# Helping Cancer Patients to Understand New 'Right-to-Try' Law

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Cancer specialists are preparing to help patients understand what a new federal law will mean in terms of allowing access to experimental medicines outside of currently established paths.

The debate around the so-called "right-to-try" law may have created unrealistic expectations about what the measure will do for patients, top officials from major oncology associations told Medscape Medical News. Patients too ill to participate in clinical trials may anticipate that the law will grant them access to promising experimental therapies, they said.

"There will be more patients asking questions because of the sense of expectation that the new law has created," Robert W. Carlson, MD, chief executive of the National Comprehensive Cancer Network (NCCN), a not-for-profit alliance, said in an interview.

Patients may think that "there are promising drugs out there that they're being denied, and that all of a sudden this law is going to make effective drugs available to them," he said.

Richard L. Schilsky, MD, chief medical officer of the American Society of Clinical Oncology (ASCO), said the measure should have been called the "right-to-ask" law.

"There's been so much hype about this, and the name has been, in a sense, so misleading," Schilsky commented in an interview.

Signed by President Donald Trump on May 30, the new law does not compel drugmakers or physicians to provide early-stage medicines to patients who seek them. It instead may bolster the cases of patients who seek these drugs outside of clinical trials. The bill is intended to encourage drugmakers to more freely provide more experimental medicines by limiting the drugmakers' liability.

The new law directs the drugmakers to submit to the Department of Health and Human Services an annual summary of use under the right-to-try provisions of their experimental products. These reports are to include the number of doses supplied, the number of patients treated, the uses for which the drug was made available, and any known serious adverse events.

Pharmaceutical companies already provide experimental medicines outside of clinical trials through the US Food and Drug Administration's (FDA's) expanded access program, under which physicians may seek consent from the agency.

ASCO has prepared a podcast about the new law to help oncologists and the public better understand it. Schilsky said physicians will need to convey to their patients the steep odds against successful treatment with experimental drugs that are offered through the right-to-try program. These medicines need only have been tested in phase 1 trials, which are initial screenings to determine whether medicines are safe enough for more advanced testing.

"Most drugs that enter into clinical development never make it across the finish line to get FDA approval," Schilsky said. "You can just sort of anticipate that a lot of these drugs that are still investigational are never going to be proven to be efficacious."

About 70% of drug candidates advance from phase 1 to phase 2 trials, where the focus is on side effects and efficacy, according to an FDA website. Only 33% of drugs then move from phase 2 to phase 3, and only 25% to 30% of drugs that advance to phase 3 succeed, the FDA's website says.

ASCO opposed the passage of the new right-to-try law, as did many other oncology groups, including the NCCN and the American Cancer Society Cancer Action Network, which outlined its objections in a letter to the House of Representatives. They argued that the new approach strips layers of supervision from use of experimental and potentially toxic drugs.

"The best way for patients to get access to investigational drug is to participate in a clinical trial of that drug," Schilsky said. Then the drug is "provided under controlled circumstances, and it can be administered safely."

Both Schilsky and Carlson also spoke in favor of the FDA's existing expanded access program for patients who are not able to enroll in clinical trials.

In a report on its Expanded Access Program in fiscal 2017, the FDA noted that it approved 1831 of 1842 applications (>99%) for expanded access through special applications and protocols. Also known as compassionate use, the program appears to meet much of the need cited by supporters of the right-to-try law, Carlson said.

**This [new] law is designed to solve a problem that does not exist.** Dr Robert Carlson, NCCN

"Most oncologists would look at this and say, 'This [new] law is designed to solve a problem that does not exist,' " he said.

Carlson and Schilsky also emphasized that the FDA's expanded access approach provides what they consider important safeguards for patients. These include institutional review boards, which can ensure that patients comprehend the balance of risks and benefits of an experimental drug. The FDA also offers physicians guidance on how to use the experimental drugs in the expanded access program.

"If you take FDA out of the picture, which is what right-to-try does, then there is no way for the doctors to get the guidance they need unless they can get it from the pharma company," Schilsky said.

The nonprofit Reagan-Udall Foundation is working to make it easier for physicians to apply for expanded access, said Blase N. Polite, MD, MPP, associate professor of medicine at the University of Chicago, Illinois, in an interview.

