Insight

Right to Try

BRITTANY LA COUTURE | AUGUST 11, 2014

In recent weeks the national news has been dominated by reports of the West African Ebola outbreak that has already claimed nearly 1,000 lives. Ebola historically has a case-fatality rate of 90 percent and has no known cure.[1] This week, for the first time in history, Ebola made it to American soil when a medical volunteer in Liberia contracted Ebola and was transferred to Emory University in Atlanta for treatment. Before being transported, the National Institutes of Health (NIH) sent him a dose of a currently non-Food and Drug Administration (FDA) approved drug called ZMapp, and within an hour his condition improved so drastically he was stable enough for the four hour flight and by the time he landed was able to walk into the hospital. He was shortly followed by the second beneficiary of this drug, another American volunteer in Liberia.

There are currently two drugs going through the FDA approval process: ZMapp and Tekmira. Tekmira has been through phase I trials[2] but was put on hold before phase II because some of the uninfected subjects were experiencing side effects from the drug.[3] Tekmira was tabled and when Americans became infected with Ebola they were given ZMapp, a drug that had so far only been tested on monkeys with less serious cases of the disease. Whether the drug will ultimately be effective enough to save their lives remains to be seen.

FDA REGULATION AND 'COMPASSIONATE USE'

Under almost any other circumstances, non-FDA approved drugs are not available for use. It is unclear whether the FDA approved providing ZMapp to the Ebola victims or if the proper process was followed, but in most circumstances accessing these unapproved drugs can take weeks or months.

The best way for patients facing serious or terminal illness to access unapproved drugs is to participate in a clinical trial during phase II or III testing.[4] However, there are many disqualifiers from participation, such as age, stage of the illness, or comorbidities. Participation is also usually limited to patients living in easy traveling distance from an academic or research institution.

For those unable to participate in clinical trials and without other treatment options, access to non-FDA approved drugs like ZMapp could be the difference between life and death. Under current law there are numerous prerequisites to obtaining one of these unapproved drugs through the FDAs expanded access or 'compassionate use' program.[5] First, the patient must have a serious or immediately life threatening illness – it is up to the FDA to determine if this threshold is met, but due to all of the other barriers in place it is unlikely anyone not in a desperate situation would apply for this program.

Next, the patient must have no other alternative treatment option available. This includes eligibility to participate in clinical trials – this is important because without that participation it would be impossible to ever get new drugs approved. If the FDA believes that the availability of expanded access to a drug is hindering the progress of clinical trials due to lack of volunteer subjects, the FDA may stop any requests for access to that drug.

Before a patient can even apply for expanded access, there must be a relationship between the patient's

physician and the drug manufacturer where both have already expressed a willingness to provide the drug to the patient. Neither the doctor nor the drug manufacturers are under any obligation to prescribe or provide non-FDA approved drugs. The patient's physician must complete and submit an application for expanded access. Though the information required is fairly straightforward, the paperwork may take a physician up to 100 hours to complete (that is over two work weeks per patient). Furthermore, due to privacy concerns, there is no way for a doctor to see or know what a successful application looks like until she herself has written one.

Once the application is submitted, the FDA has 20 days to render a decision – this is a rather long period considering the patient in question is likely in a great amount of pain or terminal. If the FDA grants the request, the application must be approved by a full Institutional Review Board (IRB). This involves convening a large panel of local, multidisciplinary experts to give an ethical opinion on the case. In places such as university hospitals IRBs may meet as often as once a week, but in more rural areas it may take a month or more for the full board to meet.

Once granted approval, the patient may receive the drug. However, there is no obligation for insurance companies or government programs to cover the cost of these experimental treatments and the patient and their family may be left to cover the high cost of the new drug. Luckily most pharmaceutical companies will donate drugs to expanded access patients – partly philanthropically, and partly to delay revealing the potential price of the drug.

RIGHT TO TRY

Though proponents of strict FDA regulation argue that barriers to treatment exist to protect consumers from 'side effects,' it is hard to imagine a side effect that is worse than being denied any hope of survival. It raises the question of whether the FDA is trying to protect patients or its own reputation by avoiding the risk of allowing someone to take a risk that may not always pay off.

Proponents of Right to Try laws take a different approach: they believe that the right to try to preserve one's life is fundamental and all other political concerns are entirely unimportant.[6]

Right to Try laws like those passed in Louisiana, Missouri, and Colorado and introduced in Arizona and Michigan allow terminal patients access to unapproved drugs that have made it through phase I trials. Physicians who take advantage of these laws are also protected from any state-level charges of professional misconduct on the basis of recommending or administering these drugs, as long as the patient gave informed consent to the experimental treatment.

Right to Try laws do not eliminate all risks though. There is a real threat that an ineffective drug could shorten an already endangered life, cause pain, or decrease lucidity or responsiveness to palliative care; it is also possible for many diseases themselves to have these effects.

There is also the fear that patients and their families are too vulnerable at this time in their lives to make informed decisions about care options, and they may waste valuable time or resources on ineffective treatment – time and resources that could be used to grieve together rather than continue to hope. This fear, while reasonable, simultaneously undermines theories of personal autonomy and ignores the fact that the feared responses are also seen in cases where FDA approved drugs are ineffective.

REMAINING OBSTACLES

The pros may outweigh the cons in debating these laws, but there are two huge obstacles to access that state laws alone cannot overcome.

No government can force drug manufacturers to provide unapproved drugs, even to the most sympathetic patients, and there are plenty of reasons for them not to. Manufacturing small quantities of a drug can be extremely expensive and beyond the budget capabilities of small labs that need all their funds to get their drugs through clinical trials. There is also the fear that patients who are terminal may be beyond the stage of the illness a drug is intended to treat. This is a recipe for failure and unwarranted bad press about a dug that has not even been approved yet. In a case like this where the drug does not work either because it is ineffective or for any other reason, there is no protection in the law to prevent families of patients from suing drug manufacturers – and even if these protections were included in state laws, the case could be brought under federal law and the patient would likely still win.

There is also no guarantee the FDA will not decide that the Food Drug and Cosmetics Act preempts these state laws and begin enforcement against doctors and manufacturers for marketing or distributing unapproved drugs. It is likely a jury would be sympathetic, especially if there was no sale involved, but the court fees alone would become prohibitive.

CONCLUSION

There are still many obstacles and ethical questions to face in considering how much access to treatment a terminal patient should have. Right to Try laws demonstrate a sense among the citizens of at least a few states that the right to try to continue to live is fundamental, as is the right to life itself, and regulatory burdens should therefore be minimized as much as possible. It is easy to understand the hesitation of supporters of the nanny-state to relinquish the power to protect Americans from themselves, but when there is a situation like the Ebola outbreak and the lives of specific, identifiable American citizens are at risk suddenly the price we pay for those regulations becomes quantifiable and simply unpalatable. It seems that once we know the person being denied care, opinions change. The unfortunate truth is that every year tens of thousands of unnamed Americans die because the FDA will not give them the same opportunity provided to the Ebola victims, and the rest of the country never even knows. It shouldn't take national publicity for people with life-threatening illnesses to have access to potential treatments; instead we should consider further expanding Right to Try.

[1] Robert Langreth et al., Ebola Drug Made from Tobacco Plant Saves U.S. Aid Workers, Aug. 4, 2014; http://www.bloomberg.com/news/2014-08-05/ebola-drug-made-from-tobacco-plant-saves-u-s-aid-workers.html.