control while taking treatment <sup>35,36</sup>
Second- or third-line (erlotinib)	Improves survival by about 2 mo vs placebo, with acceptable toxicity <sup>37</sup>
Third- or fourth-line	Response rate only 2% and 0% when patients have previously received docetaxol and platinum <sup>40</sup>
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 <sup>41</sup>
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 <sup>38</sup>
Prostate cancer	
First-line chemotherapy	Docetaxol every 3 wk improves survival by 2.4 mo, with no adverse effect on quality of life. <sup>42</sup> Second-line chemotherapy can palliate symptoms and decrease prostate-specific antigen level but does not improve survival <sup>43</sup>

**Table 2**

## Things to Do or Say (and Not to Do or Say) About Chemotherapy for Advanced Cancer

<b>Do</b>	<b>Don't</b>	<b>Comment</b>
<b>Diagnosis</b>		
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."
<b>Treatment</b>		
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."
<b>End of Life or Cancer Progression</b>		
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.



Table 3

## Studies of Concurrent Palliative Care With Oncology Care

Source	Results	Comments
Finn et al, <sup>80</sup> 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, <sup>81</sup> 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, <sup>82</sup> 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, <sup>83</sup> 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, <sup>84</sup> 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, <sup>1</sup> 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.

## Why do our patients get chemotherapy until the end of life?

### the patient

Some years ago, I treated a 21-year-old woman. During her first pregnancy, an enlarging mass appeared in her right leg. Diagnostic procedures done after delivery indicated that she had alveolar rhabdomyosarcoma. She was referred to the cancer center for isolated limb perfusion, which was deemed impossible due to inguinal masses encountered during the attempt to cannalize the femoral vessels. A computed tomography scan showed peripheral micronodules in both lungs, after which she was referred to the medical oncology department for systemic chemotherapy. By then, the primary tumor was a fungating mass requiring morphine for pain control. Treatment with cyclophosphamide, doxorubicin and vincristine led to a prolonged hospital admission for bacterial sepsis, during which she was visited by her husband daily late after work and on Sundays by her family and the baby. On the subsequent cycle, and despite reduced chemotherapy doses, she again experienced severe hematological toxicity and no antitumor effect or decreased requirement of narcotics. Next, single-agent doxorubicin was administered in the outpatient clinic as an attempt to preserve quality of life. Still no antitumor or symptom response was achieved and multiple hospital admissions due to hematological toxicity ensued. Eventually, ifosfamide was prescribed in progressively lower doses due to increasing hematological toxicity but still without clinical benefit. She finally died of fungal sepsis, 3 months after being referred to the medical oncology department.

### the problem

This case illustrates therapeutic futility at the end of life. Why are we not ceasing chemotherapy when it is useless, toxic, logistically complex and expensive? Are we prescribing chemotherapy until too late in solid tumor patients' lives? Medical oncologists have overly optimistic predictions and, sometimes excessive, treatment-prone attitude and they are criticized by other health care providers for this. Increasingly, patients, their families, advocacy groups, policy makers, journalists and society at large dwell on this topic, which is a perplexing conundrum, because sometimes they are the ones demanding not to stop aggressive systemic anticancer treatments. There is a growing culture of awareness toward preserving quality of life, palliative care, symptom-directed care, hospice referral and end-of-life issues regarding terminal cancer patients. Sadly, this issue is gaining momentum, not because oncologists are questioning their practice but because

health care costs are soaring. Whatever the motive, the reasons for administering chemotherapy at the end of life should be known. Striking a balance is not easy. Hippocrates in 400 BC wrote, about medicine in general, an aphorism that illustrates this difficulty: Life is short, the art long; the occasion fleeting; experience fallacious and judgment difficult. Medical decision making on ceasing systemic chemotherapy remains a very complex, intimate and subjective process. There are few and conflicting scientific data to guide treatments in this delicate setting.

### the available data

What data do we have that characterizes the situation? Most of available data are retrospective death-centered studies, population or institution based [1]. The institution-based studies have access to the complete medical records where eventually data can be retrieved regarding decisions and goals of interventions. On the other hand, population-based studies, such as the one by Näppä et al. [2], and the Medicare system-based studies claim to picture reality in a more unbiased way.

In the current issue, Näppä et al. [2] examine chemotherapy administration in the last month of life. They have chosen a population-based cohort from Northern Sweden in which they were able to characterize 374 adults affected by solid tumors that were treated with chemotherapy in the last month of life. Their results show that one-fourth of Swedish terminal cancer patients still receive chemotherapy, which is in agreement with reports from other geographies. In this study, patients that receive chemotherapy have a shorter duration of metastatic disease, more hospital admissions and often lack a documented decision to stop chemotherapy.