The organization's online nagivator helps physicians prepare requests to drugmakers for expanded access. The navigator walks them through the information required by the FDA's Form 3926. The Reagan-Udall efforts on expanded access may help physicians in rural areas connect patients to experimental drugs through the FDA's expanded access program, Polite said. At large academic centers, though, it is not difficult to find an early-stage study in which to enroll cancer patients who have normal liver and kidney function, Polite said.

More than 1100 cancer medicines are in various stages of testing, according to a list released recently by the Pharmaceutical Research and Manufacturers of America, a drugmakers' trade group. This list includes studies of already-approved drugs that are being studied for new uses, as well as phase 1 studies of unapproved agents.

Oncologists now are grappling with how to sequence and use newer agents, Polite said. "We're drinking from the fire hose, and that's great," he said.

## FDA Working to Speed Drugs to Market

Backers of the right-to-try law sometimes depict the FDA as an almost willful hurdle to the wishes of people facing death. "It just gives those individuals the right to choose for themselves, not have a faceless bureaucrat at the FDA make that decision," said Sen. Ron Johnson (R-WI), as he advocated for the right-to-try law in March on the Senate floor.

Last month, Johnson took exception to comments from FDA Commissioner Scott Gottlieb, MD, about a potential need to build more patient protections on the right-to-try pathway. "This law intends to diminish the FDA's power over people's lives, not increase it," Johnson wrote in a May 31 letter to Gottlieb.

However, this is not a view held by experts in the field, who see the FDA as an ally in the challenge to get new drugs to desperately ill patients.

Polite pointed out that the FDA, particularly its oncology chief, Richard Pazdur, MD, is working to speed new cancer medicines to market. The agency has proved accommodating in recent years to companies seeking approval of cancer drugs with fairly limited supporting evidence.

"When we see things that work, they are getting approved and they are getting out there," Polite said.

In recent years, the FDA has often relied on surrogate endpoints and single-arm trials that involved relatively small patient groups for approving cancer medicines. For example, in 2017, the FDA granted approval of the lymphoma drugs acalabrutinib (Calquence, AstraZenec) and copanlisib (Aliqopa, Bayer). The FDA said it approved both drugs on the basis of studies that measured how many patients experienced complete or partial shrinkage of tumors. The pivotal acalabrutinib study included 124 patients, and the key copanlisib trial included 104 patients, the FDA said.

Schilsky said drugmakers may not always be able to provide experimental products to people who seek them through the new right-to-try approach or through the FDA's established expanded access program. The firms may have manufactured only a limited supply of these drug candidates. In addition, there can be serious concern about how these potent agents would be administered in the new, less closely supervised pathway.

"The FDA is not the problem. If you want to say that there is a problem at all, the problem is with the pharmaceutical companies that are unwilling or unable to provide their drugs outside of clinical trials before they are approved," Schilsky said.

The FDA provided journalists with a copy of a note that Janet Woodcock, MD, the director of the agency's Center for Drug Evaluation and Research, sent to her staff after the enactment of the right-to-try law. The FDA is working to "develop further information" about how to respond to inquiries from those seeking to gain access to experimental medicines outside of clinical trials and the expanded access program, she wrote.

"However, we believe that sponsors are in the best position to provide information on the development status of their products (which is critical to determining whether a drug or biological product is eligible for use under Right to Try) and whether a sponsor intends to make an investigational product available under Right to Try," Woodcock said.

## Savvier Patients

Frederick M. Schnell, MD, the medical director of the Community Oncology Alliance, said he expects the right-to-try law to help some patients, although he foresees challenges ahead regarding the potential for abuse and the possibility of litigation.

"This is not going to be a free ride. This is not going to be easy," Schnell said. He maintains that the right-to-try option is "kind of what the American public has been demanding."

Patients facing death may be willing to take a chance on even toxic medicines that are long shots for stopping or slowing their cancer, he said.

"I used to sort of discourage people from doing things that I thought didn't make sense, intellectual sense, but what makes sense to me doesn't necessarily carry over to them," Schnell said.

Schnell recalled a recent patient of his for whom the right-to-try pathway would have been attractive. The patient was a cardiologist in his 50s who was battling melanoma. Although this patient would have been willing to travel far for a clinical trial, his liver test results ruled him out as a candidate for research studies, Schnell said.

"There are a lot of people out there, particularly younger people and more highly educated people, who will go to the last end to try to get something that might slow things down and buy them some more time," Schnell said.



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