

# ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

Section Editor: Mark J. Ratain, MD

## Direct-to-Consumer Advertising of Cancer Treatments



Lowell E. Schnipper, MD  
 Theodore and Evelyn Berenson Distinguished Professor  
 of Medicine in the Field of Oncology  
 Harvard Medical School  
 Clinical Director, Cancer Center  
 Chief, Hematology/Oncology Division, Emeritus  
 Beth Israel Deaconess Medical Center  
 Boston, Massachusetts

### **H&O** What have studies shown about direct-to-consumer advertising of medical treatments?

**LS** A few studies have evaluated direct-to-consumer advertising of medical treatments, but they are not the most authoritative because they are not easy to conduct. Gregory A. Abel, MD, MPH, has published studies on patient awareness and prescribing habits.<sup>1,2</sup> For the study on patient awareness, Dr Abel mailed questionnaires to patients who were receiving cancer treatments to assess their awareness of advertising. The study found that patients were highly aware of this type of advertising, and that it prompted a modest amount of discussion with their healthcare provider. Few patients, however, reported changes in therapy. The study on prescribing patterns found that for every million dollars spent on direct-to-consumer advertising for aromatase inhibitors, there was an associated increase 3 months later in appropriate prescriptions, but no significant change for inappropriate prescriptions.

In the oncology setting, direct-to-consumer advertising does not appear to have a major impact on the prescribing patterns of doctors or cause patients to insist on a particular therapy. Small changes were noted, but they were not inappropriate to the clinical indication.

### **H&O** Are there particular disadvantages to advertising treatments for cancer compared with other medical conditions?

**LS** As mentioned in an editorial I wrote with Dr Abel, there are several disadvantages.<sup>3</sup> Patients with cancer are

quite appropriately scared and oftentimes frightened of their own death. I would consider them a very vulnerable audience for advertising that depicts or even suggests an overly generous likelihood of favorable response or survival. Current television commercials tend to show relatively healthy-looking people with family members or friends; in some of them, the people look skyward with hopeful glances. At the end, the drug name appears, with the suggestion that now there is hope.

We know that patients identify with even the smallest chance of a favorable outcome—thinking, hoping, and wishing they will benefit. The concern is that the positive outcome highlighted in advertisements can create inappropriately high expectations of the treatment and the doctor, which might interfere with an honest discussion of what course the illness is likely to take. An advertisement may prompt a patient to ask his or her doctor about a different approach to treatment. It seems unlikely that the management plan will be altered, however, because oncologists are almost certainly aware of all treatment options for a given patient. Addressing the patient's question could divert the discussion the physician was planning to have about appropriate therapy and prognosis. The conversation can be a disappointment for patients with exaggerated expectations, who were hoping that a particular treatment might help them, as it appears to be helping others.

Another concern is that the current advertisements are reporting data based on clinical trials that are not definitive in every aspect. For example, in nonsquamous non-small-cell lung cancer, nivolumab (Opdivo, Bristol-Myers Squibb) improved overall survival by a median of

approximately 3 months compared with docetaxel.<sup>4</sup> The response rate was 19% with nivolumab vs 12% with docetaxel. Overall, approximately 10% to 20% of patients will do well with these therapies, so this is a small group. It is not yet possible to predict which patients will benefit from treatment, so we talk about population benefits. The advertisements do include a monotonic recitation of the adverse events, but without mentioning how common or debilitating they are. Patients require honest information about the modest improvement in survival and the risk of side effects.

Many advertisements are for drugs that were recently approved by the US Food and Drug Administration (FDA), and the long-term side effects or consequences are not known. There is a legitimate safety issue, as illustrated by the experience with epoetin alfa (Epogen, Amgen).<sup>5,6</sup> This therapy was advertised broadly to the public and to doctors as the antidote to cancer fatigue and an important adjunct to cancer therapy for all patients. It was widely utilized, although it is not possible to say to what extent advertising to the public contributed to this use. Approximately 10 years after the introduction of the drug, several studies found that death rates from cancer were higher among patients who used epoetin alfa compared with those who did not. As a result, the FDA added a black box warning stating that erythropoietin-stimulating agents should not be used within curative cancer settings.