Regarding other similar reports, two studies based on Medicare claims, encompassing roughly 8000 patients each, reported that 15% of terminal cancer patients receive chemotherapy in their last 2 weeks of life [3, 4]. In an institutional report from England, only 8% of the patients received chemotherapy in the last month of life but 7.5% and 4.3% of these patients had a toxic death or died of neutropenic sepsis, respectively [5]. Two institution-based studies from Italy showed that 23% and 15% of advanced cancer patients are receiving chemotherapy in the last month of life [6, 7]. Two similar Portuguese studies showed 37% and 13% of the patients being treated with chemotherapy in the last month of life [8, 9]. Further examples include two Korean reports, one where 30% of the patients receive chemotherapy in the last month of life and another where 50% receive treatment in the last 2 months of life [7, 10], and an Australian publication showing that 18% of cancer patients are being treated in the last month of life [11].

In these studies, the parameters presented as being predictors of receiving chemotherapy were young age, short metastatic

disease course, tumor type and chemosensitivity of the tumor. Tumor type data show that lung cancer patients are overrepresented possibly because of frequent metastatic disease at diagnosis and short life span. In fact, 43% of non-small-cell lung cancer patients treated by community oncology clinics across the United States receive chemotherapy in the last month of life and 20% in the last 2 weeks [12].

In summary, up to a fifth of cancer patients are treated with chemotherapy in the last month of life without clear benefits (e.g. no prolongation of life) and sometimes even with visible negative consequences (increased toxicity, costs and decreased quality of life). The need to critically evaluate chemotherapy prescription in this context evokes four questions discussed below.

### will the patient benefit?

Can doctors estimate patient survival in an accurate way? Most likely no; all physicians, oncologists in particular, tend to overestimate survival due to multiple reasons: strong emotional bonding, underestimating catastrophic complications and relative or forced stability during the doctor visit. A strategy to overcome this is to make frequent reassessments and ask experienced colleagues who have been shown to make more accurate predictions. It may also be beneficial to use evaluators like the Karnofsky performance score, the World Health Organization performance status, specific palliative scores or the assessment of specific symptoms. In the case of symptoms, the most informative are anorexia, weight loss, xerostomia, dysphagia and dyspnea. Among other validated variables are blood biochemical tests (e.g. low albumin, high lactate dehydrogenase, high interleukin-6) and cell counts (e.g. high white blood cell counts, low lymphocyte counts) [13]. Several attempts have been made to use algorithms for death prediction in terminal cancer patients but these have not met with general acceptance because of inefficacy, difficult implementation and ultimately because in terminal care the patient is viewed globally and thus such scoring systems are viewed as an oversimplification.

Is it appropriate to start or to continue chemotherapy? What are the symptoms? Are they cancer or toxicity related? If the main problems are pain, asthenia and cachexia, chemotherapy may not be the only and sometimes not even the most appropriate solution for them since it may exacerbate them. Performance status; asthenia; weight loss; marrow, cardiac and lung reserve as well as kidney and liver function help guiding the evaluation of the relative risks and benefits of using chemotherapy. If chemotherapy is agreed upon, this decision should be reevaluated frequently. The careful weighing of clinical benefits and risks is the core of this issue: *Primum non nocere*. In the majority of solid tumors of adults, a classic rule still stands that after three failed lines of chemotherapy the possibility of benefit with a fourth line is minute. However, there are exceptions, for example, in breast cancer, especially Her2-positive disease [14].

In short, chemotherapy should be limited to ambulatory outpatients with good performance status, except in untreated chemosensitive solid tumors or malignancies that are specifically affecting the ability to walk. The goals of palliative

chemotherapy differ from those of curative chemotherapy because metastatic solid tumors are generally incurable; the aim is to increase survival. Furthermore, instead of focusing on lesion diameter shrinkage, a clinical trial end point, clinically relevant outcome measures like symptoms are possibly more adequate.

### what does the patient want?

There are important cultural and religious variations in the acceptance of death. Data show that patients with high levels of positive religious coping tend to receive intensive life-prolonging care possibly because they believe in miracles and divine interventions [15]. However, if a religious counselor is provided from within the oncology staff, it reduces aggressive end-of-life care and increases hospice use [16]. Does the acceptance of death mean that all hope is lost? Hope is an important defensive mechanism. Somewhat paradoxically, there are data showing that giving honest information, even bad, maintains hope [17]. Some patients want to live a specific event before feeling prepared to die. If not possible, patients can find other ways to get a sense of purpose out of the event, such as writing a letter or recording a legacy. Many patients and families get great satisfaction from this.

