

Virtual Mentor

American Medical Association Journal of Ethics
August 2013, Volume 15, Number 8: 649-652.

ETHICS CASE

End-of-Life Decisions and Off-Label Drug Use

Commentary by Laura L. Tenner, MD, and Paul R. Helft, MD

With a mix of sympathy and admiration, Dr. Smith looked down at Mr. Johnson, sleeping uncomfortably on his hospital bed. Mr. Johnson had been diagnosed with lung cancer nearly 2 years before, at 70, and had remained remarkably upbeat and optimistic despite a very difficult treatment course.

“I still have a lot to live for, doc,” he routinely told Dr. Smith. “I’m gonna fight this thing. I want to be there for my family.”

Mr. Johnson had been through three rounds of chemotherapy and was now on his fourth regimen. Initially, he responded quite well, but over the past several months, his tumors continued to grow, and the side effects of treatment were becoming increasingly difficult to tolerate. He was constantly nauseated and severely fatigued. Yet he remained devoted to continuing treatment and exploring new options.

Dr. Smith had spoken with Mr. Johnson and his family several times about the possibility of moving from disease-directed therapy to palliative and end-of-life care. He felt that more chemotherapy would be likely to cause a further decline in Mr. Johnson’s quality of life without having any effect on his cancer and worried that it might even shorten Mr. Johnson’s life. Mr. Johnson’s family said they understood that prospects for recovery were bleak, but wanted to exhaust “all available options before giving up.” They approached Dr. Smith about a new drug that a family friend—also a physician—had mentioned. Dr. Smith had previously considered the drug but decided against using it for several reasons: it carried a very significant side effect profile, it had not been approved for use in Mr. Johnson’s cancer, there was only limited evidence that it had the potential to improve survival by 1 or 2 months, and it was extremely expensive.

Given this profile and Mr. Johnson’s poor condition, Dr. Smith believed starting this treatment would be an inappropriate course of action. However, both Mr. Johnson and his family seemed determined to pursue further treatment with this drug. As he contemplated how to proceed with the family meeting, Dr. Smith wondered whether he should respect Mr. Johnson’s desire to continue further cancer therapy even at the end of his life.

Commentary

This case scenario involves some of the most difficult issues practicing oncologists face in treating patients with advanced cancer nearing the end of their lives. Trying to provide compassionate, respectful, and appropriate care while navigating patient and family expectations is a challenge for any physician. Especially in the setting of

a longstanding relationship with a patient, the oncologist may find it difficult to say no to further disease-directed therapy near the end of life. Though oncologists have patients' best interest at heart, refusing to provide further therapy that has limited efficacy can often cause a rift in the patient-physician relationship.

In situations where the patient and the physician remain in disagreement over the correct therapeutic course, the patient may choose to search out other institutions or other physicians to provide the desired treatments. This is a less-than-ideal outcome insofar as the patient-physician relationship has been severed and the patient may still be exposed to further harm. Skillful and empathic communication can often aid physicians in avoiding such outcomes. While these patient and family discussions are fraught with complexity, some tools can help direct the shared decision-making process and preserve the patient-physician relationship. We address several of the concerns in this case vignette, including the ethical and communicative dimensions, and suggest ways of reframing aspects of the interaction that are among the most challenging.

An important component of any communication strategy is to validate the complex emotions the patient is experiencing. As in the above vignette, the patient told Dr. Smith that he was going to "fight this thing" because he wants to be there for his family. Timothy Quill, Robert Arnold, and others have pointed out that such statements are better understood not as literal directives about patients' preferences for therapy but rather as reflective of emotional distress [1]. In response to such statements, one adaptive strategy can be to address them as a plea for emotional support: "I hear you saying that the most important thing in your life is your family, and, more than anything else, you don't want them to have to live without you." By reiterating the sentiments, you are hearing the patient's concerns, validating his or her emotions, and allowing further exploration of fears, hopes, and wishes, but without fostering unrealistic or harmful conceptions of goals. Eliciting concerns and expressing empathy can help patients cope with negative emotions [2].

Another important part of such patient and family discussions is defining the patient's preferences and goals. In the above vignette, the patient and family are equating stopping chemo with giving up. This is a common belief among patients and families. Reframing the idea of "giving up" can be helpful. Discontinuing ineffective treatments that are more likely to cause harm than good does not mean that one is giving up. Indeed, sometimes withdrawal of chemotherapy leads to an improved quality of life that allows patients to eat more, sleep better, and become more active. In addition, therapeutic interventions often come with the risk of significant adverse events. Explaining to patients that, though some interventions may control disease by months or slow progression, this may not extend overall survival or improve quality of life [3]. Reframing the cessation of aggressive disease-directed therapy as an opportunity to refocus efforts on maximizing the quality of the patient's life can allow the patient to turn away from equating cessation of disease-directed therapy with giving up or "doing nothing."