Pharmaceutical companies are currently spending billions on direct-to-consumer advertising, whereas 10 or 15 years ago, they were spending millions. They must think it works, perhaps more so in diseases other than cancer. In the oncology setting, I do not think that direct-to-consumer advertising influences treatment decisions, but it can provide patients with misinformation or misguided hope.

The American Medical Association (AMA) and other organizations have indicated a strong position against direct-to-consumer advertising for drugs. The AMA has called for a ban,<sup>7</sup> which I support. The FDA has been unwilling to accede to these wishes because of the First Amendment of the US Constitution, which guarantees free speech. Banning these types of advertisements is therefore probably not an option, despite the fact that New Zealand and the United States are the only 2 countries in the world that permit them.

### **H&O** What regulations must direct-to-consumer advertising meet?

**LS** The FDA evaluates direct-to-consumer advertisements to determine whether they are factual and do not exaggerate, misstate claims, or promote potentially errant interpretations, particularly for medically

unsophisticated but emotionally vulnerable people—in other words, those with a serious illness. Assessment of benefit vs risk is needed for virtually all treatments, particularly cancer therapies. Advertisements should not raise expectations too high, omit the potential side effects, minimize their danger, or exaggerate the prognosis of an incurable disease.

To address misleading advertisements, the FDA can issue a Notice of Violation (known as an untitled letter), a warning letter, and an injunction.<sup>8</sup> The Notice of Violation describes the FDA's concerns. The warning letter gives the advertiser a deadline to respond to the concerns. The FDA can ask companies to stop running a particular advertisement, and to create new ads to correct any misleading claims. If the warning letter does not work, then the FDA can ask the Department of Justice to issue an injunction. Further options include civil monetary penalties, product seizures, and withdrawal of approval for sale. These actions are rare.

It is not known how much the feedback from the FDA influences advertisers. The compiled data show that the FDA has focused its warning letters concerning improper direct-to-consumer advertising disproportionately to the oncology community, meaning oncology drug producers. There is a perception within the FDA that some of these advertisements contain exaggerations and/or fail to accurately describe adverse events.

### **H&O** Have you noticed any differences in patient behaviors or expectations since direct-to-consumer advertising became more common?

**LS** I have not noticed any differences in patient behavior. However, there were some interesting data from a recent study performed by my colleague Jennifer S. Temel, MD, a lung cancer oncologist at Massachusetts General Hospital.<sup>9</sup> In Dr Temel's study, patients with incurable lung or gastrointestinal cancer were given a detailed explanation of the gravity of their illness and the treatment possibilities. Patients were told that treatments were available, but that they were not curative. Patients in the study could choose to be in a control group, which received usual oncologic supportive care, or to enroll in a palliative care program to help manage their cancer symptoms and any emotional issues.

In a personal communication, Dr Temel stated that a substantial portion of the patients in the study still thought that their cancer was curable, even after being informed that it was not. So what does that tell us? As oncologists know, patients have a healthy degree of denial. It is not necessary to tamper with this denial if it appears to be beneficial; patients should not be living in terror. However, you do not want patients to make unrealistic decisions based on inaccurate expectations.

A patient's hope and denial can be fueled by a beautiful television advertisement that shows healthy-looking cancer patients gazing skyward. This type of advertising can touch spiritual buttons and raise hope that might be inappropriate in many cases.

**H&O** Do you think that direct-to-consumer advertising has impacted the way clinicians practice and/or interact with patients?

**LS** I do not think so.

**H&O** Are there any benefits to direct-to-consumer advertising?

**LS** There are potential benefits. Direct-to-consumer advertising could lead to some degree of education about how to approach a given illness. Cancer is unique in that patients must receive treatment from physicians with specialized expertise. This type of advertising could raise questions that stimulate the patient to seek answers from his or her physician, and this can lead to a discussion that illuminates the illness as well as the possibilities or limitations of treatment.