There are tools and checklists for communicating bad news. During consultation, one can follow the stepwise approach of the SPIKES acronym: choose a setting (i), assess perception of the disease (ii), invite the patient to hear (iii), transmit knowledge (iv), assess emotional reaction with empathy (v) and summarize the care plan (vi) [18]. Why is not communication more effective? It is not because patients and families cannot bear to be informed on prognosis, it is because oncologists are insufficiently trained and, even for experienced physicians, giving bad news is just too hard. A simulated consultation study reported that poor performance was correlated with emotional burnout and fatigue but not inexperience [19]. In a study that recorded hematological oncology consultations in tertiary centers, cure was not discussed quantitatively or at all in half of them [20]. A prospective study on palliative chemotherapy versus watchful waiting in advanced cancer patients showed that only 39% of patients reported discussing prognosis with the attending oncologist. In a longitudinal study, in admitted terminally ill cancer patients, 39% of the patients and 62% of the families said that the possibility of death had not been discussed [21]. Research shows that patients know more about their disease and their treatments at the time of diagnosis than at the time of relapse, progression and near death. One of the reasons for this discrepancy is that the established closer proximity between doctor and patient interferes with the physicians' capacity to communicate unpleasant news [22]. Data show that when information is given to patients, it is provided with a range of values and patients cope with it by hoping to belong to the favorable tail of the distribution [21].

Information pays off. If physicians have discussed care at the end of life with their patients, patients are more likely to receive care according to their needs and preferences [23]. Additionally, when informed about their terminal illness, patients more often choose symptom-directed care [23].

Regarding biased or lack of information, a randomized trial of the use of the decision aid Adjuvant! for adjuvant breast cancer chemotherapy prescription concluded that only 58% (35 of 60) of the women who used the tool chose chemotherapy, while 87% (33 of 38) of the women that were informed by physicians chose it [24]. This is an indication that patients have unrealistically optimistic expectations on the benefits of chemotherapy.

In summary, fully understanding terminal patients' wishes and goals, realistically addressing the potential and limitations of palliative chemotherapy and discussing end-of-life logistics are items of successful communication that might help spare useless treatments.

### can the patient get better care?

It is harder to provide a good death than to cure a patient. Research has shown that terminal patients want to die at home, with loved ones, with symptom control, feeling independent and as conscious as possible [25]. For most cancer patients, this is difficult but achievable with the aid of specific skills that unfortunately are not widespread. For example, in a survey to second-year oncology fellows, only 23% carried out correctly an opioid conversion [26]. Cancer death is predictable, i.e. bedridden, pain, dyspnea, cachexia, anorexia, constipation, dehydration, fleeting consciousness and coma; therefore, it is easy to prepare families for it. After death, there might be an urge to move on, but, families in bereavement need follow-up, provide feedback and studies show it to be insufficient [27].

In the last decade, there was an expansion of palliative care units with doctors, nurses and supportive staff, dedicated full time to the terminally ill, that have shifted gear from a cancer-centric approach to a patient-centered approach. Palliative care should be gradually integrated so that the patient, family and medical oncology team do not feel as they are getting rid of the patient to die under the care of another team, away from the environment they lived in during the most extensive and easier part of the disease. The intervention of a palliative care team should start at the time of distant dissemination because the majority of metastatic patients are incurable. As the disease progresses, the emphasis slowly shifts from one of aggressive antitumor treatment to more focus on palliation. Near death, the only treatment is palliation with no blood tests, artificial feeding, emergency room or intensive care unit admissions because families communicate by phone with the staff that visits at home. Why, then, are patients and families sometimes reluctant to accept this? Apparently due to lack of information. Studies have shown higher use of hospice care by informed patients [21]. Additionally, palliative care should not be a one-way road. Different reimbursement systems in some countries might preclude the utilization of hospice care because patients transferred to hospice lose the rights to cancer center care. It would be an improvement if in this setting patients gained rights instead of losing rights.

Is chemotherapy more effective than best supportive care as treatment of metastatic cancer? This depends on how one defines 'effective'. If it is survival, then, yes, chemotherapy prolongs survival in the majority of metastatic solid tumors of adults. So the question is not if it should be administered but

rather until when should it be administered. On the other hand, if effective means achieving a 'good death', with symptom control and quality of life, chemotherapy is not as good. But, do hospice patients die sooner? A retrospective study designed to answer this question actually found either prolongation of life, in case of lung cancer, or no difference, in case of three other common solid tumors (breast, colon and prostate carcinomas). This study is based on Medicare records and the inclusion criteria for the hospice care group is one Medicare claim. Therefore, it might reflect better care in general and not necessarily capture the dichotomy between chemotherapy administration and symptom control [28].