Other points to consider are the physician's responsibility to uphold the ethical principles of beneficence (the promotion of well-being) and nonmaleficence (the avoidance of harm) [4, 5]. Though patient preferences should guide physician care, the physician should not feel ethically bound to provide aggressive disease-directed therapy that he or she deems to offer a poor risk-benefit ratio. If the physician truly feels that the therapy is more likely to harm than benefit the patient, then the value of the principles of nonmaleficence and beneficence should outweigh the value of preserving the patient's autonomy. In other words, a patient's request or demand for treatment does not obligate a physician to provide it, if the physician thinks it will cause more harm than good. *Primum non nocere*.

Mr. Johnson has already experienced significant side effects from the four regimens, and the off-label treatment he is requesting carries a significant side-effect profile with limited data to support its benefits. For off-label treatments, especially, substantial evidence of safety and efficacy must be present before they are considered for use outside a clinical trial [6]. In the setting of a decrease in overall functioning and significant accumulated side effects from prior treatments, further off-label experimental drugs will most likely cause more harm than benefit.

The number one recommendation on the American Society of Clinical Oncology's "top five list" of tests and treatments that are commonly performed in oncology despite a lack of evidence that they provide meaningful benefit states that "for patients with advanced solid-tumor cancers who are unlikely to benefit, do not provide unnecessary anticancer therapy, such as chemotherapy, but instead focus on symptom relief and palliative care" [7]. The physician is ethically obligated to refuse to offer a therapy with an unacceptably poor risk-benefit ratio. It is essential, however, to stress that this "compassionate refusal," must emphasize that the reasons for refusal arise from of the physician's resolute commitment to the patient's best interest.

Cost considerations, mentioned in the vignette may play a role in physician decision making or shared decision making, but it is unknown whether physicians feel comfortable exploring this avenue of discussion with patients. In a 2010 *New England Journal of Medicine* article, Cooke claims that "being a physician is not just about finding benefit for patients; it is also about helping them to understand value" [8]. As in our case above, the great expense coupled with limited data on efficacy suggest that using an unproven therapy such as the drug the patient requests represents poor value. Further challenges are that cost consideration must be, as Cooke states, explicit, transparent, and consistent, and, furthermore, "physicians must be provided with the skills to discuss value with patients honestly, effectively and compassionately" [9]. Further study in cost communication with patient and family members is needed, so that physicians can feel better prepared to engage in conversations about costs with patients.

In conclusion, physicians should not feel bound to provide care that they think will harm the patient. However, physicians should, without compromising their values, maintain the physician-patient relationship to the best of their ability through open

communication and empathic listening, incorporating the techniques of emotional validation and goal-directed therapy.

References

1. Quill TE, Arnold R, Back AL. Discussing treatment preferences with patients who want “everything.” *Ann Intern Med.* 2009;151(5):345-349.
2. Evans WG, Tusky JA, Back AL, Arnold RM. Communication at times of transitions: how to help patients cope with loss and re-define hope. *Cancer J.* 2006;12(5):417-424.
3. Peppercorn JM, Smith TJ, Helft PR, et al. American Society of Clinical Oncology statement: toward individualized care for patients with advanced cancer. *J Clin Oncol.* 2011;29(6):755-760.
4. Beauchamp TL, Childress JF. *Principles of Biomedical Ethics.* 6th ed. New York: Oxford University Press; 2009.
5. Luce JM. Physicians do not have a responsibility to provide futile or unreasonable care if a patient or family insists. *Crit Care Med.* 1995;23(4):760-766.
6. Peppercorn JM. Off-protocol therapy in oncology [2009]. <http://meetinglibrary.asco.org/sites/meetinglibrary.asco.org/files/Educational%20Book/PDF%20Files/2009/09edbk.ethics.01.pdf>. Accessed July 10, 2013.
7. Schnipper LE, Smith TJ, Raghavan D, et al. American Society of Clinical Oncology identifies five key opportunities to improve care and reduce costs: the top five list for oncology. *J Clin Oncol.* 2012;30(14):1715-1724.
8. Cooke M. Cost consciousness in patient care—what is medical education’s responsibility? *N Engl J Med.* 2010;362(14):1254.
9. Cooke, 1255.

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