**H&O** Are there ideas on how to expand regulation of direct-to-consumer advertising?

**LS** Physicians from Dartmouth proposed the use of a Drug Facts Box, a 1-page summary of data listing the benefits and harms for each indication of a drug.<sup>10</sup> The Drug Facts Box aimed to provide clear, balanced content about drugs or a class of drugs. Many therapies on the market are just “me-too drugs,” and it can be difficult for patients to distinguish among them. The Drug Facts Box was presented to the FDA, but it was dismissed as too complicated and impractical to implement.

**H&O** Are there ways to counterbalance direct-to-consumer advertising?

**LS** Physicians should provide detailed, balanced information when they meet with the patient and his or her family. This is an idealized scenario, however. Doctors are being forced to see patients in shorter and shorter time frames. The kinds of discussions that enable a broad understanding of the particular place for a given therapy must be integrated with discussion of prognosis, interpretation of symptoms, and a management plan for symptoms. Assuming that the patient and the

doctor have a positive line of communication based on trust, this type of detailed discussion can address any misunderstandings and misapprehensions, and provide a reality-based consideration of the patient's illness. That would be a boon to all.

**H&O** Do you have any suggestions on how to improve communication with patients?

**LS** Doctors must be sensitive to the needs of the patient, in terms of how much information to provide, and at what point in the illness and at what level of detail. Doctors must be aware of the nuances inherent within different cultural backgrounds, and how they might influence the patient. The sociomedical dimensions of medicine—meaning the dialogue, communication, and emotional and intellectual understanding between patient and doctor—should be valued as much as prescribing a drug that is eligible for reimbursement. Doctors must spend time with their patients, and because that time is very valuable, it must be viewed as a critically important part of the care equation and compensated no differently than other, more measurable areas of compensation, such as a cost of a prescribed or dispensed drug.

#### Disclosure

*Dr Schnipper is the co-Editor-in-Chief of the UpToDate oncology content.*

#### References

1. Abel GA, Burstein HJ, Hevelone ND, Weeks JC. Cancer-related direct-to-consumer advertising: awareness, perceptions, and reported impact among patients undergoing active cancer treatment. *J Clin Oncol.* 2009;27(25):4182-4187.
2. Abel GA, Chen K, Taback N, Hassett MJ, Schrag D, Weeks JC. Impact of oncology-related direct-to-consumer advertising: association with appropriate and inappropriate prescriptions. *Cancer.* 2013;119(5):1065-1072.
3. Schnipper LE, Abel GA. Direct-to-consumer drug advertising in oncology is not beneficial to patients or public health. *JAMA Oncol.* 2016;2(11):1397-1398.
4. Borghaei H, Paz-Ares L, Horn L, et al. Nivolumab versus docetaxel in advanced nonsquamous non-small-cell lung cancer. *N Engl J Med.* 2015;373(17):1627-1639.
5. Brower V. Erythropoietin may impair, not improve, cancer survival. *Nat Med.* 2003;9(12):1439.
6. Debeljak N, Solár P, Sytkowski AJ. Erythropoietin and cancer: the unintended consequences of anemia correction. *Front Immunol.* 2014;5:563.
7. AMA calls for ban on DTC ads of prescription drugs and medical devices. <https://www.ama-assn.org/content/ama-calls-ban-direct-consumer-advertising-prescription-drugs-and-medical-devices>. Posted November 17, 2015. Accessed August 24, 2017.
8. Direct-to-consumer advertising of prescription drugs. <https://www.everycrsreport.com/reports/R40590.html>. Posted May 20, 2009. Accessed August 24, 2017.
9. Nipp RD, Greer JA, El-Jawahri A, et al. Coping and prognostic awareness in patients with advanced cancer. *J Clin Oncol.* 2017;35(22):2551-2557.
10. Schwartz LM, Woloshin S. The drug facts box: improving the communication of prescription drug information. *Proc Natl Acad Sci U S A.* 2013;110(suppl 3):14069-14074.