Finally, research must be conducted regarding end-of-life care to identify which patients are best managed with etiological versus symptomatic approach. Qualitative outcomes and health services research increased through the 90s and peaked in 2000 [29]. Futility, toxicity and aggressiveness are measured by following patients with a predicted reduced life span prospectively and collecting data on the justifications, decisions and goals of terminal care interventions and recording indicators of aggressiveness, like emergency room, intensive care unit admissions and surgeries.

### are there conflicts?

Oncologists are frequently subject to pressure sometimes from patients but more often from families to continue therapies of doubtful efficacy [30]. Conflict often starts with members of the family that are absent or health illiterate [31].

There are health care systems in which the physician and the institution are better reimbursed for chemotherapy administration and by requesting radiological examinations than for carrying out a complex cognitive discussion. In fact, there are systems where burdensome family conferences are not reimbursed. This creates a perverse incentive because the hardest actions are poorly compensated, while the easier ones are more lucrative. This would be avoided if reimbursement was done on the basis of consultation with the physician with no link to drug administration. Additionally, admitting that there are better alternatives for symptom control and quality of life preservation might include the referral to another team of physicians and the potential loss of the patient as client of the clinic.

Lastly, why is not there more research on terminal cancer care, as has been discussed? Clinical cancer research mainly asks drug-oriented questions by doing clinical trials. But even academic trials led by institutions and collaborative groups are exquisitely dependent on pharmaceutical industry funding to happen. It is extremely difficult to fund applied clinical research questions that do not involve drugs; this might be one of the reasons it is less attractive.

### the patient, again

At this point, I return to the initial story and imagine how I could have done better. Regarding the first question, I should have assumed that widely metastatic alveolar rhabdomyosarcoma was likely to be chemoresistant. The specific disease had taken an aggressive biological behavior, the

lesion was increasing daily and the natural history of the untreated primary had only 4 months. I should have set my goals accordingly. The patient, who was supposedly a fit young woman, had feeble marrow reserve, possibly because of infiltration, which I should have diagnosed. Her performance status was three, i.e. she was partially bedridden, with lung metastases, so the potential for infectious complications, with the regimens used, was high. Her symptoms were pain in the primary lesion, which was well controlled with morphine, and she was not dyspneic.

Regarding the three other questions: What did she want? She wanted to be with her baby daughter, husband and parents, at home. Was there a better team to care for her? Possibly, yes. I do not think that she would have objected to a discussion about therapeutic futility and end-of-life care by different staff, provided the medical oncology team could remain available. Were there conflicts? Not at all. They had accepted distressingly peacefully the catastrophe of incurable cancer at a young age.

What went wrong? Why did this young woman get chemotherapy until the end of life? Clearly because I failed. I hope I have learned the lesson.

## funding

The Programme for Advanced Medical Education is sponsored by Fundação Calouste Gulbenkian, Fundação Champalimaud, Ministério da Saúde e Fundação para a Ciência e Tecnologia, Portugal.

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## disclosure

The author declares no conflict of interest.

## references

- Earle CC, Ayanian JZ. Looking back from death: the value of retrospective studies of end-of-life care. *J Clin Oncol* 2006; 24: 838–840.
- Näppä U, Lindqvist O, Rasmussen BH, Axelsson B. Palliative chemotherapy during the last month of life. *Ann Oncol* 2011; 11: 2375–2380.
- Emanuel EJ, Young-Xu Y, Levinsky NG et al. Chemotherapy use among Medicare beneficiaries at the end of life. *Ann Intern Med* 2003; 138: 639–643.
- Earle CC, Neville BA, Landrum MB et al. Trends in the aggressiveness of cancer care near the end of life. *J Clin Oncol* 2004; 22: 315–321.
- O'Brien ME, Borthwick A, Rigg A et al. Mortality within 30 days of chemotherapy: a clinical governance benchmarking issue for oncology patients. *Br J Cancer* 2006; 95: 1632–1636.
- Andreis F, Rizzi A, Rota L et al. Chemotherapy use at the end of life. A retrospective single centre experience analysis. *Tumori* 2011; 97: 30–34.
- Matsuyama R, Reddy S, Smith TJ. Why do patients choose chemotherapy near the end of life? A review of the perspective of those facing death from cancer. *J Clin Oncol* 2006; 24: 3490–3496.
- Braga S, Miranda A, Fonseca R et al. The aggressiveness of cancer care in the last three months of life: a retrospective single centre analysis. *Psychooncology* 2007; 16: 863–868.
- Gonçalves J, Goyanes C. Use of chemotherapy at the end of life in a Portuguese oncology center. *Support Care Cancer* 2008; 16: 321–327.
- Kear B, Oh DY, Lee SH et al. Aggressiveness of cancer-care near the end-of-life in Korea. *Jpn J Clin Oncol* 2008; 38: 381–386.
- Kao S, Shafiq J, Vardy J, Adams D. Use of chemotherapy at end of life in oncology patients. *Ann Oncol* 2009; 20: 1555–1559.
- Murillo JR, Koeller J. Chemotherapy given near the end of life by community oncologists for advanced non-small cell lung cancer. *Oncologist* 2006; 11: 1095–1099.
- Christakis NA, Lamont EB. Extent and determinants of error in doctors' prognoses in terminally ill patients: prospective cohort study. *BMJ* 2000; 320: 469–472.
- Smith TJ, Hillner BE. Bending the cost curve in cancer care. *N Engl J Med* 2011; 364: 2060–2065.
- Phelps AC, Maciejewski PK, Nilsson M et al. Religious coping and use of intensive life-prolonging care near death in patients with advanced cancer. *JAMA* 2009; 301: 1140–1147.
- Balboni TA, Paulk ME, Balboni MJ et al. Provision of spiritual care to patients with advanced cancer: associations with medical care and quality of life near death. *J Clin Oncol* 2010; 28: 445–452.
- Smith TJ, Dow LA, Virago E et al. Giving honest information to patients with advanced cancer maintains hope. *Oncology (Williston Park)* 2010; 24: 521–525.
- Back AL, Arnold RM, Baile WF et al. Efficacy of communication skills training for giving bad news and discussing transitions to palliative care. *Arch Intern Med* 2007; 167: 453–460.
- Brown R, Dunn S, Byrnes K et al. Doctors' stress responses and poor communication performance in simulated bad-news consultations. *Acad Med* 2009; 84: 1595–1602.
- Alexander SC, Sullivan AM, Back AL et al. Information giving and receiving in hematological malignancy consultations. *Psychooncology* 2011. Published online in Wiley Online Library ([wileyonlinelibrary.com](http://wileyonlinelibrary.com)). DOI: 10.1002/pon.1891.
- Harrington SE, Smith TJ. The role of chemotherapy at the end of life: "when is enough, enough?" *JAMA* 2008; 299: 2667–2678.
- Hoff L, Tidefelt U, Thaning L, Hermerén G. In the shadow of bad news—views of patients with acute leukaemia, myeloma or lung cancer about information, from diagnosis to cure or death. *BMC Palliat Care* 2007; 6: 1.
- Mack JW, Weeks JC, Wright AA et al. End-of-life discussions, goal attainment, and distress at the end of life: predictors and outcomes of receipt of care consistent with preferences. *J Clin Oncol* 2010; 28: 1203–1208.
- Peele PB, Siminoff LA, Xu Y, Ravdin PM. Decreased use of adjuvant breast cancer therapy in a randomized controlled trial of a decision aid with individualized risk information. *Med Decis Making* 2005; 25: 301–307.
- Goodman D. End-of-life cancer care in Ontario and the United States: quality by accident or quality by design? *J Natl Cancer Inst* 2011; 103: 840–841.
- Buss MK, Lessen DS, Sullivan AM et al. Hematology/oncology fellows' training in palliative care: results of a national survey. *Cancer* 2011. Published online in Wiley Online Library ([wileyonlinelibrary.com](http://wileyonlinelibrary.com)) DOI: 10.1002/cncr.25952.
- Chau NG, Zimmermann C, Ma C et al. Bereavement practices of physicians in oncology and palliative care. *Arch Intern Med* 2009; 169: 963–971.
- Connor SR, Pyenson B, Fitch K et al. Comparing hospice and nonhospice patient survival among patients who die within a three-year window. *J Pain Symptom Manage* 2007; 33: 238–246.
- Borreani C, Miccinesi G, Brunelli C, Lina M. An increasing number of qualitative research papers in oncology and palliative care: does it mean a thorough development of the methodology of research? *Health Qual Life Outcomes* 2004; 2: 7–7.
- Morita T, Akechi T, Ikenaga M et al. Communication about the ending of anticancer treatment and transition to palliative care. *Ann Oncol* 2004; 15: 1551–1557.
- Smith AK, Sudore RL, Pérez-Stable EJ. Palliative care for Latino patients and their families: whenever we prayed, she wept. *JAMA* 2009; 301: 1047–1057, E1.